2004-11-01

Comparison of Auto-adjusting and Fixed Level Continuous Positive Airway Pressure Therapy in Patients with Mild to Moderate Obstructive Sleep Apnoea Hypopnoea Syndrome

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Comparison Of Auto-Adjusting And Fixed Level Continuous Positive Airway Pressure Therapy In Patients With Mild To Moderate Obstructive Sleep Apnoea Hypopnoea Syndrome

By

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A thesis presented to

The School of Physics

Dublin Institute of Technology

For the Degree of Master of Philosophy

November 2004

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Abstract

Obstructive Sleep Apnoea Hypopnoea syndrome (OSAHS) is a potentially serious medical disorder associated with increased morbidity and mortality. It is estimated to affect 4% of males and 2% of females between the ages of forty and sixty. Nasal continuous positive airway pressure (CPAP) is the first choice treatment for this condition and it is extremely effective at controlling OSAHS. However, not all patients can tolerate this therapy, in particular those within the mild to moderate category, and there are also many others who are unable to comply with the minimum usage requirements of at least four hours every night. A newer type of positive airway treatment, auto adjusting positive airway pressure (APAP), has been developed in the last decade, which theoretically should improve tolerance and therefore lead to higher compliance rates. The aim of this study was to determine whether patients with mild to moderate OSAHS tolerated auto-adjusting positive airway pressure better than traditional fixed positive airway pressure therapy by using the device for longer. No differences were found in respiratory abnormalities or daytime sleepiness, as assessed by the Epworth Sleepiness Score (ESS) between the two modes of treatment, but all measured parameters were significantly improved from the baseline, untreated values. Mean APAP pressure was significantly lower than CPAP pressure (6.2 ± 1.4 *v* 8.4 ± 1.7 cmH_2O, $p < 0.001$). Patient compliance and duration of use were similar with both treatments, although there was a statistically significant proportion of patients requiring higher fixed pressure (> 8 cm H_20), who preferred APAP while those requiring lower pressure (< 8 cm H_2O) preferred CPAP. In conclusion APAP and CPAP are equally effective in resolving sleep related breathing disturbance and improving daytime sleepiness in patients with mild to moderate OSAHS, although compliance may be affected by fixed CPAP pressure requirements.

Declaration

I certify that this thesis which I now submit for the award of Master of Philosophy, is entirely my own work and has not been taken from the work of others save and to the extent that such work has been cited and acknowledged within the text of my work.

This thesis was prepared according to the regulations for post graduate study by research of the Dublin Institute of Technology and has not been submitted in whole or in part for an award in any other Institute or University.

The work reported on in this thesis conforms to the principles and requirements of the Institute's guidelines for ethics in research.

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Signature Geraldine Nolan Date 26/8/05
Candidate

Acknowledgements

I would like to thank Professor Walter Mc Nicholas, director of the Sleep Disorders Unit at St Vincent's University Hospital, for his support and encouragement during this project. I would also like to thank my supervisors at DIT, Kevin Street, Dr Pat Goodman, Dr James Walsh and Dr Matt Hussey for all the help and advice they have given to me. I am especially grateful to Dr Goodman for initially proposing to me the idea of postgraduate study.

I would like to extend my appreciation to my colleagues in the Sleep Disorders Unit who helped me throughout this busy time.

Finally, I would like to thank my family who have had to put up with me while I juggled between them, work and study.

I dedicate this work to my parents Mathew and Carmel Nolan, who encouraged me to always ask questions

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1. INTRODUCTION

1.1 Aim of the Study

This study forms part of the research into the treatment options available at present for patients who are diagnosed with mild to moderate obstructive sleep apnoea hypopnoea syndrome, a common and potentially serious medical disorder[1,2]. The broad aim of this study is to assess the relative compliance of two positive airway pressure (PAP) devices, both of which are currently available to treat this condition, but which use different applications of positive airway pressure. This study was carried out in the Respiratory Sleep Disorders Unit of St Vincent's University Hospital. Ethical approval was obtained from the Ethics committee in the hospital and each patient gave informed consent before participating in the study.

1.2 Obstructive Sleep Apnoea Hypopnoea Syndrome

First described by Gastaut[3] in 1965 Sleep Apnoea Syndrome (SAS) is a complex disease characterised by brief interruptions of breathing during sleep. Obstructive Sleep Apnoea Hypopnoea Syndrome (OSAHS) occurs when the tongue and soft palate relax (Fig 1.1) during sleep and block the upper airway, so that air cannot flow into or out of the person's nose or mouth, although efforts to breathe continue. It is a serious, potentially life-threatening condition that is estimated to occur in 4% of middle-aged men and 2% of middle-aged women [4,5], although many cases remain undiagnosed. OSAHS is one of 88 known sleep disorders and it is one of 13 diagnoses that are classified as "intrinsic dyssomnia" (Appendix A)[6].

People most likely to develop OSAHS include those who snore loudly, are overweight[7], or have high blood pressure[8-13], those who have some abnormality in the nose, throat or

other part of the upper airway[14-16] and as the condition runs in some families, there may also be a possible genetic basis[17,18].

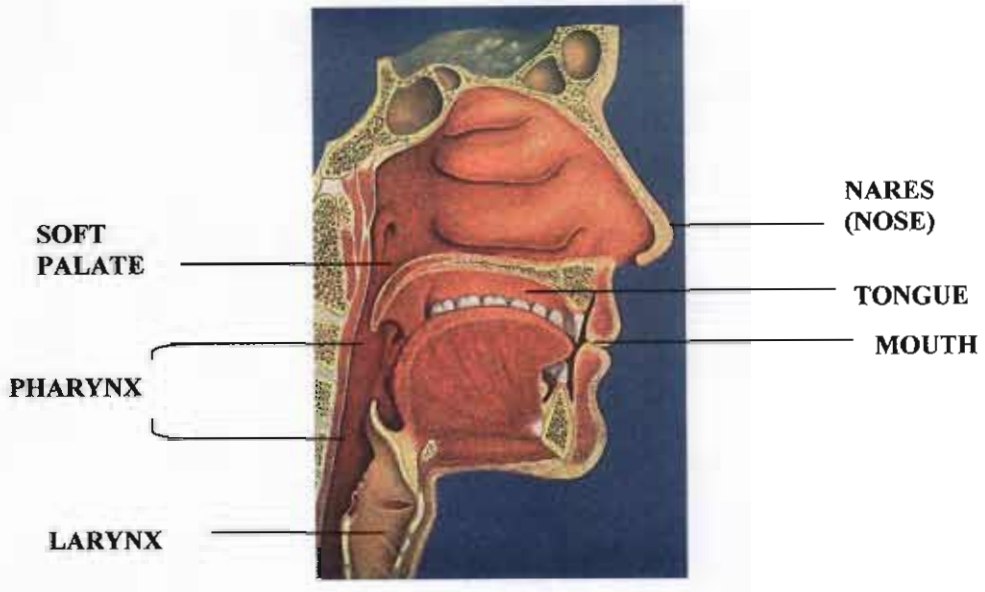


Fig 1.1 Structure of the Upper Airway[1]

1.3 How is OSAHS Diagnosed?

The diagnosis of OSAHS requires two main components, a high number of abnormal respiratory events during sleep and compatible clinical symptoms[19]. OSAHS patients complain about their daytime symptoms, the most common being excessive daytime sleepiness[20] or somnolence. Impairment of alertness could make these patients susceptible to occupational or car accidents, and or to poor social functioning[21-25]. However, because this sleepiness may be progressive over many years, it is often not seen as abnormal by the patient and may be just attributed to age. Their bed partners complain about their behaviour during sleep, primarily loud snoring and apnoea episodes, which are periods when there is a cessation in breathing.

[1] Image taken from www.alltheweb.com

Snoring is the earliest and probably the most consistent symptom of upper airway (UA) dysfunction that can lead to OSAHS. Snoring results from an imbalance between the collapsing and dilating forces in the area of the pharynx (Fig1.1). Vibration of the soft tissue of the pharynx, soft palate and uvula produces the sound we hear. In OSAHS patients, snoring is usually heavy, occurring nearly every night, for most of the night and in all sleep positions.

However, not all people who snore will be diagnosed with OSAHS. As a result, the clinical picture alone has not enough sensitivity to confirm the diagnosis of OSAHS or exclude the possibility of other sleep disorders[26]. All well defined clinical sleep disorders, including OSAHS, can be diagnosed or excluded by means of the Cardiorespiratory Polysomnography (CRPSG) test, a non-invasive multichannel recording of sleep pattern and respiratory events. A standardised procedure for this diagnostic test has existed since 1968[27-29].

1.4 Sleep Assessment

The classical hallmarks of sleep are lack of movement, reduced postural tone, closed eyes, changes in breathing pattern and lack of response to limited stimuli. All these features can be used to assess if someone is likely to be asleep, but for adequate quantification of sleep it is necessary to assess electroencephalography (EEG), electrooculography (EOG) and electromygraphy (EMG).

EEG is a measure of the electrical activity of the brain recorded across the scalp. The electrodes are arranged in a montage (group) to detect action potentials of the cortex that are then amplified and displayed on a computer. The amplifiers used can measure AC (alternating current) frequencies in the range of 0.1 – 90 Hz. Table 1.1 shows the EEG frequencies generally associated with wake and sleep.

Table 1.1 EEG Frequencies during Wake and Sleep

Alpha Rhythm:	8-13 Hz	Relaxed closed eyes
Theta Rhythm:	3-7 Hz	Drowsiness and sleep
Delta Rhythm:	<13 Hz	Stages 3 + 4 sleep
Beta Rhythm:	>13 Hz	Infants + children

Electrodes are placed on the scalp using the international 10/20 system for EEG placement[27] (Fig 1.2). All EEG patterns associated with sleep are well defined in areas C3 and C4. These two electrodes are referenced to an electrode placed contra-laterally on the mastoid bone (behind the ear), A1, and A2, to give C3:A2 and C4:A1 configuration (Fig 1.3).

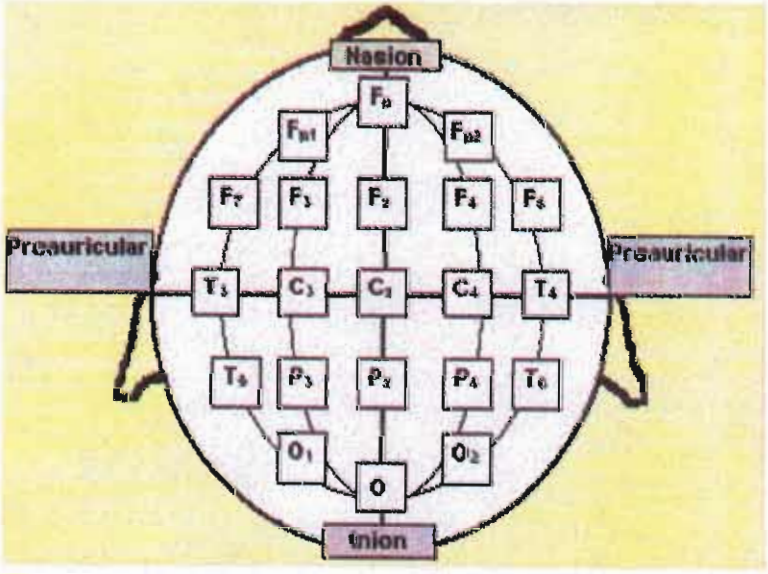


Fig 1.2 10/20 System of EEG Electrode Placement[2]

[2] Image taken from SleepMultimedia

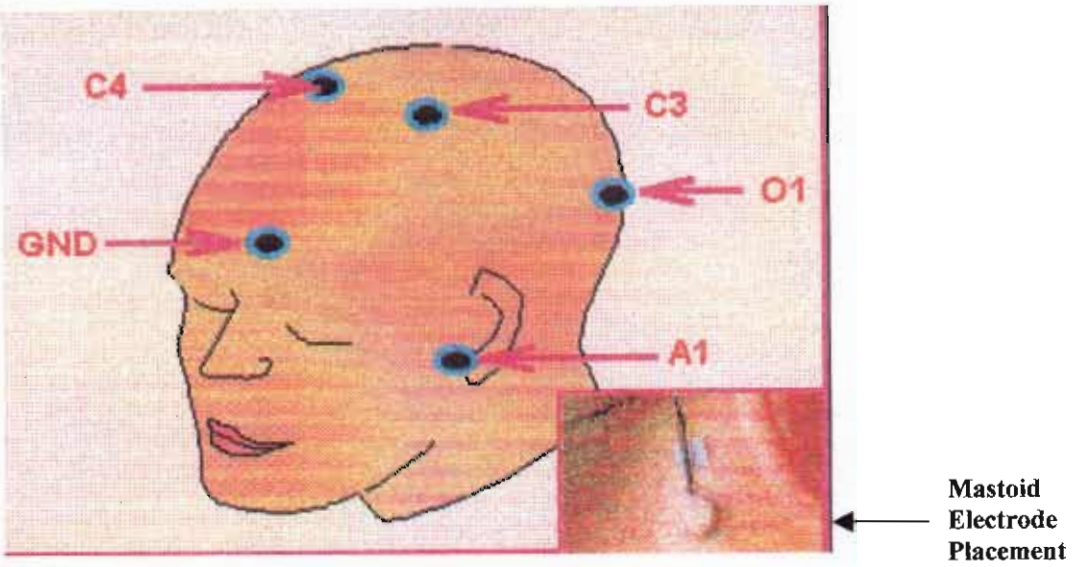


Fig 1.3 EEG Electrode Placement[3]

EOG is a measure of the electrical potential differences between the front and back of the eye, the cornea being positive with respect to the retina (Fig 1.4). EOG is essential to document the rapid eye movements found in rapid eye movement (REM) sleep. An electrode is placed at the outer canthi of each eye 1 cm above the centre and 1 cm below centre. They are referenced to the same side mastoid electrode, giving Right EOG, A2 and Left EOG, A1 configuration (Fig 1.4).

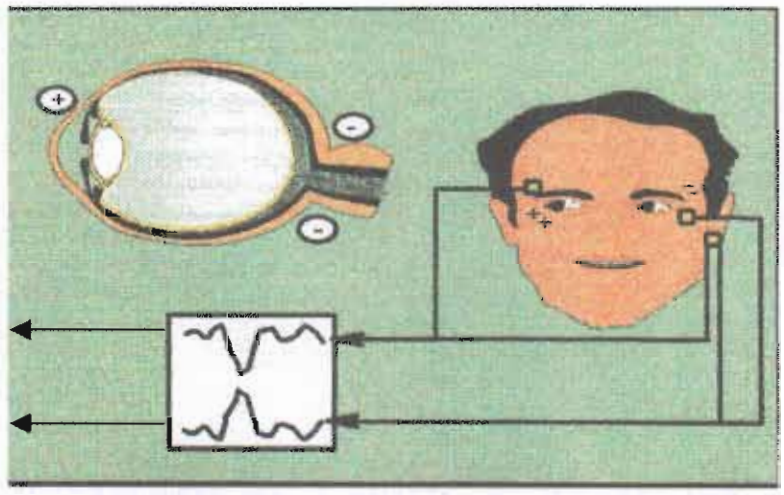


Fig 1.4 EOG Electrode Placement[3]

[3] Image taken from SleepMultimedia

The EMG signal represents the electrical activity of a muscle. Muscle tone is elevated during wakefulness, but is greatly reduced or absent during different stages of sleep. Two electrodes are placed beneath the chin

With the information from all these measurements (EEG, EOG and EMG) it is possible to classify sleep into its various stages. The analysis of these data is carried out manually according to the internationally accepted Rechtschaffen and Kales[27] (R&K) guidelines. These were two eminent members of a large committee of experienced sleep researchers, that produced a consensus set of rules in 1968 for sleep staging of normal adult sleep based on 30 second sections (epochs) of recording.

1.4.1 Sleep Staging

Sleep is not homogenous but rather it is divided into two alternating phases, REM (rapid eye movement) and NREM (non-rapid eye movement). NREM sleep accounts for the bulk of sleep and consists of four sleep stages, each representing progressively deeper levels of sleep. Stage 1 occurs as the subject falls asleep and is associated with drowsiness. Stage 2 accounts for 50% or more of the total sleep time. Stages 3 and 4 are referred to as slow wave sleep.

REM sleep is associated with dreaming and occurs in cycles of between 90-120 minutes in normal adult sleep. There are usually 4-6 discrete episodes of REM each night of sleep, with an increase in the duration of these episodes during the last third of the night.

Table 1.2 summarises the various signals displayed while awake and during sleep in adults. Each page (epoch) of recording is assigned a stage according to the criteria listed.

Table 1.2 Physiological Signals during Wake and Sleep

Sleep Stage	EEG	EOG	EMG
Stage wake	Low amplitude, mixed frequency, alpha rhythm	Mainly blinks, lots of irregular eye movements	High tonic activity
Stage 1	Low amplitude, mixed frequency, theta activity	Slow rolling lateral eye movements	Slightly lowered tonic activity
Stage 2	K complexes, sleep spindles	Eyes still, but EEG activity seen in eye channels	Tonic activity maintained
Stage 3	Delta waves < 2Hz & > 75uV occupy 20-50% each epoch	Dominated by EEG activity	Tonic activity maintained
Stage 4	Delta waves 2Hz & > 75uV occupy > 50% of each epoch	Dominated by EEG activity	Very low tonic activity
REM	Low amplitude, mixed frequency (like stage1)	Phasic rapid eye movements	No measurable tonic activity

Any epoch that displays movement or artefact for more than 50% of the time is assigned Stage wake. Fig 1.5 shows the EEG waveforms associated with the different stages of sleep. The EEG pattern for wake is also included, as it is necessary to have evidence of Stage wake to correctly analyse sleep stages manually, particularly as the waveforms for both Stage 1 and REM sleep are very similar to those found during wake.

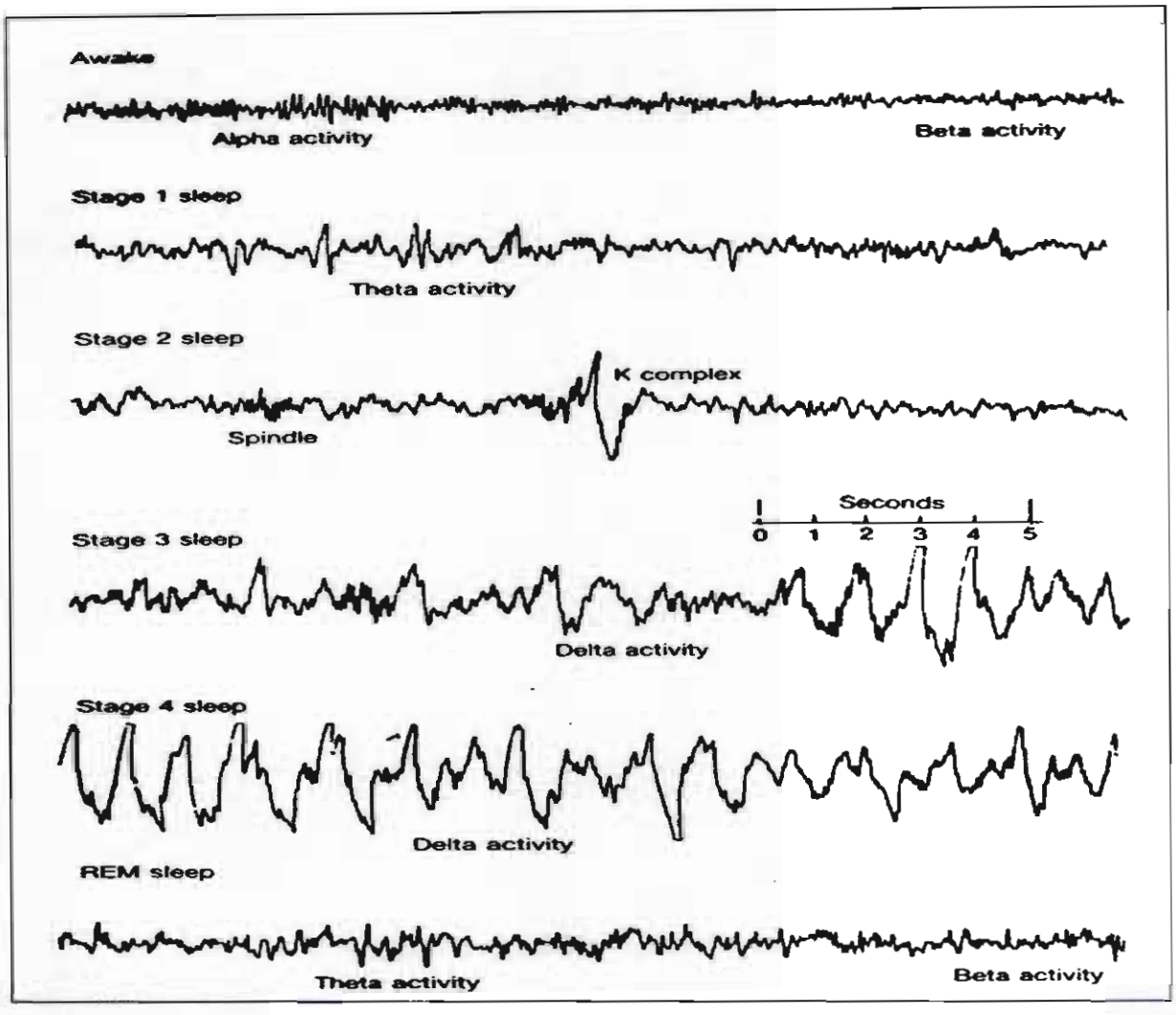


Fig 1.5 EEG Waveforms associated with Wake & Sleep Stages[4]

1.4.2 Sleep Architecture

Sleep architecture describes the pattern of sleep during the night. The alternating pattern of NREM and REM can be plotted on a histogram, which graphically depicts the distribution of sleep stages during the night (Fig 1.6). There are other calculations made during sleep analysis that can be used to assess sleep quality. These are summarised in Table 1.3.

[4] Image taken from www.alltheweb.com

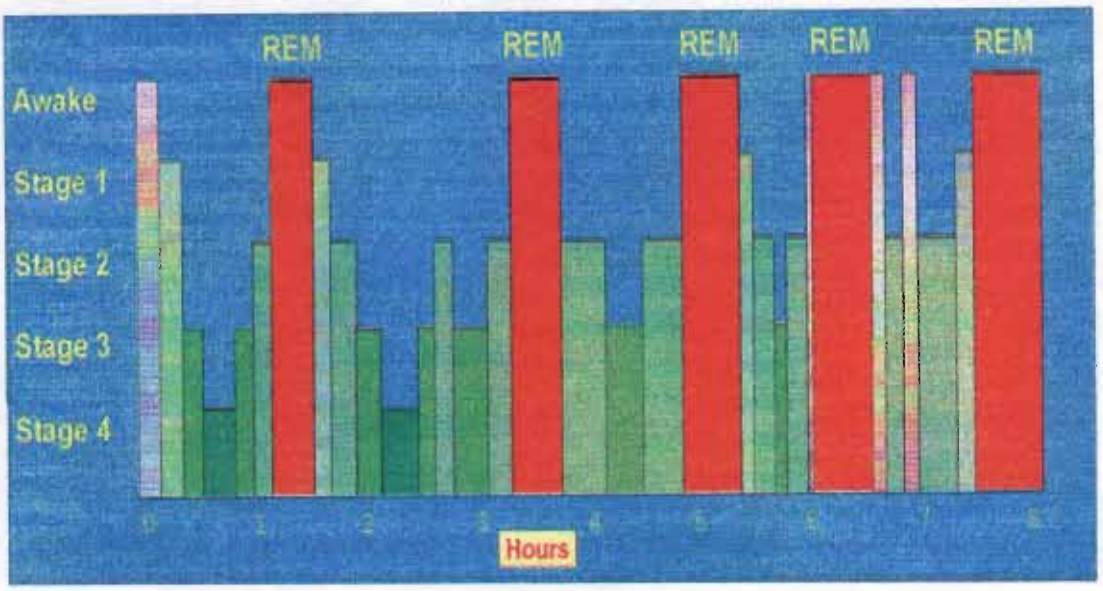


Fig 1.6 Sleep Histogram of Normal Adult Sleep[5]

Table 1.3 Sleep Terminologies

Term	Definition
Total Recording Time (TRT)	Time from lights out to lights on
Total Sleep Time (TST)	Total sleep time from lights out to lights on
Sleep Maintenance Efficiency (% TRT)	% of total recording time asleep
Sleep Efficiency (TST/TRT)	% of time in bed actually asleep
Sleep Latency	Lights out to first 5 minutes of sleep
REM Latency	Time from sleep onset to 1.5 minutes of REM
Wake during Sleep	Amount of time awake after sleep onset
Movement Time	Period recording was obscured by artefact

1.5 Normal Adult Sleep Pattern

Man generally has one episode of sleep and one main episode of wakefulness per day. Sleep pattern can vary from night to night even in the same subject, but there is general

[5] Image taken from SleepMultimedia

agreement on what constitutes a "normal" nights sleep in adults. Sleep is entered via NREM, initially Stage 1 and then through Stages 2, 3 and 4. NREM and REM alternate within 90-120 minutes throughout the night and REM is entered via Stage 2. The percentage of time spent in the different stages will also vary but the following table (Table 1.4) summarises the generally accepted ranges.

Table 1.4 Sleep Stages in Normal Adult Sleep

Wakefulness accounts <5% Total Sleep Time (TST)
NREM accounts 75/80% of TST, divided into 4 stages:
Stage 1: 2-5% TST
Stage 2: 45-55% TST
Stage 3 + 4: 13-23% TST
REM accounts for 20/25 % of TST and occurs in 4-6 discrete episodes

The amount of time asleep varies from person to person, but the average is about eight hours in adults. The amount of sleep needed is considered to be the amount that permits us to be wide-awake, alert and energetic throughout the day. However, several factors influence the quality and quantity of sleep obtained, even in persons who do not have a sleep disorder.

1.5.1 Factors Affecting Normal Sleep Patterns in Adults

Sleep patterns are affected by age[30], alcohol[31] caffeine[32], nicotine[33] and circadian disturbances[34] i.e. shift work[35], jet lag[36] etc. The need to sleep remains constant during life, but the ability to sleep decreases with age, resulting in an increase in the number of awakenings and leading to a reduction in sleep efficiency.

Small quantities of alcohol can help to initiate sleep but even a moderate drinking session, more than 3 and less than 8 units of alcohol, can create sleep maintenance problems, because as the alcohol metabolises (approximately 1 unit per hour) it leads to increased awakenings.

Caffeine increases wakefulness also, reduces the total sleep time and has a five-hour half-life. An average cup of coffee contains 100 mg of caffeine, a strong cup can be double this amount, with tea and cola containing between 50 to 75 mg of caffeine each. Caffeine intake of more than 500 mg per day can have disturbing effects on sleep patterns in some people, resulting in insomnia. Caffeine has also been shown to have significant acute effects on blood pressure. In one study non-coffee drinkers received 250 mg of caffeine and on average their systolic blood pressure rose by 14 mmHg and the diastolic by 10 mmHg[37]

Nicotine is relaxing and sedating in low concentrations, but like caffeine, in higher concentrations it can produce an increase in the number of awakenings[33]. Nicotine has a half-life of 1-2 hours. So, either individually or interacting together, alcohol, caffeine and nicotine can profoundly alter sleep maintenance and efficiency.

Humans synchronise sleep and wake behaviour to changes in light and temperature. Body temperature changes over the course of the day. It peaks late morning and early evening, with the lowest point between 4-6am. It rises just before or around the time of morning wakening. Therefore, persons who work shift hours, in particular during the night may not have good quality sleep during the daytime[35]. However, none of the study group involved in this project work through the night and all adhered to a regular bedtime and wake time, which helps to develop good sleep habits and promote good quality sleep[38].

In summary, sleep is an active process of the brain and although it is generally governed by homeostatic and circadian rhythms it can be overridden by behaviour. Profound age related changes occur to sleep patterns[30]. Certain chemicals and drugs can alter sleep pattern and quality and there are individual differences in sleep requirements even in the normal population.

1.6 Breathing during Sleep

During sleep most physiological functions decrease, including breathing which becomes deeper and slower. Sleep alters the breathing pattern and respiratory responses to many external stimuli. In fact sleep has no positive effect on breathing at all and indeed there are many adverse consequences. With the onset of sleep there is a reduction in the overall drive to breathe from the respiratory drive centre in the hypothalamus in the brain, which affects the diaphragm, the major muscle in the lungs, leading to a reduction in ventilation. There is also an increase in resistance in the upper airway. Reduction in the general postural muscle tone, especially during the pronounced muscle hypotonia of REM stage sleep further aggravates these two factors[39].

Arousal responses to gas exchange deterioration is reduced during sleep and can be further suppressed by sedatives, sleep deprivation etc. This can lead to even more of a reduction in ventilatory drive caused by rising carbon dioxide levels and falling oxygen levels in the blood.

1.6.1 Respiratory Assessment during Sleep

Respiratory parameters that are measured during a Cardiorespiratory Polysomnography test (CRPSG) include airflow, respiratory movements, tracheal sound and arterial blood oxygen saturation by pulse oximetry. An electrocardiogram (ECG) can reveal nocturnal

cardiac arrhythmias. Nasal and oral airflow are measured by placing thermistor tips at the nose and mouth, which record the presence or absence of airflow based on the temperature differences between inhaled and exhaled air.

Ventilatory effort is measured by recording thoracic and abdominal movements using elastic bandage devices containing transducer coils which are wrapped around the chest and abdomen. They produce a signal that is proportional to volume. Although this is not an accurate measure of volume, it is sufficient to show the differences between normal and abnormal breathing patterns. In normal breathing during sleep there is continuous synchronised movement of airflow and ventilatory effort in the same direction while arterial blood oxygen saturation (SaO_2) levels remain relatively constant and close to 100% (Fig 1.7).

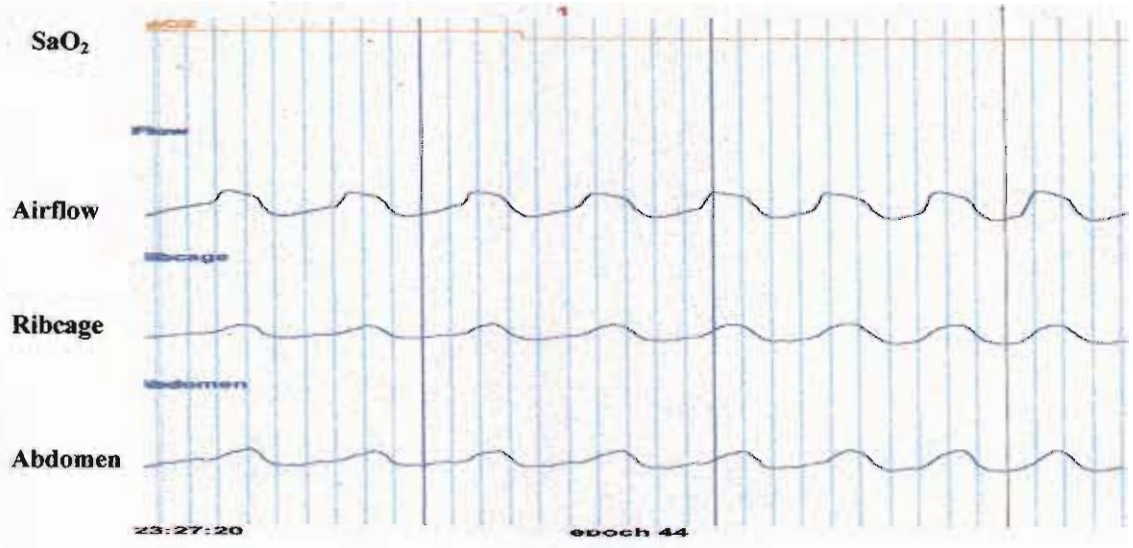


Fig 1.7 Normal Breathing Pattern[6]

However, in patients with sleep apnoea syndrome the breathing pattern alters during sleep so that airflow, ventilatory effort and oxygen saturation produce a range of different signals.

[6] Image taken from PSG recording

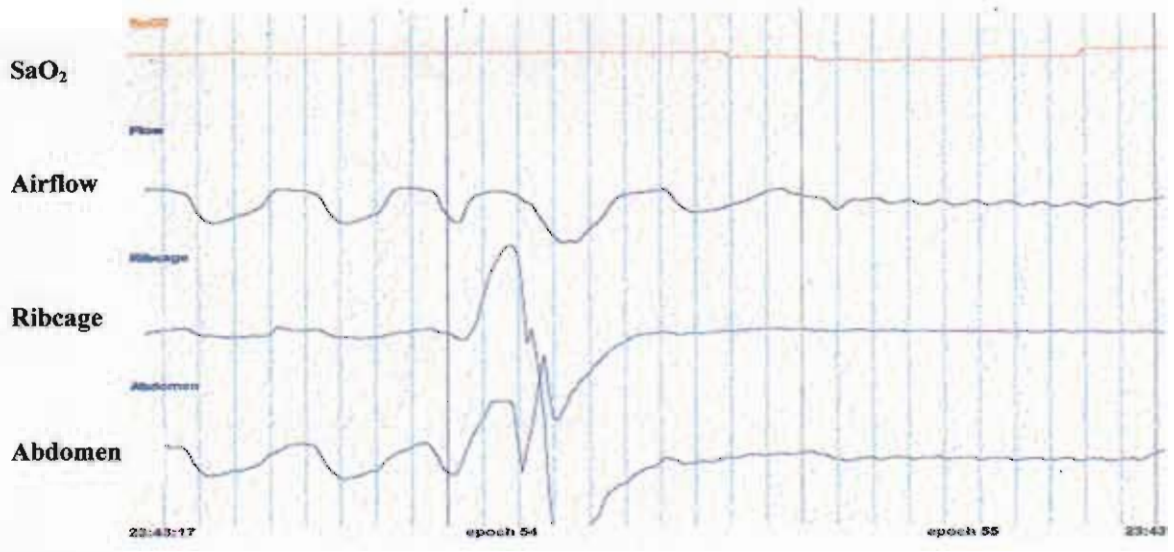


Fig 1.8 Central Apnoea Event[7]

Apnoeas are either central (Fig 1.8), where respiratory effort is diminished or absent, or obstructive (Fig 1.9) when respiratory effort continues against a closed glottis producing paradoxical movement in the thoracic cavity.

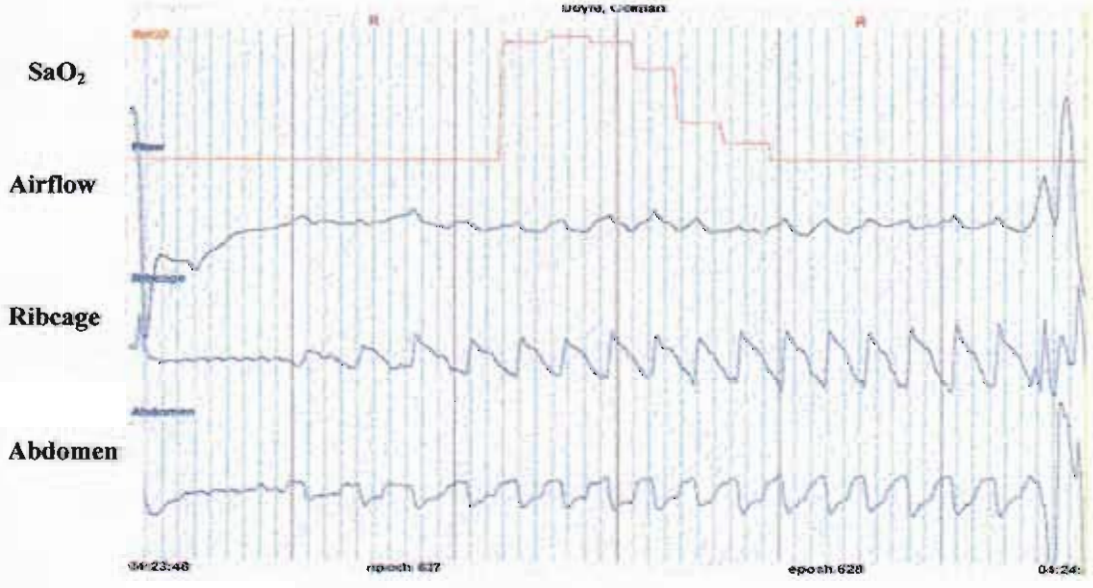


Fig 1.9 Obstructive Apnoea Event[7]

[7] Image taken from PSG recording

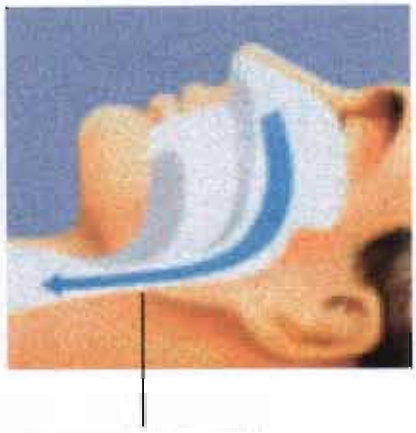
Mixed apnoeas or hypopnoeas start as a central event and develop into an obstructive one. The dominant types of events in OSAHS are obstructive apnoeas and hypopnoeas.

A pulse oximeter with a sensor probe attached to a digit is used to measure oxygen blood levels continuously during the night (see section 4.2.1. for further information on this device).

1.6.2 The Apnoea Hypopnoea Index

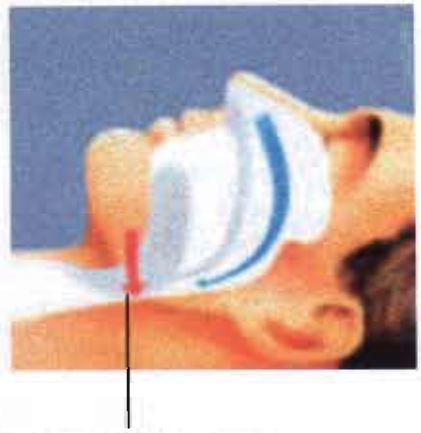
An apnoea (no breathing) is defined as a reduction of 80% or more in the airflow signal, measured at the nose, mouth or larynx, when it is compared to the previous two minutes of stable breathing. The reduction in airflow must last for at least 10 seconds. A hypopnoea (reduced breathing) is defined as a reduction in airflow by more than 50%, but no more than 80%, when compared to the previous two minutes of stable breathing. Airflow can be measured at the mouth nose or larynx and the hypopnoea must last for at least 10 seconds.

Apnoeas and hypopnoeas can be further classified into central or obstructed events. A central apnoea or hypopnoea is due to an intermittent failure in the respiratory drive centre of the brain to signal the lungs to breathe in and out. There is then a reduction or cessation in airflow at the mouth and nose with a corresponding loss of movement in the chest wall and abdomen. The upper airway is usually not obstructed in this situation (Fig 1.10). An obstructive apnoea or hypopnoea is also detected by a reduction or cessation in airflow, but with visible paradoxical movement of the ribcage and abdomen. In this type of respiratory event the upper airway is either partially or completely obstructed (Fig 1.11). Obstructive apnoeas in particular are usually accompanied by an oxygen desaturation of > 3% but hypopnoeas or central apnoeas may not have an associated desaturation event.



Open upper airway

Fig 1.10 Normal breathing[8]



Closed upper airway

Fig 1.11 Obstructive apnoea[8]

Therefore, during sleep when there are short periods of reduced breathing (hypopnoea) or no breathing (apnoea), these result in reductions in arterial blood oxygen saturation (nocturnal desaturations) and in central nervous activation reactions (arousals), which cause short interruptions of sleep. These frequent arousals, although necessary for breathing to restart, prevent the patient from getting enough restorative deep sleep. Therefore, the daytime somnolence (sleepiness) experienced by the OSAHS patient is most likely to be due to sleep disruption and fragmentation by the repeated arousal after each apnoea or hypopnoea.

In OSAHS patients a cyclical pattern develops, consisting of obstruction, asphyxia, arousal, and gasping snores, which may be repeated several hundred times per night. In fact, it is the number of apnoeas and hypopnoeas per hour of sleep that indicates the presence and severity of the condition. This index is called the Apnoea Hypopnoea Index (AHI)[40].

The following classifications have been proposed by the American Academy of Sleep **Medicine Task Force**[41] **on sleep rela**ted breathing disorders in adults.

[8] Image taken from www.alltheweb.com

Table 1.5 Classifications of Sleep Disorder Breathing in Adults

A. Sleepiness

1. **Mild**: Unwanted sleepiness or involuntary sleep episodes occur during activities that require little attention (such as watching TV or reading). Symptoms produce only minor impairment of social or occupational function.

2. **Moderate**: Unwanted sleepiness or involuntary sleep episodes occur during activities that require some attention (such as attending concerts or meetings). Symptoms produce moderate impairment of social or occupational function.

3. **Severe**: Unwanted sleepiness or involuntary sleep episodes during activities that require active attention (such as eating or driving). Symptoms produce marked impairment in social or occupational function.

B. Sleep-related obstructive breathing events
(apnoea, hypopnoea and respiratory effort-related arousals)

1. Mild: 5-15 events/hour of sleep
2. **Moderate**: 15-30 events/hour of sleep
3. **Severe**: > 30 events/hour of sleep

1.6.3 The Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS) is a commonly used questionnaire, which is a self-evaluation of "objective" sleepiness[42,43]. It scores the patient's daytime sleepiness on a scale between 0-24. It asks the patient to number appropriately, the likelihood of falling asleep in certain daily situations. Some of these situations are passive (e.g. lying down, watching TV), others are very active (e.g. driving, conversation), where O = never doze, and a score of up to 3 = high chance of dozing. Whilst this scale cannot establish a diagnosis of sleep apnoea syndrome (SAS) it is a very simple way to demonstrate the response of daytime sleepiness to treatment with continuous positive airway pressure (CPAP) therapy in clinical practice (Appendix B)[44,45].

1.7 How is OSAHS Treated?

The most successful treatments for OSAHS to date have all been aimed towards a mechanical solution to the problem of upper airway closure. In the past a severe surgical solution called a tracheostomy, whereby the upper airway is bypassed completely by the insertion of a permanent rigid tube inserted into the trachea, was initially the only effective option for patients with OSAHS. However, this procedure was only indicated or accepted by patients with very severe disease. So it was very fortunate that Dr Colin Sullivan *et al* in 1981[46] developed another mechanical solution that of continuous positive airway pressure (CPAP) delivered via a nose mask. This development was a crucial step, in providing a highly effective, but non-invasive, modality of treatment for OSAHS[47], which has revolutionised the whole field of sleep medicine.

Nasal CPAP acts like a pneumatic splint preventing collapse of the pharyngeal airway (Fig 1.12).

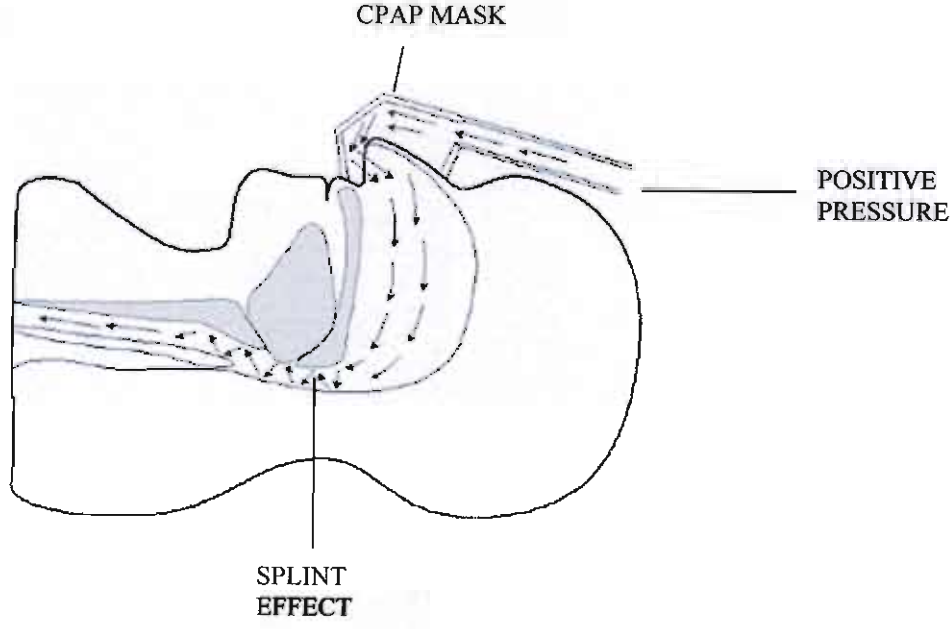


Fig 1.12 CPAP Therapy Keeps Upper Airway Open[9]

[9] Image taken from www.alltheweb.com

The device is a quiet pump, which blows air continuously past the nose, via a well fitting nasal mask, which is strapped to the patients nose (Fig 1.13, 1.14). The applied pressure can be adjusted to achieve a positive pressure of between 4 to 20 cm H_2O depending on the severity of the condition. The consequences of upper airway collapse disappear as soon as the effective positive pressure is applied. Sleep architecture improves, respiratory efforts decrease, snoring is abolished, arterial blood oxygen saturation is higher and pulse rate stabilises. A large number of patients can obtain substantial clinical improvement, particularly with daytime somnolence using this therapy[48-57]. In the Respiratory Sleep Disorders Unit at St Vincent's University Hospital we have also shown that CPAP therapy is associated with improvements in quality of life of partners of OSAHS patients as well as the patients themselves[58]. OSAHS is prevented immediately and continues for as long as the mask is worn and CPAP pressure remains adequate (optimal pressure) for the patient.

Fig 1.13 Fitting a nasal CPAP mask[10]

[10] Image taken from www.alltheweb.com

However, CPAP is a constraining therapy and acceptance and compliance of CPAP appears to be linked to the balance between perceived improvements in daytime symptoms and side effects[59-62]. Throat and nose problems occur in approximately 40% of patients using CPAP and consist to variable degrees of dry mouth, rhinnorrhoea, sneezing, nasal congestion, and pain[59-61]. The important mechanism for dry mouth and nasal symptoms is air leak through the mouth[62-64]. Correct mask sizing and fitting will eliminate air leaks[65]. A warm air humidifier can greatly reduce the magnitude and duration of the increased nasal resistance, which is a consequence of inhaling cold dry room air at pressure[66]. Compliance has also been shown to increase by attendance at a group CPAP clinic, where education, training, support of symptoms, treatment and equipment queries can be shared[67].

Objective data, for the purposes of evaluating the patient's progress on treatment, can be downloaded from the positive airway pressure (PAP) devices. All CPAP units have a built-in machine time counter, which records the number of hours that the pump is running. An additional microprocessor in some models, in particular the APAP devices records both the machine runtime and the actual time spent by the patient wearing the mask at the prescribed pressure[68,69].

CPAP abolishes but does not by itself cure OSAHS. Interruption of CPAP is soon followed by the return of obstructive sleep apnoea. Only up to 10% of patients can be successfully weaned off CPAP after one to several years of regular use[70,71]. Therefore the majority of patients are committed to a prolonged life long treatment.

Fig 1.14 Sleeping with a CPAP system[11]

1.7.1 How to Determine Optimal Pressure

The optimal pressure, in CPAP treatment, is defined as the lowest pressure that eliminates different respiratory events in all positions and sleep stages, resulting in normalised sleep architecture. However, the concept of a single ideal level of positive pressure for any individual is over-simplistic. Upper airway resistance is dependent on multiple factors including, body position, sleep stages, sleep deprivation, body weight, and fluctuations in nasal congestion. The level of fixed pressure required therefore, to maintain upper airway patency, the so-called "optimal" pressure may vary considerably from night to night or even during the night.

Titration is the process of making a trade-off, between eliminating all obstructive events by increasing the pressure, and reducing side effects by using the lowest possible effective pressure. If the prescribed fixed pressure is too low, snoring and apnoeas will persist. If the pressure is too high, there could be problems with mask removal during

[11] Image taken from www.alltheweb.com

sleep, air leaks and disturbed sleep. Incorrect pressure setting could also reduce tolerance and compliance with treatment in the long term.

Traditionally, the gold standard for selecting a fixed pressure for home therapy has been manual titration in association with a Cardiorespiratory Polysomnography (CRPSG) test overnight in the sleep laboratory[47]. Patients are connected to a nasal CPAP system and the pressure is gradually increased in steps of 1 cm H_2O (range 4-20 cm H_2O) until the optimal fixed pressure setting is reached. This fixed pressure must resolve respiratory events, snoring and associated arousals. As a consequence of the high costs involved in this detailed and time consuming procedure and the demands on the CPRSG equipment for diagnostic purposes, cheaper and shorter procedures have been developed over the past decade.

Automatic titrating systems are such devices and they are engineered to continuously adjust the pressure at the "optimal" level[72]. They use the pressure flow signals to detect apnoea and hypopnoeas or flow limitation. Most machines are piloted by an algorithm based on detection of apnoea and hypopnoea alone, or in combination with snoring. One such algorithm is based on inspiratory flow limitation derived from the shape of the inspiratory flow time relationship[73-75].

1.7.2 Inspiratory Flow Limitation

Analysis of the inspiratory flow-time curve is the most effective method to assess flow limitation. It is derived from the way the inspired airflow changes during the breathing cycle. Airflow rises smoothly and gradually at the start of inspiration and falls smoothly at expiration. Therefore, a rounded curve indicates a normal unobstructed breath (Fig 1.15). But as the upper airway begins to narrow, causing flow limitation and upper airway resistance, the shape of the curve will flatten (Fig 1.16). By applying a numerical

value to this flattening rate it is possible to calculate the presence of airflow abnormalities. The flattening index for a normal unobstructed breath will have a value in the range 0.2 to 0.3. But when upper airway narrowing is present the flattening index will have a value in the range of 0 to 0.15. This means that a flattening index of less than 0.15 is considered to be an indication of upper airway obstruction. This principle of assessing the upper airway is utilised in the clinical auto-titrating and home therapy APAP devices used by the patients in this study.

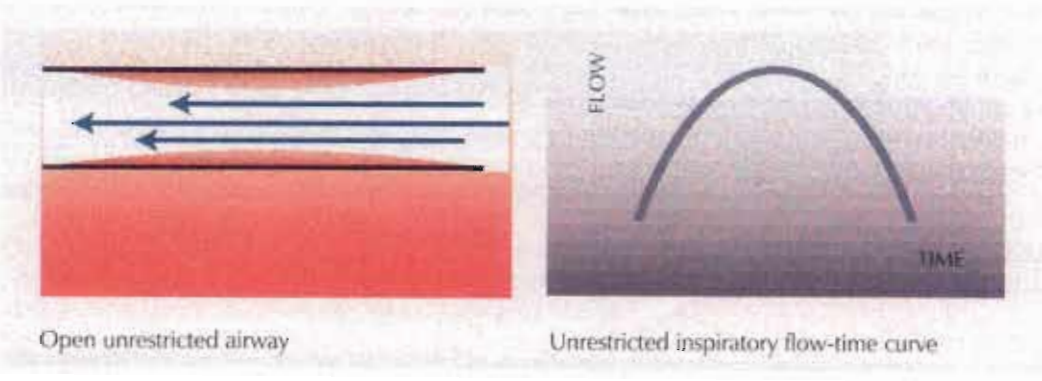


Fig 1.15 Normal Open[12]

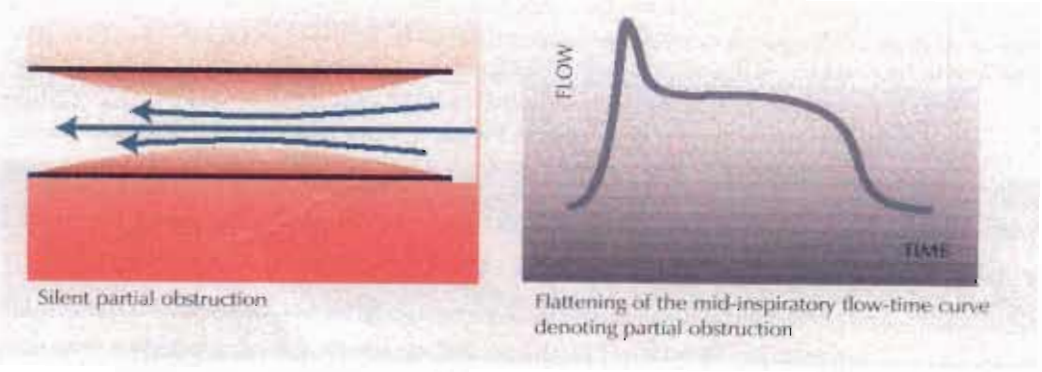


Fig 1.16 Flow Limitation[12]

[12] Image taken from Autoset Portable II Plus, Overview and Interpretation Guide

1.8 Treatment with CPAP Therapy

As already mentioned, nasal continuous positive airway pressure (CPAP) therapy has become the first choice treatment for obstructive sleep apnoea hypopnoea syndrome (OSAHS) over the past two decades[46]. It is extremely successful in treating this condition, by reducing the number of episodes of upper airway obstruction during sleep and improving or completely resolving clinical symptoms, the adverse physiological consequences of obstructive sleep apnoea. But not all patients can tolerate this form of treatment. Hoffstein *et al*[59] pointed out that nasal CPAP is unlike any other conventional medical therapy and therefore a great deal of commitment is required on the part of the patient to accept this form of treatment. Mechanical characteristics of the devices especially the noise level, nocturnal awakenings, tolerance by the bed partner and side effects, relating to the mask and air pressure, all influence the acceptance of this treatment by patients.

1.9 Factors that Affect Compliance

Three main factors appear to affect nasal CPAP compliance. One is motivation, which is tied to the severity of the symptoms and satisfaction with the mode of therapy. Second are the perceived complications or discomfort from the use of the device. The third is the degree of education about and understanding of OSAHS and the importance of treating it. Several long-term studies have shown compliance rates of between 65-90%[76-80]. In addition other groups have shown that CPAP usage averages only between 3 – 6 hours nightly[81-83]. Built-in time counters and microprocessors in the CPAP units can objectively detect the number of hours that the pump is running, as well as the percentage of time that the mask is worn, therefore the effective fixed pressure delivered to the patient. Kreiger *et al*[56] found that, both within and between groups, objective disease

severity, as measured by the respiratory event index e.g. apnoea/hypopnoea index (AHI), rather than patients' symptoms or complaints seemed to play a role in the quality of compliance to treatment. This was comparable to the earlier findings of Rolfe *et al*[84].

1.9.1 The AHI and Compliance Relationship

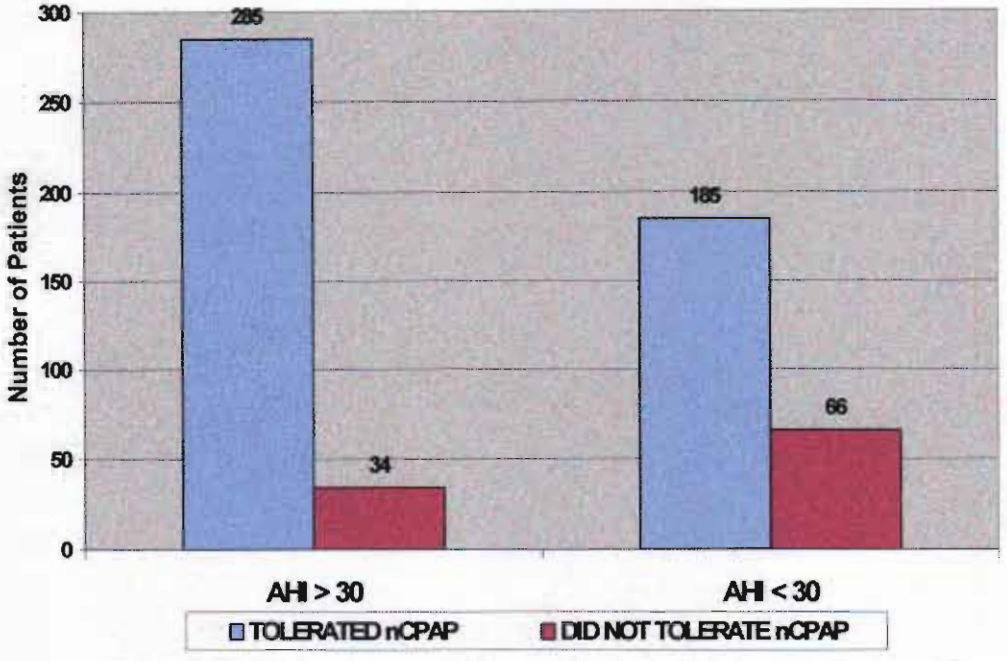


Fig 1.17 Patients Assessed for nasal CPAP between 1990-2000[13]

A random selection of 570 patients, 496 (87%) males and 74 (12%) females, who had been assessed for nasal CPAP therapy over the past ten years in the Respiratory Sleep Disorders Unit of St Vincent's University Hospital, revealed the following information (Fig 1.17). 319 (55%) of the patients had a diagnostic AHI greater than thirty events per hour of sleep, and 251 (45%) had less than thirty. A group of 100 (17%) of these patients were unable to tolerate nasal CPAP treatment. Of this group of 100 non-tolerant patients, 66 (66%) recorded initial baseline AHI of less than thirty, whilst 34 (34%) had values more than thirty. In other words, of the 100 patients who could not tolerate CPAP

[13] Data taken from Sleep Disorders Unit, SVUH

therapy almost two thirds recorded an AHI of less than thirty. This would seem to indicate that mild to moderate OSAHS, as based on an AHI of between five and thirty, implies less compliance.

As previously mentioned, it has been practice to perform a manual pressure titration in the sleep laboratory during a full Cardiorespiratory Polysomnography recording, gradually increasing the pressure by 1 cm H_2O (range 4-20 cm H_2O) until the optimal fixed pressure setting is reached. This pressure must successfully resolve respiratory events, including snoring and associated arousals[47]. In practice though, all patients may not tolerate this optimal pressure and the final fixed pressure is often set to a lower one. This means, there is usually a trade-off made between increasing effectiveness at eliminating respiratory related events and avoiding unpleasant side effects.

1.10 Clinical APAP Systems

During the early 1990's clinical auto-titrating systems were developed that provided a method for determining a single fixed positive airway pressure, suitable for subsequent long term home treatment with a conventional nasal CPAP device[72,85,86]. The goal of these systems was to avoid the cost and labour of a manual titration. Since auto-titrating or auto-adjusting positive airway pressure (APAP) devices apply at any time the minimally required pressure to normalise breathing, it has been hypothesised that this ability to vary pressure means the patient's needs could be met on a night by night basis. This should improve patient comfort and therefore lead to an increase in patient compliance. Also the anticipated reduction in the mean pressure could eliminate troublesome side effects with air leaks and noise, as pressure is only applied when it is needed, and yet at the same time guarantee that peak pressure demands are met[87].

1.11 APAP Therapy Compared to CPAP Therapy

Several groups have compared APAP systems to conventional nasal CPAP devices, but have yielded varying results. Konermann *et al*[88] demonstrated that APAP is as reliable in suppressing respiratory disturbances as CPAP in patients with severe obstructive sleep apnoea, and that patient compliance and sleep quality were better in the group using the APAP device. Comparable efficacy was also found by Boudewyns *et al*[89] in an uncontrolled study of 15 OSAHS patients. Ficker *et al*[90] achieved identical therapeutic effects with both systems but they did not achieve the anticipated lower mean pressure with the APAP type.

Conversely, Teschler *et al*[91] did find a 23% reduction in the median pressure using the APAP device but showed no increase in compliance. In recent studies, d'Ortho *et al*[92] and Wiltshire *et al*[93] both demonstrated that although APAP is as effective as CPAP, patient tolerance, compliance and duration of use were similar for both treatments.

1.12 Purpose of this Study

The majority of patients in these earlier study groups included patients with severe OSAHS e.g. AHI greater than thirty, and therefore APAP did not specifically target the potentially poor compliant group e.g. AHI less than thirty. Evidence from recent epidemiological studies, suggests that even subjects with mild sleep breathing abnormalities may have associated hypertension[94], neurocognitive deficits[95] and increased motor vehicle accidents[96].

Furthermore, in three randomised controlled trials[97-99] in patients with mild OSAHS, which looked at the effect of nCPAP therapy results, there appeared to be an improvement in some areas of neuro-behavioural function and self-reported symptoms. Although this number of failed users of one hundred non-tolerant patients represents only

14% of the total number commenced on treatment, a small increase in cardiovascular incidence or hypertension or behavioural morbidity attributable to OSAHS in this group could have a large impact from a public health point of view. Therefore it appears that getting all patients with OSAHS, irrespective of the severity category, compliant with treatment is a very important clinical objective for all sleep service providers.

With this in mind the aim of the study was to see if APAP was tolerated better than CPAP in patients with mild to moderate OSAHS. If there was conclusive evidence that APAP was better tolerated than CPAP, then APAP could become the first choice treatment for mild to moderate OSAHS sufferers.

The following chapters discuss the methods and techniques used to collect and interpret the data needed to determine the outcome of this hypothesis. In particular, Chapter two looks at the methodology of the study protocol, while Chapter three discusses in detail the measurement equipment used during the study. Chapter four presents the results of the data analysis and in Chapter five the results of this study are compared and discussed with results from previous studies. The final chapter outlines the main conclusions that can be drawn from this study and also discuss the limitations and possible future work that could be carried out in this area.

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2. METHODOLOGY

2.1 Study Protocol

The study consisted of four separate study nights in the sleep laboratory spread over approximately seventeen weeks, depending when the night 1 diagnostic data were collected. The patients spent a total of sixteen weeks at home on treatment devices comprised of two eight-week sessions, one eight-week period on CPAP, the other 8 weeks on APAP. A total of 115 days of data were collected during the study on each patient. Ethical approval was obtained from the Ethics Committee of St Vincent's University hospital prior to the commencement of the study. The flow chart (Fig 2.1) gives an overview of the study protocol in relation to the tests carried out each night in the Sleep Laboratory. The following sections outline the set up on each of the nights of the study, as well as details regarding the information that was recorded during them.

2.2 Study Criteria

The patient group comprised a total of forty-five patients (Appendix C) all who had an AHI of less than thirty[1] by Cardiorespiratory Polysomnography (CRPSG), with an Epworth Sleepiness Score (ESS) of more than 6[2]. All patients had a history of snoring, with no evidence of unstable cardiovascular disease. All patients had been previously diagnosed with OSAHS[3] and were on the clinical waiting list in the respiratory Respiratory Sleep Disorders Unit in St Vincent's University Hospital, awaiting a trial of nasal CPAP therapy.

2.3 Lab Night 1 Set-Up in the Sleep Laboratory

On the first night, written informed consent was obtained from the patients. The patients were also asked to fill in a questionnaire regarding current sleep patterns, caffeine (tea,

coffee, and cola) and alcohol intake. The ESS was completed to determine the degree of daytime sleepiness that was being experienced at that time. A CRPSG test was then performed and analysed according to international guidelines[4].

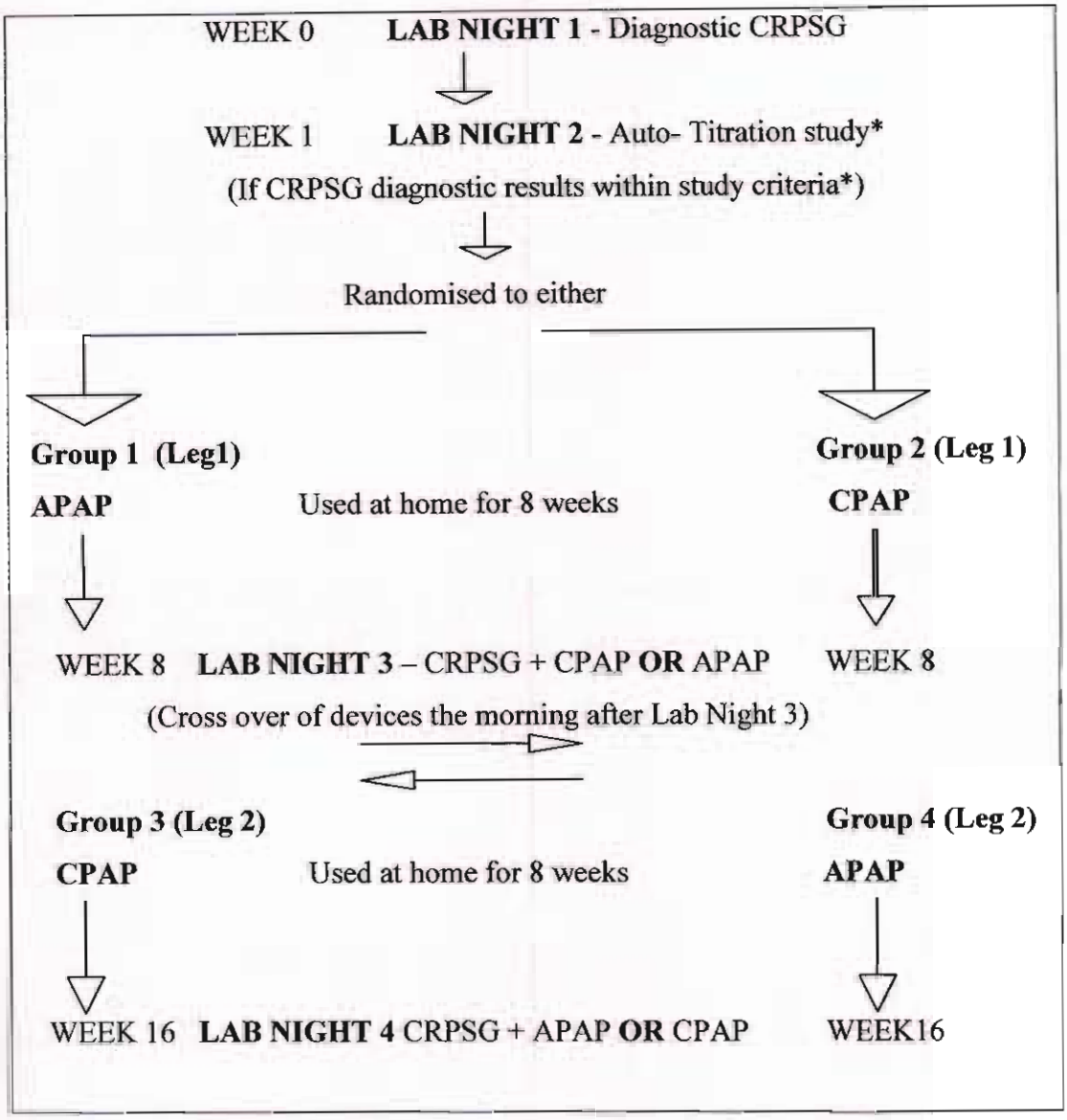

Fig 2.1 Flow Chart of Study Tests

The CRPSG procedure consisted of the placement of bands containing transducer coils around the upper chest and lower abdomen, which allowed monitoring of the breathing pattern. This method of assessing thoracic and abdominal efforts during sleep is called respiratory inductance plethysmography. An oronasal thermistor was taped onto the face

to record airflow through the nose and mouth. This device provided information about the presence or absence of airflow based on the temperature differences between inhaled and exhaled air. Abnormal respiratory events were analysed from the airflow signal in conjunction with the readings from the transducer coils (Fig 3.2, page 51).

Small metal skin electrodes were attached to the scalp (no = 2), forehead (1), chin (2), eyes (2) and behind the ears (2) in order to record electroencephalogram (EEG, brain activity), electromyogram (EMG, muscle activity) and electroocculogram (EOG, eye movements). A position sensor with microphone and ECG electrodes (2) were taped onto the chest area to record sleep position, snoring and heart rate. A pulse oximeter probe was taped to a finger to record the percentage saturation of oxygen in the arterial blood.

When this lab night 1 study was analysed and if the apnoea hypopnoea index (AHI) and Epworth sleepiness score (ESS) met the criteria set for the study (see section 2.1) the patient proceeded to lab night 2. Otherwise they were excluded from the study. These excluded patients were commenced on standard nasal CPAP treatment according to the clinical protocol in the sleep laboratory at that time.

2.4 Lab Night 2 Set-Up in the Sleep Laboratory

On lab night 2 (usually one week after the baseline, lab night 1 data had been obtained) an automatic titration of fixed positive airway pressure therapy was performed using a clinical auto-titrating system[5]. Treatment education took place in a group therapy setting[6] and included a mask-fitting session and a thirty-minute video viewing of positive airway pressure treatment. The partners or spouses were encouraged to attend on this night so as to learn about the condition and positive airway pressure treatment. A question and answer session followed on OSAHS and the proposed therapy was then covered.

The home device for leg 1 of the trial, either CPAP or APAP, which was randomly assigned, was fully demonstrated to the patient. Those who received APAP for leg 1 belonged to Group 1, while those who received CPAP for leg 1 were in Group 2. (Group 3 used CPAP for leg 2 of the trial, whilst Group 4 used APAP for leg 2 of the trial). The patients were not aware of the different mechanisms by which these two devices worked. This type of clinical trial format is known as a single blind randomised study. The patient is "blinded" to the device, but the operator is aware which device is being used for each leg of the trial.

The patient wore a soft nasal cushion fitted snugly over the nose during the night (Fig 1.13, page 23). This nasal mask is connected via a hose to a small compressor type device, which blows air continuously up the hose and through the mask into the nose and down into the lungs (Fig 1.14, page 25). The oximeter probe was taped to the finger to measure arterial blood oxygen saturation. The results of this night 2 automatic titration study were reviewed by a doctor and then the patient was randomly assigned a device, either CPAP or APAP to use nightly at home for eight weeks.

The patient was requested to complete a simple diary card (Appendix D) every morning during the eight weeks of home usage on each device. The diary card assessed the user's opinion on the quality of sleep and any ear, nose, and / or throat (ENT) discomfort of the previous night's sleep with the treatment[7]. A steroid nasal spray (Flixonase) or a warm air humidifier can help to relieve the ENT symptoms[8]. The diary card recorded the addition of either or both the nasal spray and the humidifier each night. Alcohol intake was also recorded for the previous day[9].

2.5 Lab Night 3 & Lab Night 4 Set-Up in the Sleep Laboratory

Lab nights 3 and 4 in the sleep laboratory were therapy assessment nights after leg 1 and leg 2 treatment periods respectively. Group 1, who had used APAP treatment at home for 55 nights, used this device on the 56th night of treatment in the sleep laboratory (lab night 3). They then started leg 2 on CPAP therapy and became Group 3. On the 56th day of this treatment they were reassessed in the sleep laboratory with CPAP (lab night 4). Group 2, who started leg 1 on CPAP therapy had this treatment assessed on lab night 3 in the laboratory, which was the 56th night of this treatment. They then started leg 2 of the trial on APAP therapy and became Group 4 and were on this device for 55 nights at home and were then reassessed again on the 56th night in the laboratory with the APAP device (lab night 4).

A CRPSG with either CPAP or APAP was performed on these nights (lab nights 3 and 4) in the laboratory. The set up was similar to lab night 1 except that an oronasal thermistor was not required, as the patient was wearing the nasal mask in conjunction with either a CPAP or APAP device. The mask was connected to a channel on the CRPSG system, which recorded the positive pressure values throughout the night's study.

The patients were once again asked to fill in the questionnaire regarding current sleep patterns as well as the ESS questionnaire. The diary card was also completed each morning during the second eight weeks of the trial.

After completing each 56 nights of treatment the APAP and CPAP device memories were downloaded onto the sleep laboratory computer to assess the hours of use by the patient over the previous eight week home therapy session. The patient and their partner (where applicable) also recorded their preference for device at the end of the total sixteen-week treatment period.

2.6 References

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3. MEASUREMENT EQUIPMENT

3.1 Overview

Several pieces of equipment were used during the study, both in the sleep laboratory for monitoring purposes and at home as treatment devices by the patient. The flow chart (Fig 3.1) lists the equipment used each night of the study and at home. A brief description of each device, the basic principle of operation and its primary function in the study are given in the later sections of this chapter.

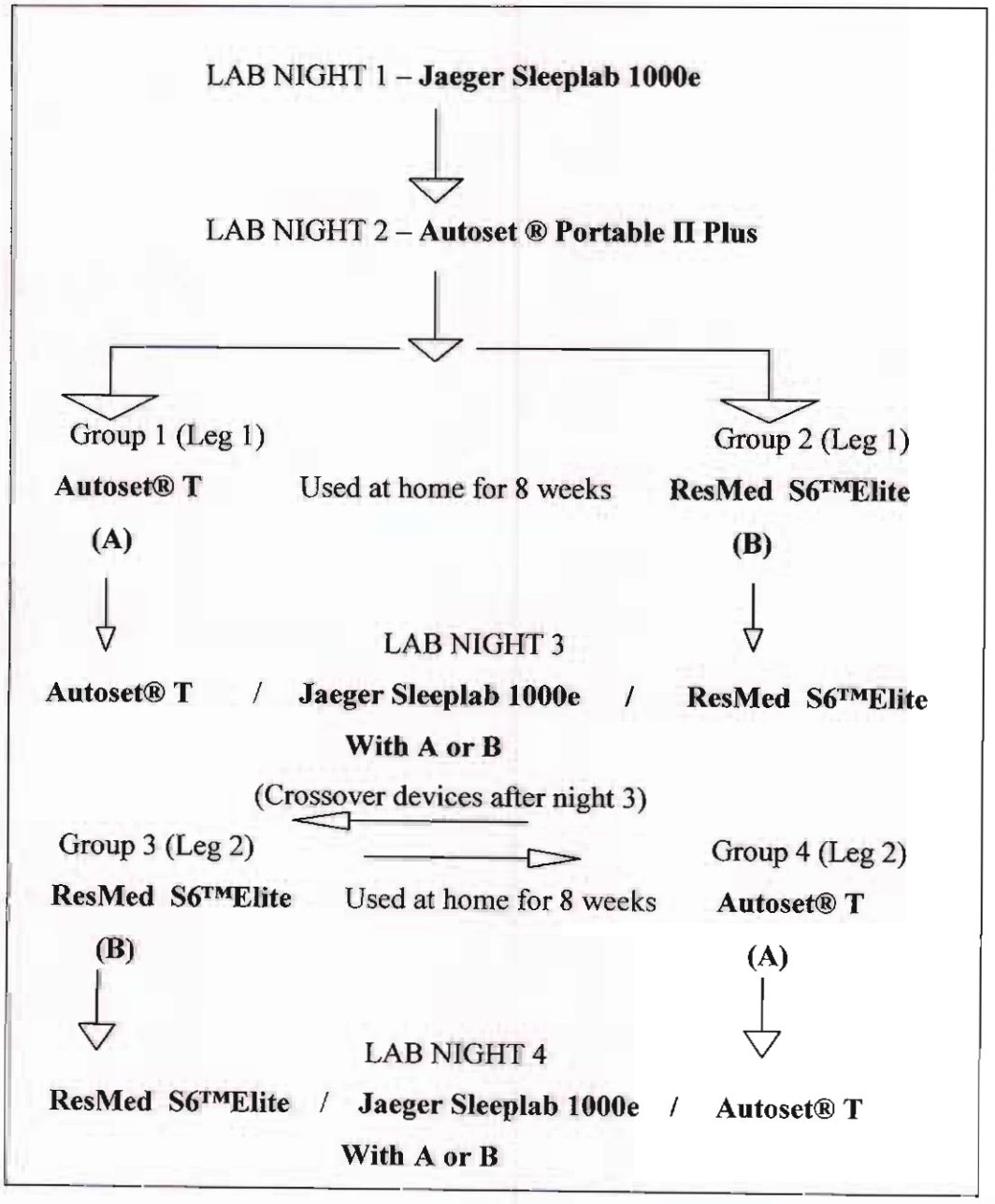

Fig 3.1 Flow Chart of Equipment used during Study

3.2 Cardiorespiratory Polysomnography System

The Jaeger Sleeplab 1000e (SL1000e) Version 2 is a portable computerised polysomnography system for recording physiological sleep signals overnight (Appendix E). The system is a networked two-bedded system utilising Windows NT. Each bed unit was comprised of eight AC amplifier channels, with another eight channels that could have been used as AC amplifier channels, RT channels or auxiliary channels. Channels 1-8 displayed EEG, EOG, EMG and ECG signals recorded from the patient via the patient junction box (PJB). These channels were connected to eight internal AC amplifiers.

Respiratory signals (Fig 3.2) were recorded via the patient yoke box, and included oral and nasal airflow via an oronasal thermistor and thoracic and abdominal efforts via inductance belts. Snoring was detected through a tracheal microphone located at the neck. A Sims BCI 3304 Oximeter provided fast, reliable arterial blood oxygen saturation (SaO_2), pulse rate and pulse strength measurements.

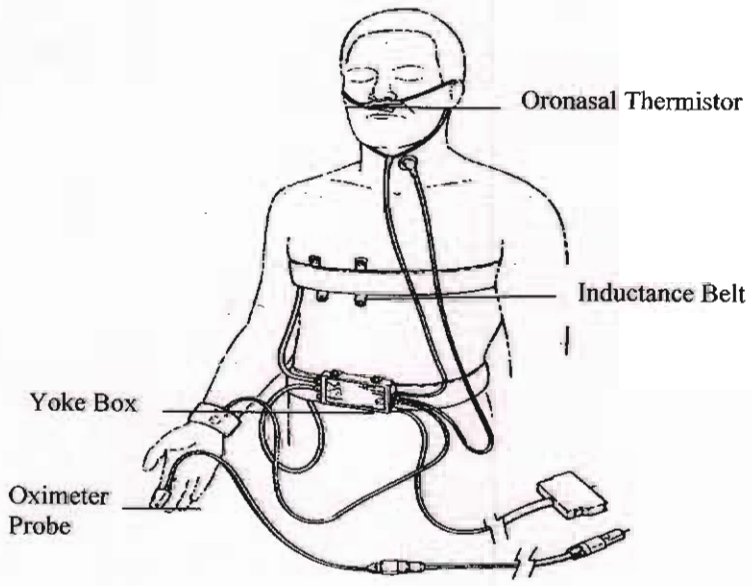

Fig 3.2 Respiratory set-up for CRPSG Study[1]

[1] Image taken from Sleeplab 1000e Operator Manual

The oximeter operated accurately over an ambient temperature range of 0 to 40° C..

The sleep system was provided with an efficient software program, the Aequitron Matrix Sleep™ Analysis for Windows™. The Matrix Analysis software allowed for a comprehensive and fully automated evaluation of both sleep and respiration at the end of the recording session. However, a manual analysis of these readings was also conducted, which was reported as the final result (Appendix F). This test procedure could be used as either a diagnostic test (lab night 1) or as a treatment assessment test (lab nights 3 and 4). In the treatment assessment configuration the patient was connected to either an APAP or CPAP device while the CRPSG study was carried out.

3.2.1 Principle of Operation of a Pulse Oximeter

A pulse oximeter determines arterial blood oxygen saturation and pulse rate non-invasively by passing two wavelengths of low intensity light, one red (660 nm), and one infrared (940 nm), through body tissue in a digit to a photo-detector. Oxygenated haemoglobin found in arterial blood and non-oxygenated haemoglobin found in venous blood, absorb these wavelengths of light differently. Oxygen saturation percentage values can be calculated using the ratios of received light intensities at each wavelength (application of Beer-Lambert law). Oximetry screening using a BCI pulse oximeter (Appendix G) was continuously monitored during study nights in the sleep laboratory. No calibration process was required to set up the oximeter, but it was necessary to confirm that both zero (0% SaO_2) and maximum values (subject's awake SaO_2) were recorded correctly by the computer, prior to commencement of each CRPSG study.

3.3 General Information on AutoSet ®T and AutoSet ®Portable II Plus

The AutoSet Portable II Plus and AutoSet T (ResMed (UK) Ltd, Abington, UK) are flow generators that are part of a computer controlled automatic CPAP treatment system. The flow generator uses a low inertia and high speed integrated motor/fan combination. The motor speed is electronically controlled and is included in a feedback loop monitoring the mask pressure. At all times, the mask pressure measured by a pressure transducer in the circuit governs the motor speed through the computer. By assessing the contour of the inspiratory flow-time curve on a breath-by-breath basis, both these devices pre-emptively increase pressure in response to inspiratory flow limitation, which typically precedes snore and obstruction. Prevention of snoring and apnoea events normalises the work of breathing thereby reducing arousals, which cause sleep fragmentation.

The two systems also maintain pressure by compensating for mask leak. Mask leak is measured by analysing the inspiratory and expiratory volumes, which should be equal, leading to an average airflow of zero. However, if the long-term average is greater than zero there is a leak, usually at the mask. If mask leak is greater than 0.4 l/s the flow generator can inappropriately increase pressure. Once mask leak reaches 0.7 l/s there is no increase in response to flow limitation.

3.3.1 Flattening Index

As previously mentioned the flattening or flow limitation index is a measure of upper airway obstruction. The most effective method to assess flow limitation is by analysis of the inspiratory flow-time curve (Fig 1.16, page 27). In both the Autoset Portable 11 Plus and the Autoset T, the system software assigns a flattening index value in the range 0.2 to 0.3, to a normal unobstructed breath. Values in the range of 0 to 0.15 indicate some degree of airway narrowing, generally due to upper airway obstruction. This value is

calculated continuously by averaging the previous 5 breaths. The algorithms in the two devices adjust the pressure according to the extent of flattening, in order to maintain airflow and restore the flattening index to a value greater than 0.2.

However one point to mention is that in central apnoea events or open airway apnoeas, as they are also referred to, the airway is widely patent, i.e. held open by either muscle tone or by the existing CPAP pressure. Therefore there is no need to increase mask pressure, because the airway is already open. In fact increasing the pressure would needlessly add to patient discomfort and increase vagal inhibition of breathing via the Hering-Breuer reflex, thus aggravating the central apnoeas further.

3.4 AutoSet® Portable II Plus

Fig 3.3 AutoSet ®Portable II Plus - Clinical Auto-Titrating Device[2]

The Autoset Portable II Plus (Fig 3.3) is a clinical laboratory system that includes nasal mask, built-in Nonin pulse oximeter and an optional respiratory band and body position sensor (Appendix H).

[2] Image taken from www.alltheweb.com

The system can operate in three modes. The diagnostic mode is used to diagnose obstructive sleep apnoea, but without reference to sleep stages. The manual mode is used for assessing respiratory parameters at a given set pressure and the automatic mode for automatic pressure titration. During automatic titration the Autoset Portable II Plus detects and automatically adjusts pressure in response to inspiratory airflow limitation, snoring and obstruction.

The patient wears a nasal mask containing a pneumotachometer, a calibrated flow-sensing device that measures airflow and volume in the upper airway. The basic principle of a pneumotachometer is to produce a signal that is proportional to gas flow. This signal can then be integrated to provide a measure of volume. At six seconds into a period of zero or near zero airflow, indicating the commencement of an apnoea, pulses of air at a pressure of 0.25 cm H_2O are sent into the mask at a frequency of 4 Hz. If no flow is detected, the apnoea is classified as closed and the pressure is increased by 1 cm H_20 every 15 seconds until the apnoea is terminated and airflow resumes. The maximum rate of increase in response to any event is 1 cm H_2O per second. If there is no evidence of further snore, obstruction or flow limitation then there will be a gradual decrease in pressure towards 4 cm H_2O. However, if flow is detected, indicating an open airway, the pressure is not increased.

Oxygen saturation, nasal ventilation, snoring and apnoeas are also recorded. The oxygen saturation is recorded continuously during the study. It is sampled, averaged and logged every second and is plotted in a scale of 0-100%. The snore index is averaged and logged every 15 seconds. Arbitrary units are used to represent the snore intensity (e.g. dBa stands for adjusted decibels, which are used to express relative levels of noise). Silent breathing generates less than 0.2 units, whereas a value of 1 equates to approximately 75

dBa measured from the nares. (Fig 1.1, page 6). Therefore, a value greater than two indicates loud snoring.

Nasal ventilation is logged every 2 seconds and it is measured in litres per minute from the pneumotachometer attached to the nasal mask. The reading is semi-quantitative and more useful readings can be taken from nasal thermistors. Airflow is measured every two seconds and then averaged over a moving hundred second interval. If at any time, the airflow falls below this moving hundred second average by 75% for at least 10 consecutive seconds then an apnoea is scored. The airflow is also averaged every 8 seconds over the same moving hundred seconds, and if there is a reduction in airflow of between 50-75% from this second hundred average value for at least 10 consecutive seconds then a hypopnoea is scored.

3.4.1 AutoView™ 98 Software

The recorded data were downloaded using Autoview 98 software (ResMed UK). AutoView 98 is a user-friendly, software program that is Windows 95, 98 and NT 4 compatible. Before using the Autoset Portable II Plus on individual patients, patient identification numbers, biographical details as well as mode selection are configured by the software. At the end of a recording session, the data was presented in a summary report as an eight-hour session, which gave a concise view of the entire study. The graphical summary report gave information on all the overnight respiratory events, pressure changes, oxygen saturation, heart rate as well as a measurement of mask leak (Appendix I). The report also included an apnoea hypopnoea index, and a suggested fixed pressure for home treatment this is referred to as the 95th Centile (Appendix J). This is the pressure that is only exceeded 5% of the night. It is very important when interpreting the results to always inspect the leak tracing first as leaks greater than 0.4 l/s

reduce the accuracy of the other measurements. A mask leak less than 0.2 l/s for the majority of the study equates to a well-fitting mask.

3. 5 AutoSet® T

Fig 3.4 AutoSet® T – Auto-adjusting Positive Airway Pressure Device[3]

The AutoSet T or AutoSet Therapeutic (Fig 3.4) is an automatic titration system for the long-term home treatment of obstructive sleep apnoea (Appendix K). The internal computer in the system adjusted the pressure on a breath-by-breath basis to adapt to the patient's changing needs throughout the night. As a result the patient receives the minimum pressure required for effective therapy. The AutoSet T algorithm responded to three key respiratory parameters.

- Inspiratory Flow Limitation – the greater the flow limitation the more pressure it delivers
- Snore – the louder the snoring the more pressure it delivers
- Apnoea – the longer the apnoea the greater the increase in pressure

[3] Image taken from www.alltheweb.com

Additionally, the AutoSet T maintains pressure by compensating for mask leak. A visual display is also available to check the quality of mask fit. The operating and clinical parameters of the system are configured using the front panel display or via a computer utilising the AutoScan™ software. The pressure transducer located in the AutoSet T measures delivered pressure and snore.

The flow sensor located in the flow generator measures the patient's airflow and enables the AutoSet T to detect apnoeas and inspiratory flow limitation. The AutoSet T increases pressure by up to 0.3 cm H_2O for every 0.01 unit below a flattening index value of 0.15 units. The maximum rate of increase in pressure is 1 cm H_2O per second. When no further decreases in the flattening index are detected the pressure is gradually reduced to the minimum set pressure over twenty minutes. However, unlike the AutoSet Portable II Plus, the AutoSet T does not differentiate between a closed airway apnoea i.e. obstructive apnoea and an open apnoea i.e. central apnoea. For this reason it does not increase pressure in response to apnoeas once the pressure of 10 cm H_2O was reached, unless there is evidence of flow limitation or snore. The AutoSet T increased pressure by up to 0.2 cm H_2O per second for snore above 0.2 snore units and until snore was less than 0.2 units.

3.6 ResMed S6™ Elite

As mentioned previously a CPAP flow generator unit provides pressurised air through a nasal mask to keep the airway open. The ResMed S6 Elite unit (Fig 3.5) is set to deliver a fixed pressure, usually the 95th Centile calculated from a previous automatic titration study. This system contains a microprocessor-controlled motor that maintains constant pressure (Appendix L). There are built-in delay timer controls for 5, 10 or 20 minutes. These delay timer controls allow the patient to reduce the set fixed pressure value to 4 cm

H_2O. Then the pressure is gradually increased up to the maximum fixed pressure setting over the following 5, 10 or 20 minutes, depending on the control selected. It also has an automatic internal power converter and automatic leak adjustment to maintain therapy when mask leaks are present.

Fig 3.5 ResMed S6™ Elite CPAP – Continuous Positive Airway Pressure Device[4]

The SmartStart® feature allows automatic stop and start of the device. The hour meter displays the total number of hours that the motor is running and so can provide some information on therapy compliance. It is located on the underside of the flow generator.

3.7 AutoScan™ Software for Compliance Monitoring

AutoScan™ (ResMed UK) is a Windows© based software tool for managing the patient's therapy. This software will download the recorded compliance data from both APAP and CPAP treatment devices, which can be viewed in graphic or numeric report formats (Appendix M).

[4] Image taken from www.alltheweb.com

This compliance data was downloaded at the end of each treatment leg, following lab night 3 and lab night 4 studies. The software reported data in four main profiles, usage profile, statistical summary, treatment profile and night profile. The last two profiles were only available from the Autoset T (Appendix N).

3.8 Ultra Mirage® Nasal Interface

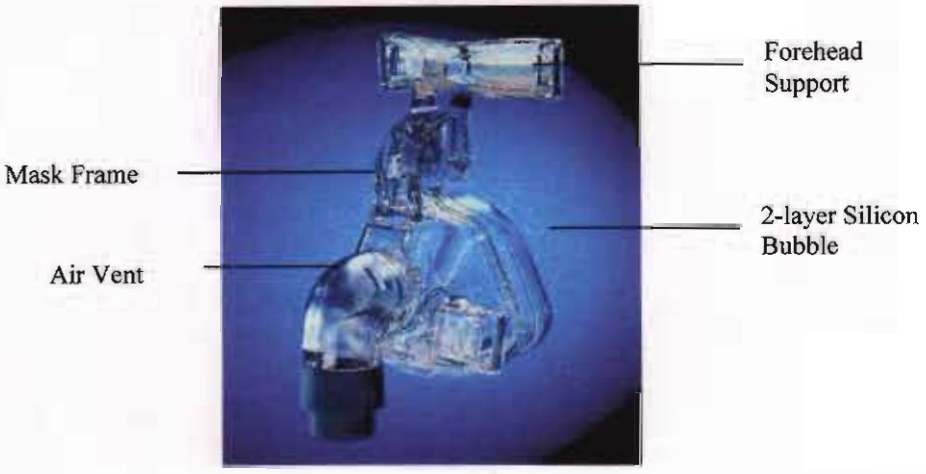

Fig 3.6 Ultra Mirage® Nasal Mask –Interface for AutoSet T & ResMed S6 ™Elite[5]

The Ultra Mirage® mask (ResMed UK) is a nasal mask interface between the patient and the flow generator (Fig 3.6). It is designed with several unique features that ensure comfort and fit. A two-layer cushion on the silicon bubble provides comfort and stability. The forehead support provides fit and stability, which is further enhanced by the four-point headgear attachment that fastens with Velcro®. The quiet air vent minimises noise and enables efficient carbon dioxide washout. The silicon bubble comes in two sizes, standard and large. The standard size fits approximately 80% of patients. This interface

[5] Image taken from www.alltheweb.com

was used by the patients during the sixteen weeks of treatment. It was compatible with both the AutoSet T and ResMed S6 Elite devices.

3.9 HumidAire® Humidifier

Studies indicate that heated humidification provides the most effective treatment for patients who experience nasal irritation or sore throat side effects. The HumidAire® (ResMed UK) heated system effectively humidifies and warms room air with low heat and minimal condensation (Fig 3.7). The large heater plate heats (range 20-26°C) the water in the 600mls chamber in less than twenty minutes. The automatic heater plate shut-off prevents plate temperature exceeding 75°C thereby reducing risk along with other safety features, which ensure that all electronic components are isolated from the water chamber. When humidification is required in conjunction with positive airway pressure (PAP) therapy, either CPAP or APAP, it is placed in-line. Room air is first passed through the warm air humidifier before being passed through the hose leading to the nasal mask.

Fig 3.7 HumidAire® Humidifier - use with AutoSet® T and ResMed S6™ Elite[6]

[6] Image taken from www.alltheweb.com

4. DATA ANALYSIS AND RESULTS

4.1 Introduction

This chapter presents the results of the data analysis from the study. Large amounts of data, both objective and subjective, were recorded during the course of this trial. Details regarding technical difficulties with the data and the statistical methods employed in the analysis are addressed first. Secondly the details about the group's characteristics leads into data analysis about sleep quality. Finally, respiratory data and treatment compliance are discussed. At the conclusion of this chapter sub group analysis is performed to ascertain if there were any variables present at the baseline assessment that may have pre-determined end preference by the patients.

4.2 Recruiting Subjects

Sixty-four patients received a written invitation to join the study (Appendix C). These patients were all on the CPAP titration list awaiting assessment at the time. Forty-five (70%) of these responded positively to this invitation. The other nineteen patients were followed up separately in the sleep laboratory at a later stage. Ethical approval was requested and granted by the Ethics committee of St Vincent's University Hospital. Informed patient consent was also obtained for all the patients who participated in the study.

Thirty-one (69%) of the forty-five patients completed the trial, but only twenty-nine patient's data were included in the final analysis. Two patients were excluded from the final analysis, as they were no longer categorised with obstructive sleep apnoea following review of their baseline CRPSG data, treatment data and clinical findings at the end of the study.

4.3 Technical Problems

Minor problems with recording hardware, software applications and incomplete questionnaires resulted in some missing data. Each measuring device connected to the patient is checked that it is producing a correct signal at the onset of the study as per standard methodology (Section 1.3, page 6). However, during the study as the patient sleeps and moves about some of the devices may become dislodged. These can be re-sited but care must be taken to minimise waking the patient and thus interfering with their sleep pattern.

Also in the clinical setting the devices used to measure respiratory events (snore, ventilation and respiratory movements) are not accurate devices, but rather qualitatively assess these signals over the duration of the night. It is the trend of the signals changing with time that determine if there are abnormalities present or not. To perform accurate measurements of ventilation and to determine the presence and type of apnoeas and hypopnoeas it is necessary to insert an oesophageal balloon into the upper airway. This is a very invasive method and not one used in the clinical setting of a Respiratory Sleep Disorders Unit.

The system hardware problems included an intermittent fault with the microphone used to detect snoring during (Cardiorespiratory Polysmnography) CRPSG recording. This was a very difficult problem to detect as the devices worked intermittently throughout several nights and it was only after many sleep studies had been analysed that the problem manifested itself. This affected eighteen patients in total and resulted in some missing data in twenty-three of the eighty-seven CRPSG studies recorded.

One CRPSG study with CPAP and one CRPSG study with APAP were not recorded correctly leaving twenty eight CRPSG with APAP and twenty eight CRPSG with CPAP studies to analyse, compared to twenty nine baseline CRPSG studies.

During the APAP leg of the trial, when usage was less than 50% of the time (in this case 5/29 patients) a software limitation prevented full compliance data download. A complaint about this software limitation was forwarded to the manufacturer and a upgraded version of the software became available, but unfortunately, it could not be used to recalculate previously recorded data.

High levels of artefact in 4/87 studies, during pulse oximetry monitoring while recording CRPSG studies, led to difficulty analysing these data. Artefact is a very common problem with oximeter probes during overnight recording of sleep, as patients will not lie still once they fall asleep and the bulky probe is liable to become dislodged. In an effort to correct this problem affecting all the patients (clinical and research) attending the sleep laboratory, the original probe was replaced with a new one. The SIMS BCI 3044 reusable sensor probe, in use at the start of the study, was replaced with a disposable sensor probe, a Nellcor Oximax Max A adult oxygen sensor probe. When both probes were placed on a pulse oxygen simulator (Smart Sats®, Clinical Dynamics Corporation, USA) differences in the region of 2-3% were found across the range. Although the new probe recorded overall higher values than the previous one, it was necessary to conclude the study using the original reusable probe. Note that the oximetry data presented here have not been altered to take this difference into account.

Blood pressure was not recorded on some visits, affecting eight patients and 10 out of the 87 studies. Subjective questionnaires were not completed fully by twenty-four of the twenty-nine patients. However, only 83 cells of 1711 cells of information on the questionnaires were missing and so this represents a very small percentage (<5%) of missing data.

4.4 Statistical Methods

In order to power a study, such as this one, the application of a statistically rigorous algorithm such as those described in the "Interpretation and Uses of Medical Statistics"[1] could be utilised. However, within the time constraints of this research project it was considered appropriate to target a relatively small group of about 30 subjects. Nevertheless, we must consider the possibility that a larger sample group might produce different results.

In all, two hundred and thirty individual variables were entered onto a spreadsheet. The statistical package used to record and analyse the data was SPSS (Statistical Package for Social Sciences), versions 9 and 11. The variables were grouped as shown in Table 4.1.

Table 4.1 Parameter Groupings in SPSS database

Quantitative sleep and respiratory assessment	105 variables
Qualitative sleep pattern assessment	59 variables
Treatment characteristics	55 variables
Characteristics of the patient group	20 variables

All numeric values are given as means ± standard deviation. The SPSS program excluded missing values when making calculations. As the study sample size was relatively small and the data was quantitative, non-parametric tests were chosen as the most suitable tests for evaluating the data in this study. Comparisons were made using the Wilcoxon matched pairs non-parametric test between the data from baseline lab night 1 and treatment lab nights 2, 3 and 4. This study was also a cross over type study, where data was collected before and after two different therapies (CPAP and APAP), therefore the patient groups were self-pairing or in other words, the patients acted as their own controls. As a result, where comparisons were made between the two treatment modes, CPAP and APAP, the independent *t* test was used to assess the significance of the

relationship. Statistical significance was taken at $p < 0.05$ level. The diary cards given to patients to complete each morning at home during both treatment legs of the study have proven too time-consuming to analyse at this stage and were not included in the final analysis.

4.5 Quality of Laboratory Sleep

The patients were allocated the same single bedroom on each night they stayed in the sleep laboratory, which helped them become familiar and comfortable with the lab environment. But to assess the affect of the lab environment on the sleep pattern we asked the patients to subjectively categorise each of their night's sleep. The reason for determining lab sleep quality was to ensure that any differences determined during either therapy mode (CPAP and APAP) were not subjected to influences outside of the actual treatment process. As mentioned previously adult sleep pattern varies from night to night and can be altered by many factors, even in normal subjects, so in this current study it was essential to ensure patients slept as close to their "normal" nights sleep as possible. In Fig 4.1 we find that less than a quarter of patients on any night felt that the sleep in the lab was not close to their normal sleep at home. More than 80% of the patients felt they had slept close or very close to their normal sleep at home when they were assessed in the sleep lab on lab night 1. When they were reassessed on lab night 3 and lab night 4 after completing leg 1 and leg 2 of treatment at home, more than 74% of the patients still felt that they had slept fairly close, even very close to their normal night's sleep at home. Therefore in the majority of this group the data obtained on each of the lab nights were a reasonable representation of their usual sleep pattern at home. Considering the amount of equipment attached to them and the fact that they were sleeping in a hospital bed and lab

environment these figures are reassuring about the quality of the sleep data obtained on the nights spent in the sleep laboratory

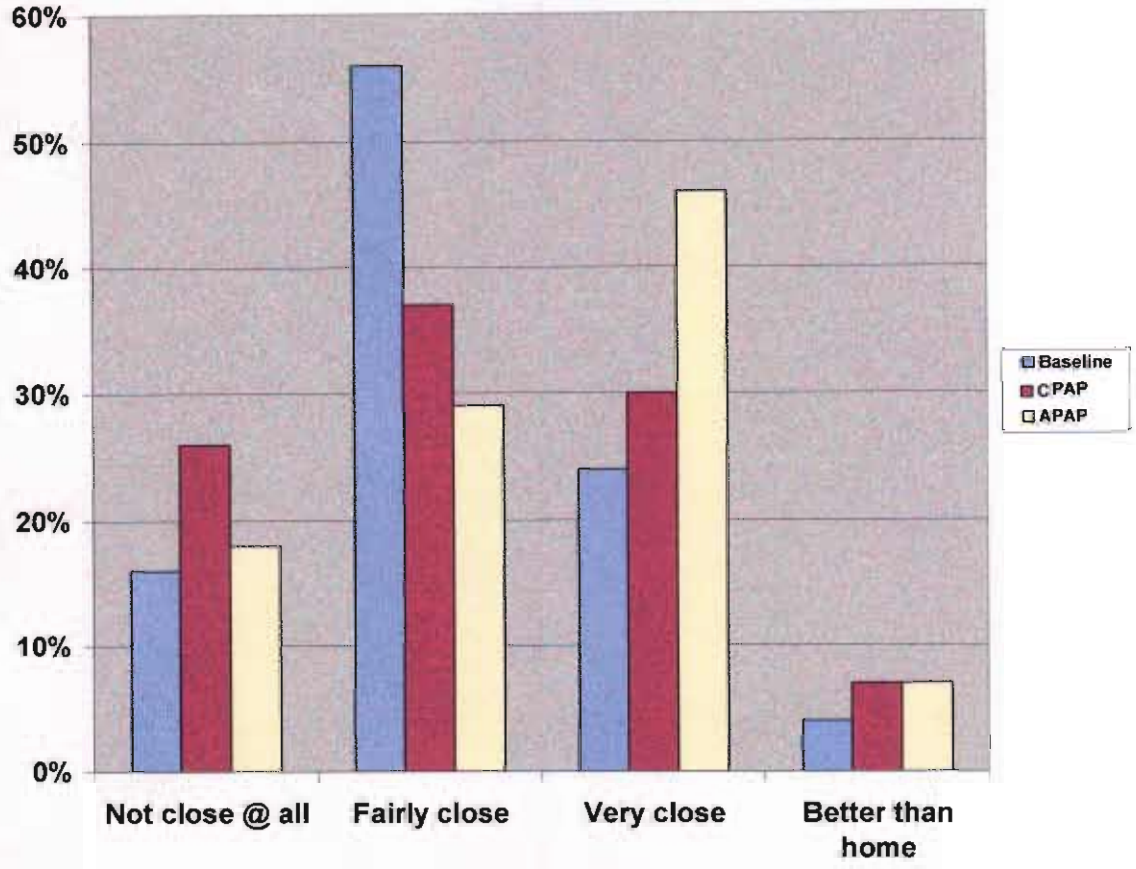

Figure 4.1 Perceived Quality of Sleep in the Laboratory

4.6 Group Characteristics

Table 4.2 shows the anthropometric, social and work characteristics of the group, presented as mean values ± standard deviations (SD). All the patients in this study were middle aged (40-60 years) and overweight (BMI 26-29 kg/m^2), with 55% (16/29) falling into the obese category, i.e. BMI > 30 kg/m^2. There was a male to female ratio of 8:1. The mean neck circumference of the group was 16 inches (42 cm), while the mean blood

pressure (BP) was within normal limits (<140/90mmHg). However, 14/29 (48%) of the patients were hypertensive based on either a systolic pressure of ≥140 mmHg or a diastolic pressure of ≥ 90 mmHg[2]. Four of these patients were already on hypertensive treatment and two more, who recorded normal blood pressure at baseline, were also taking regular medication for hypertension.

Table 4.2 Group Characteristics

Parameter	**Mean ± SD** (where applicable)
Sex	26 males / 3 females
Age	52.8 ± 8.3 years
BMI	29.9 ± 4.7 kg/m² (Healthy range 20 –25 kg/m²)
Neck Circumference	41.7 ± 2 cm
Blood Pressure	132 / 84 ± 23 / 13 mmHg
Alcohol	4 (14%) non drinkers, 25 (86%) drink 10 units/week
Cigarettes	19 (65%) non smokers, 10 (35%) smoke 18 cigarettes /day
Caffeine	6 ± 3 cups/day
Occupation	26 (90%) work, 3 (10%) retired/work in the home
Shift work	7 (24%) work shift hours, but not after midnight
Hours worked per week	46.9 ± 10.3 (total group) ***(48.5 ± 11.2 non- shift) (42.5 ± 5.9 shift)***

Twenty five (86%) of the group drank alcohol, but the amount per week on average (range 1-30 units), was well within the acceptable limits of < 14 units for females and < 21 units for males, except for one male patient who drank more than 21 units per week. 35% were smokers, which was slightly above the national average of 31% based on figures released from the Central Statistics Office (CSO) at the time of the trial[3]. The average number of cigarettes smoked per day was 18 (range 2 - 40 per day). The average amount of caffeine (tea, coffee or cola) consumed each day per patient was approximately 6 cups, although one subject drank twice this amount.

Twenty six (90%) of the patients worked outside the home, with (7/29) 24% of them doing some type of shift hours, although no one worked throughout the entire night. This number was higher than the estimated 11% of the Irish population who worked outside the traditional 9am – 5pm hours between March and May 2001 (CSO figures)[3]. The national average hours worked per week was 39.4 hours, (March-May 2001) whereas the patients in this study group worked a mean of 46.9 hours according to the data recorded at the baseline lab night 1. The mean hours worked per week by the patient group at the end of the study had fallen to 43.9 hours per week, but this was not significantly different to the baseline night value. However, overtime was not counted separately from normal working hours, as was done by the Central Statistics Office, in that the patient group were asked how many hours they worked in total each week, irrespective of overtime.

Table 4.3 Trend of Group Characteristics over 16 week trial period

Parameter	**Start of study** (mean ± SD)	**End of study** (mean ± SD)
BMI (kg/m²)	29.9 ± 4.7	30.4 ± 4.3
Blood Pressure (mmHg)	132 ± 23 / 84 ± 3	128 ± 18 / 84 ± 17
Alcohol units /week	10 ± 8	11 ± 7
Cigarettes per day	18 ± 11	22 ± 17
Caffeine cups per day	6 ± 3	6 ± 3
Non-shift workers hours/week	48.5 ± 11.2	44.1 ± 11.6
Shift workers hours/week	42.5 ± 5.9	43.6 ± 6.1

There was no significant change (Table 4.3) over the course of the study in BMI, blood pressure, units of alcohol, cigarettes or caffeine (tea, coffee or cola) consumed, or hours worked in this particular group of patients.

4.7 Blood Pressure Measurements

Six of the twenty-nine patients were on blood pressure (BP) treatment. As data were missing on some of the nights, only eighteen out of the twenty-three patients in the non-BP treatment group were included in this analysis (Table 4.4).

Table 4.4 Blood Pressure Measurements

BP Treatment	**Baseline Night** (mean ± SD)	**Last night Leg 1** (mean ± SD)	**Last night Leg 2** (mean ± SD)
Non-Treatment (n=18)	131 ± 22 / 84 ± 12	121 ± 14 / 82 ± 13	126 ± 86 / 86 ± 17
Treatment (n=6)	145 ± 28 / 81 ± 17	130 ± 30 / 78 ± 22	144 ± 22 / 78 ± 19

(values expressed in mmHg)

There was no significant difference in mean blood pressure between the treated and untreated groups on any of the three nights. Neither was there any significant change in blood pressure recorded over the course of the study between baseline and the last night, of leg 1 treatment (lab night 3) or baseline and the last night of leg 2 treatment (lab night 4) in either the treated or untreated groups.

4.8 Sleep Assessment

Several subjective and objective measurements were recorded to assess sleep and sleepiness during the course of the trial. Subjective measures were recorded using questionnaires, including the validated Epworth Sleepiness Scale (ESS)[4]. Objective measurements were made during the Cardiorespiratory Polysomnography (CRPSG) recording.

4.8.1 Daytime Sleepiness Assessment

We assessed the patient's perception of daytime sleepiness at baseline and after each eight-week leg of treatment. This information was obtained from the ESS questionnaire.

Table 4.5 presents the data obtained from the ESS over the course of the study. At baseline (lab night 1) a mean ESS value of 12.3 reflects a mild degree of sleepiness in this group (< 11 suggests mild or no sleepiness and > 18 implies significant degree of sleepiness)[4]. Both APAP and CPAP treatments had the effect of significantly reducing the degree of daytime sleepiness perceived by the patients, but there was no significant difference between the two modes of treatment.

Table 4.5 ESS at Baseline and after APAP and CPAP Therapy

Baseline Night (mean ± SD)	**APAP Therapy** (mean ± SD)	**CPAP Therapy** (mean ± SD)
12 ± 4	9 ± 4*	8 ± 5*

* p value = <0.001 between baseline + treatment therapies

4.8.2 Sleep Pattern – Subjective Assessment

Patients in this study were also asked questions relating to sleep pattern, including time of going to bed, time of getting up and estimated time spent asleep. This subjective information was obtained from the perception of sleep pattern section of an in-house sleep hygiene/lifestyle questionnaire (Appendix M). The questionnaires were completed on baseline (lab night 1), the last night of leg 1 treatment (lab night 3) and the last night of leg 2 treatment (lab night 4) in the sleep laboratory. Fig 4.2 shows the data obtained when the group was divided in three, those who were retired (n=3), those on shift work (n=7) and the non-shift workers (n=19).

The falling asleep time for shift workers ranged between 11.15pm and 01.30am and for non-shift workers and those retired it was between 10.30pm and 01.30am. The wake up time in the shift worker group ranged between 05.30 am and 9.30am and for non-shift workers and retired the time range was 04.30 am to 9.45am. On average, each group each night perceived that they slept for a little over seven hours per night. There was no

significant difference in the estimated number of hours asleep, or the falling asleep and waking up times between baseline night or during the APAP or CPAP treatment periods.

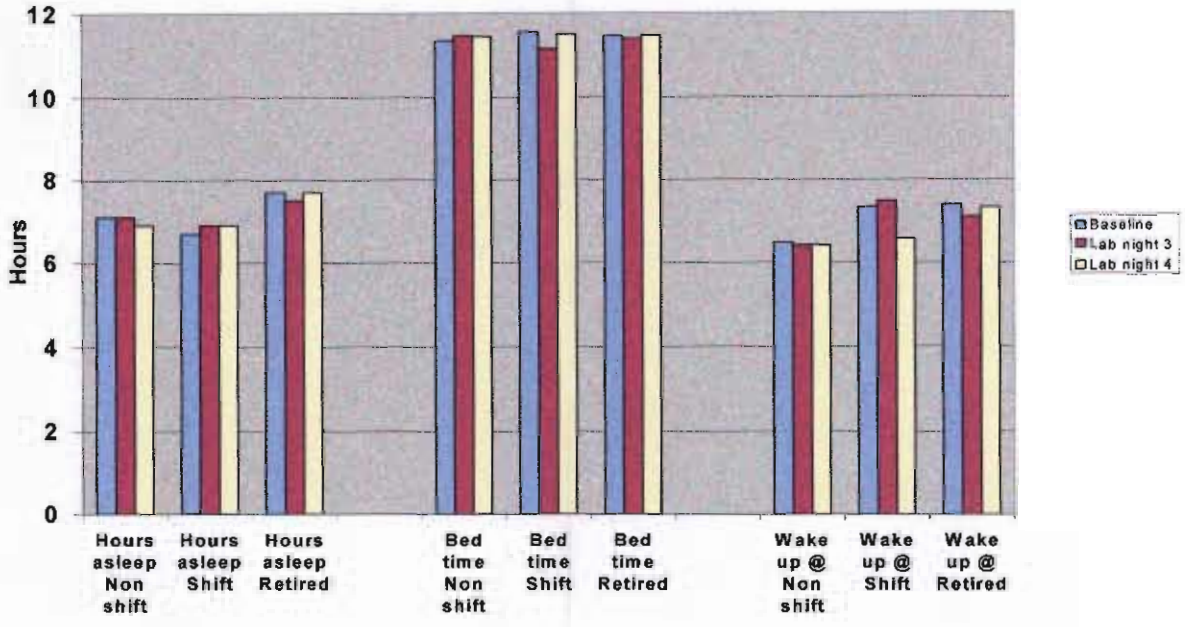

Figure 4.2 Sleep Pattern –Subjective Assessment

4.8.3 Sleep Quality – Objective Assessment

Tables 4.6 and 4.7 summarise the sleep quality data from the study population obtained on baseline night and both APAP and CPAP treatment nights. There was no difference in the Total Sleep Time (TST) recorded on the three nights. Sleep efficiency and sleep maintenance were statistically different between baseline and CPAP nights, but not between baseline and APAP nights. Sleep latency time was reduced significantly on both treatment nights when compared to baseline night, but there was only a significant difference in REM latency time on CPAP treatment nights.

Total NREM as a percentage of TST and Stage REM as a percentage of TST were not statistically different on any of the three nights. However, there was a significant reduction in the amount of Stage 1 and wake time after sleep onset on the two treatment nights compared to Baseline night.

Table 4.6 Sleep Quality Comparisons between Baseline and APAP Therapy

Parameter (n=28)*	**Baseline Night** (mean ± SD)	**APAP Therapy Night** (mean ± SD)	**p value**
Total Sleep Time (mins)	344 ± 49	335 ± 43	ns
Sleep Efficiency (%)	79 ± 9	83 ± 8	ns
Sleep Maintenance (%)	85 ± 7	87 ± 10	ns
Sleep Latency (mins)	30 ± 22	12 ± 7	**0.00**
REM Latency (mins)	106 ± 59	92 ± 40	ns
Stage 1 (% TST)	15 ± 6	12 ± 6	**0.02**
Stage SWS (%TST)	14 ± 8	15 ± 7	ns
Total NREM (% TST)	82 ± 5	82 ± 7	ns
Stage REM (% TST)	18 ± 5	17 ± 7	ns
Wake after sleep onset (mins)	64 ± 31	51 ± 27	**0.05**

Table 4.7 Sleep Quality Comparison between Baseline and CPAP therapy

Parameter (n=28)*	**Baseline Night** (mean ± SD)	**CPAP Therapy Night** (mean ± SD)	**p value**
Total Sleep Time (mins)	342 ± 49	349 ± 55	ns
Sleep efficiency (%)	79 ± 9	84 ± 10	**0.02**
Sleep Maintenance (%)	85 ± 7	89 ± 7	**0.00**
Sleep Latency (mins)	30 ± 22	15 ± 13.0	**0.00**
REM Latency (mins)	107 ± 59	84 ± 46	**0.02**
Stage 1 (% TST)	15 ± 6	15 ± 8	**0.03**
Stage SWS (% TST)	14 ± 8	15 ± 8	ns
Total NREM (%TST)	82 ± 5	80 ± 7	ns
Stage REM (% TST)	18 ± 5	20 ± 7	ns
Wake after sleep onset (mins)	63 ± 31	47 ± 31	**0.01**

(ns = not significant)

* Although 29 baseline PSG studies were recorded, only 28 studies with APAP and 28 studies with CPAP were recorded, therefore the baseline data is slightly different in Tables 4.6 and 4.7

4.8.4 Comparison of Study Group to "Normal" Adult Sleep

When we compared the study group to the 'normal' adult sleep pattern (refer to section 1.5, page 13) we found that the amount of NREM and REM sleep was reduced in the study group and that there was an increase in the amount of wakefulness after sleep onset too (Table 4.8). There was also an increase in the amount of Stage 1 sleep in the study group on all nights compared to the 'normal' adult range. Factors that may have affected the study group included their sleep disorder and the effect of sleeping in a laboratory environment. The sleep pattern and sleep quality of this particular group of patients was not significantly different to the 'normal' population, but APAP and CPAP treatments appeared to improve some aspects of sleep in this group when compared to the untreated baseline data (Fig 4.3).

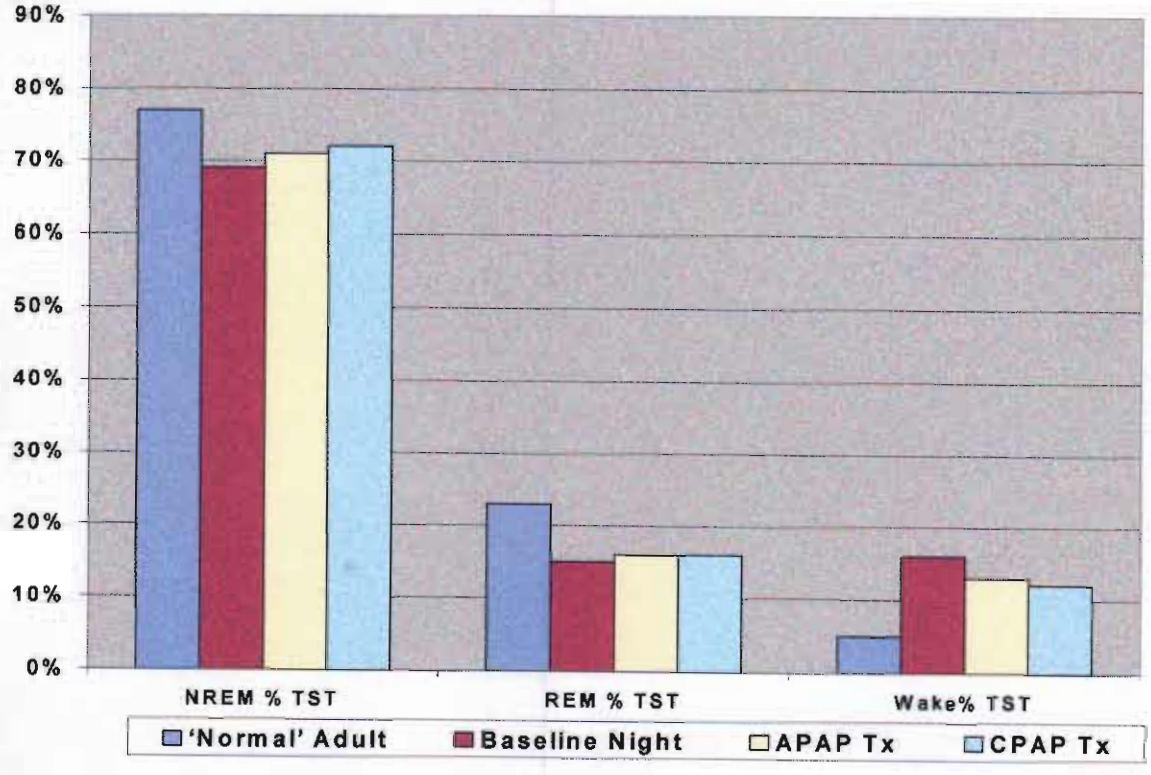

Fig 4.3 Comparison of Study Patients Sleep to "Normal" Adult Sleep

Table 4.8 Comparison of study group to "Normal" Adult Sleep

	"Normal" (mean ± SD)	Baseline night* (mean ± SD)	APAP night* (mean ± SD)	CPAP night* (mean ± SD)
NREM% TST	77	69	71	72
REM % TST	23	15	16	16
Wake % TST	5	16	13	12

* not significantly differently from "Normal"

4.8.5 Age Related Difficulties with Sleep

As mentioned earlier the ability to sleep decreases with age not the need to sleep. We saw this effect clearly in the current study group when we looked at the information, which displays the patient's subjective perception of difficulties either falling asleep or staying asleep (Fig 4.4). Note that the difficulty "falling asleep" improved with treatment, in particular with APAP therapy. But on the other hand, approximately half the patients experienced difficulty "staying asleep" on baseline (lab night 1) and this problem was not greatly improved on either APAP or CPAP treatment.

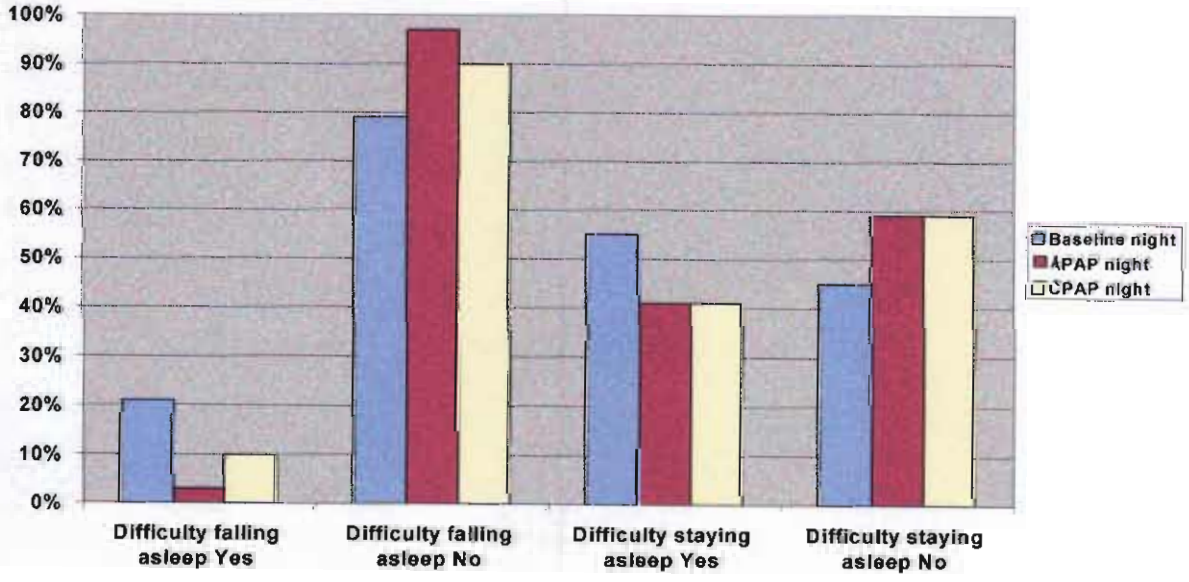

Fig 4.4 Difficulties Falling or Staying Asleep

We know that this particular group of patients consumed minor to moderate amounts of alcohol, nicotine and caffeine and that these factors therefore may have had only a small effect on sleep quality in general. This suggests that age may possibly be the major contributing factor affecting this group of patient's ability to stay asleep.

4.9 Respiratory Assessment during Sleep

Tables 4.9 and 4.10 summarise the respiratory events between the baseline and the two therapy assessment nights in the sleep laboratory. On the baseline night (lab night 1) we found that the mean AHI of 15 was at the cut off limit of ≥ 15 set for a moderate degree of OSAHS. The AHI is comprised predominantly of obstructive apnoeas and hypopnoeas (mean duration of both of less than twenty seconds on baseline night), as would be expected in this particular patient group. The mean total number of desaturations recorded was 87 with an average arterial blood oxygen saturation of 92% on the baseline night. All parameters with the exception of mean apnoea duration on both treatment nights were improved very significantly on either therapy when compared to baseline night values. However, there was no significant difference between the two treatment nights. APAP and CPAP treatment both had a similar effect therefore in reducing the number of respiratory abnormalities during sleep, resulting in fewer arterial blood oxygen desaturations and a higher overall mean oxygen saturation during the night.

Table 4.9 Respiratory Assessment between Baseline and APAP Therapy Nights

Parameter (n=28)*	**Baseline Night** (mean ± SD)	**APAP Night** (mean ± SD)	**p value**
AHI	15 ± 8	3 ± 2	**0.000**
Obstructive Apnoeas (Total)	39 ± 38	2 ± 2	**0.002**
Obstructive Hypopnoeas (Total)	59 ± 31	13 ± 12	**0.000**
Mean Apnoea Duration (sec)	19.1 ± 7.0	17.5 ± 5.2	ns
Mean Hypopnoea Duration (sec)	19.8 ± 3.8	14.6 ± 3.9	**0.000**
Total Number Desaturations	79 ± 48	15 ± 15	**0.000**
Mean Oxygen Saturation	92.0 ± 2.1	93.3 ± 1.7	**0.001**
Total Snore Events	326 ± 287	16 ± 11	**0.001**
Respiratory Arousals/hour	16 ± 14	2 ± 2	**0.000**

(ns=not significant)

Table 4.10 Respiratory Assessment between Baseline and CPAP Therapy Nights

Parameter (n=28)*	**Baseline Night** (mean ± SD)	**CPAP Night** (mean ± SD)	**p value**
AHI	15 ± 8	4 ± 4	**0.000**
Obstructive Apnoeas (Total)	23 ± 22	1 ± 1	**0.000**
Obstructive Hypopnoeas (Total)	54 ± 27	17 ± 16	**0.000**
Mean Apnoea Duration (sec)	19.1 ± 7.0	14.2 ± 3.8	ns
Mean Hypopnoea Duration (sec)	19.8 ± 3.8	15.2 ± 2.5	**0.000**
Total Number Desaturations	82 ± 45	15 ± 11	**0.000**
Mean Oxygen Saturation	92.0 ± 2.1	93.2 ± 1.8	**0.000**
Total Snore Events	313 ± 259	17 ± 16	**0.001**
Respiratory Arousals/hour	16 ± 14	4 ± 4	**0.000**

(ns = not significant)

* Although 29 baseline PSG studies were recorded, only 28 studies with APAP and 28 studies with CPAP were recorded, therefore the baseline data is slightly different in Tables 4.9 and 4.10

4.10 Problems with Treatment – Subjective Assessment

Side effects from the treatment were monitored subjectively (Fig 4.5) on each night in the laboratory when treatment was applied i.e. auto-titration night 2, APAP therapy and CPAP therapy nights. The first night positive airway pressure (PAP) treatment was applied, a third of patients expressed "major discomfort" with treatment, but this fell to 15% and 10% respectively on APAP and CPAP nights. The discomfort with treatment was categorised into mask problems, nasal problems (which included dry mouth, blocked or runny nose), device problems (pressure too high, air too cold and machine too noisy) and feelings of claustrophobia.

On night 2 auto titration night, 65% of patients complained of mask leaking, but this problem only affected 22% and 24% on APAP and CPAP nights respectively. The main reason for the reduction in mask leaking problems was probably due to the fact that patients had become competent with fitting the mask during the fifty-six days of treatment on each device. About 40% of patients across all nights complained of nasal problems, either blocked or runny nose or a dry mouth. This is a similar percentage to those found in other studies[5-7].

With regard to problems with the actual device, 20% of patients found the pressure too high on all nights, but cold air was only a problem on the first night when 21% of patients were affected. The noise of the machine was a problem for 15% of patients on the APAP night and 21% on the CPAP night, but this affected a much higher number of patients (45%) on lab night 2, when a clinical system was used in the laboratory. This was due in part to the patients acclimatising to treatment, but also due to the fact that the home therapy units (APAP and CPAP) are quieter than the clinical ones used in the sleep laboratory. Feelings of claustrophobia affected over a third of patients on the night 2, but this fell to 22% and 14% on the APAP and CPAP treatment nights respectively.

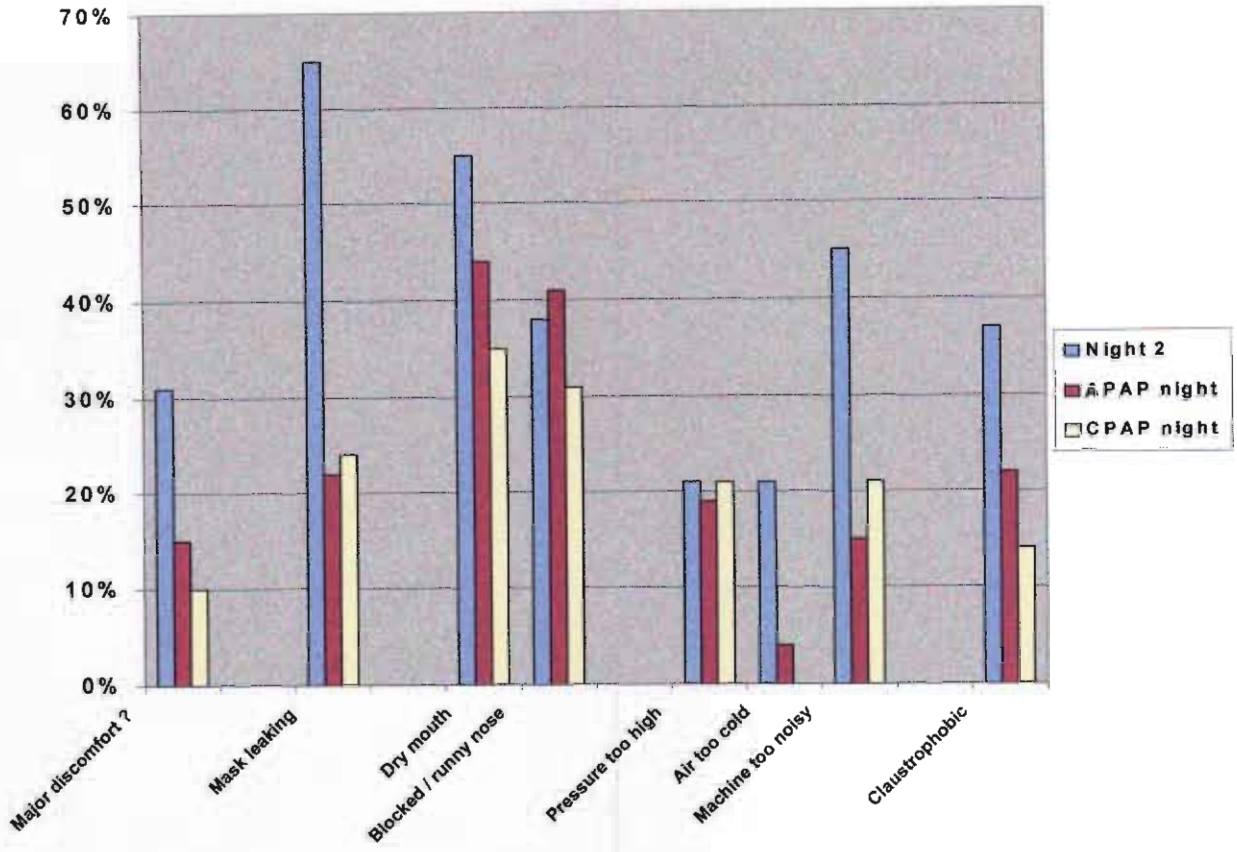

Fig 4.5 Problems with Treatment – Subjective Assessment

4.11 Patient and Partner Preference

At the end of the study patients and their partners were asked which machine they preferred. Fig 4.6 shows the breakdown of these preference results. There are a couple of important points about these data. Firstly, twenty-six out of twenty-nine patients and twenty-three out of twenty-seven partners expressed a definite preference. Secondly, out of the thirteen that preferred APAP, 85% of these had started APAP on the first leg and of the thirteen that choose CPAP, 77% had begun leg 1 on this device. Therefore there appears to be a strong order effect that influenced end preference. Of minor note, 10% (3) of patients liked either device and 17% (5) preferred the device they had used on the second leg of the study.

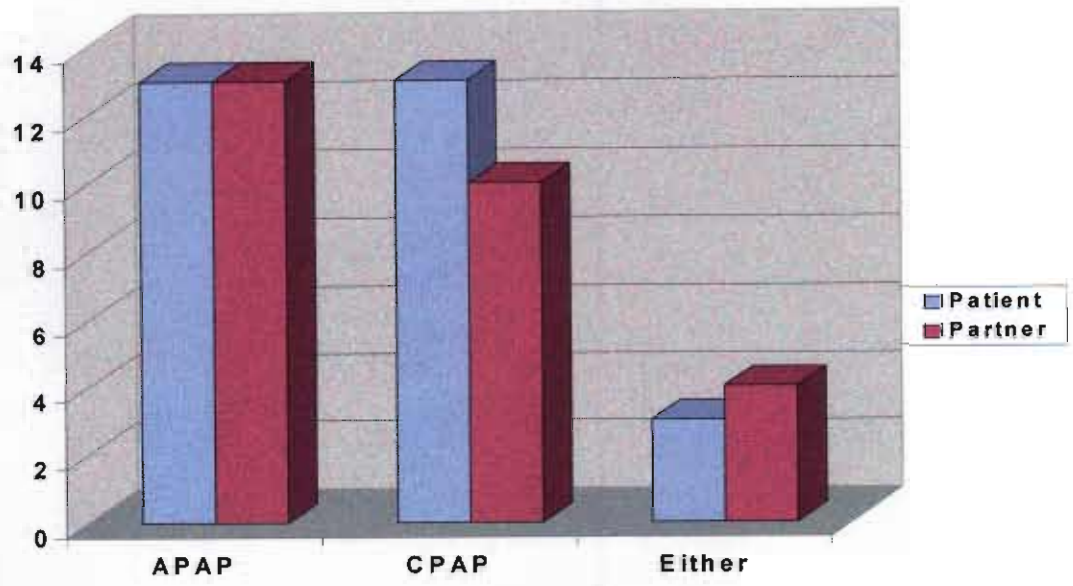

Fig 4.6 Patient and Partner Device Preference

4.12 Compliance Data

According to the Concise Oxford Dictionary the definition of compliance is " to act in accordance with wish". In medical terms compliance can be defined as "the consistency and accuracy with which a patient follows the regimen prescribed by a physician". As mentioned already, positive airway pressure treatment is only effective for as long as the nasal mask is worn and optimal pressure is being applied to the upper airway. Ideally we want patients to use the treatment every night (100% usage days) and all the time they are asleep (> 7 hours). However the minimum acceptable compliance data is 70% of nights and for at least four hours each night (median hours per night). Both the APAP and CPAP devices have built-in microprocessors, which record these parameters along with other information (Appendix M & N).

The whole group (Table 4.11) compares the usage and median hours for both devices in the total group of study patients. The results show that there was no significant difference

between the two treatments in terms of compliance. Also both devices were used for more than the minimum acceptable compliance time of more than 70% nights used and for more than 4 hours per night.

Table 4.11 Compliance data for Whole Group

Whole Group (n=29)	**APAP (n=29)** (mean ± SD)	**CPAP (n=29)** (mean ± SD)	**p value**
% Nights used	79 ± 29	81 ± 25	ns
Median hours per night	5 ± 2	5 ± 2	ns

(ns = not significant)

However, the study was a cross over trial and therefore each patient started with one device, which was randomly assigned to them, and then changed over to the second device half way through the trial. As a result each patient belongs to three of the following six subgroups. Group 1 (Table 4.12) started APAP on the first leg and then crossed over to CPAP and became Group 3. Group 2 (Table 4.12) started CPAP first and then crossed over to APAP and became Group 4. These four groupings are based on random assignment of therapy. Group 5 (Table 4.13) started and preferred APAP and Group 6 (Table 4.13) were those who started CPAP and preferred CPAP. These two groupings are based on end preference.

When we looked at the compliance data in first five groups (Groups 1-5), we found that both devices were used for more than 70% of nights and on average for more than four hours each night the machine was used. But the last group, Group 6, which was the group that used the APAP device on the second leg of the trial, but who actually preferred CPAP, did not use the APAP device for either the minimum acceptable % usage nights (>70%) nor the median hours per night (>4 hours/night). Group 5 on the other hand, those who used CPAP as their second device, but who started and preferred APAP, were

able to use both devices within acceptable limits, but they did use their preferred device significantly longer than the non-preferred one. In fact they used the APAP device (preferred) for the most nights (93%) and for the longest median hours (6 hours) of all the groups.

Table 4.12 Compliance Data for APAP + CPAP Based on Random Assignment

Group 1 + 4 APAP data*	**Group 1 (n=14)** (mean ± SD)	**Group 4 (n=15)** (mean ± SD)	**p value**
% Nights used	88 ± 18	70 ± 34	ns
Median hours per night	5 ± 2	5 ± 2	ns

Group 2 + 3 CPAP data**	**Group 2 (n=15)** (mean ± SD)	**Group 3 (n=14)** (mean ± SD)	**p value**
% Nights used	81 ± 26	81 ± 25	ns
Median hours per night	5 ± 2	5 ± 2	ns

Table 4.13 Compliance data for APAP and CPAP based on End Preference

Group 5 + 6 APAP data***	**Group 5 (n=13)** (mean ± SD)	**Group 6 (n=13)** (mean ± SD)	**p value**
% Nights used	93 ± 9	60 ± 33	**0.00**
Median hours per night	6 ± 1	4 ± 2	**0.01**

Group 5 + 6 CPAP data***	**Group 5 (n=13)** (mean ± SD)	**Group 6 (n=13)** (mean ± SD)	**p value**
% Nights used	87 ± 13	73 ± 33	ns
Median hours per night	5 ± 1	4 ± 2	ns

(ns = not significant)

*Group 1 started APAP first. Group 4 used APAP second leg

**Group 2 started CPAP first leg and Group 3 used CPAP on second leg

***Group 5 preferred APAP and Group 6 preferred CPAP

4.13 Baseline Comparisons between APAP and CPAP Groups

In order to determine if there were baseline characteristics that had an effect on end preference, the baseline data between the different subgroups were compared. Table 4.14 compares the baseline night data based on random assignment of treatments APAP (Groups 1+4) and CPAP (Groups 2+3).

Table 4.14 APAP v CPAP Baseline Data Comparison based on Random Assignment

Parameter	**Groups 1+4 (n=14) APAP** (mean ± SD)	**Groups 2+3 (n=15) CPAP** (mean ± SD)	**p value**
Sleep Architecture			
Sleep Efficiency (%)	81 ± 9	77 ± 8	ns
NREM (% TST)	82 ± 5	83 ± 6	ns
REM (%TST)	18 ± 5	17 ± 6	ns
Respiratory Pattern			
AHI	14 ± 7	15 ± 9	ns
Desaturation Index	14 ± 9	17 ± 10	ns
Mean Oxygen Saturation	92.3 ± 2.3	91.7 ± 2.0	ns
Pressure Requirements			
Fixed Pressure (CPAP)	9 ± 2	8 ± 2	ns
Mean Pressure (APAP)	7 ± 1	6 ± 2	ns
Anthropometric Data			
Age	52 ± 9	54 ± 7	ns
BMI	29.2±1.9	30.6±5.1	ns
Neck circumference	41.6±1.9	41.9±2.2	ns
Social Characteristics			
Caffeine per day	6 ± 2	6 ± 3	ns
Alcohol per week	9 ± 8	12 ± 9	ns
Cigarettes per day	16 ± 8	19 ± 13	ns
Hours worked per week	43 ± 15	44 ± 17	ns
Daytime Sleepiness			
ESS	13 ± 4	12 ± 4	ns

(ns = not significant)

Table 4.15 compares the baseline night data when end study preference for either APAP (Group 5) or CPAP (Group 6) therapy had been taken into account.

Table 4.15 APAP v CPAP Baseline Comparisons based on End Preference

Parameter	**Group 5 (n=13)** **APAP** (mean ± SD)	**Group 6 (n=13)** **CPAP** (mean ± SD)	**p value**
Sleep Architecture			
Sleep Efficiency (%)	83 ± 9	76 ± 9	ns
NREM (% TST)	82 ± 5	84 ± 5	ns
REM (%TST)	18 ± 5	16 ± 5	ns
Respiratory Pattern			
AHI	16 ± 7	14 ± 9	ns
Desaturation Index	16 ± 8	17 ± 11	ns
Mean Oxygen Saturation	92.1±2.4	91.7±2.0	ns
Pressure Requirements			
Fixed Pressure (CPAP)	9 ± 1	7 ± 1	**0.01**
Mean Pressure (APAP)	7 ± 1	6 ± 1	**0.04**
Anthropometric Data			
Age	52 ± 10	53 ± 7	ns
BMI	30.6±3.8	28.5±5.1	ns
Neck circumference	41.9±18	41.5±1.9	ns
Social Characteristics			
Caffeine per day	5 ± 3	7 ± 3	ns
Alcohol per week	8 ± 6	11 ± 10	ns
Cigarettes per day	16 ± 8	19 ± 13	ns
Hours worked per week	44 ± 18	47 ± 10	ns
Daytime Sleepiness			
ESS	13 ± 4	12 ± 4	ns

(ns = not significant)

There were no differences seen between the measures of disease severity (AHI), perception of daytime sleepiness (ESS), sleep architecture (REM, NREM and sleep

efficiency) or social and anthropometric characteristics in any of the six subgroups when their baseline night 1 data was compared between the two treatments (APAP and CPAP). Two parameters did show significant differences related to the fixed pressure and median pressure but only when end preference (Groups 5 + 6) was taken into account. The indirect post hoc inference therefore might be that end preference is related to fixed pressure requirements.

4.14 Further Subgroup Analysis

In order to tease out the effects on end preference, the whole group was subdivided in three ways. Firstly, the sub grouping was based on disease severity using the AHI, according to AHI < 15 and AHI ≥ 15 (Table 4.16). Secondly, a subdivision, based on perception of sleepiness using the ESS limits of < 12 and ≥ 12 (Table 4.17) was used. In the third case, the groups were divided based on fixed pressure requirements, into < 8 cm H_20 and ≥ 8 cm H_2O (Table 4.18).

In the subgroup divided by AHI (< 15 and ≥ 15) there was only a significant difference between the AHI as expected. Preference for APAP and CPAP was similar in this subgroup.

When the group was subdivided by ESS, there was only a significant difference between ESS and age. There was no significant difference between the end preference and the ESS.

In the final subgroup based on fixed pressure requirements < 8 or ≥ 8 cm H_20, the variables of fixed pressure, median pressure, BMI and neck circumference were significantly different between the two groups. End preference also displayed significant difference, in that a higher proportion of those requiring ≥ 8 cm H_2O fixed pressure

preferred APAP and an significantly higher number of those requiring < 8cm H_20 preferred CPAP.

Table 4.16 Comparison of Baseline data based on Subgroup of AHI

Parameter	**AHI < 15 (n=14)** (mean ± SD)	**AHI ≥ 15 (n=14)** (mean ± SD)	**p value**
AHI	8 ± 4	22 ± 5	**0.000**
ESS	13 ± 4	11 ± 4	ns
Sleep Efficiency	81 ± 7	77 ± 10	ns
Desaturation Index	13 ± 9	18 ± 9	ns
Fixed Pressure CPAP	8 ± 2	8 ± 2	ns
Median Pressure APAP	6 ± 2	6 ± 1	ns
Age	55 ± 7	51 ± 9	ns
BMI	29.7±5.0	30.2±4.7	ns
Neck circumference	41.4±2.4	42.1±1.4	ns
Preferred APAP	6/13	7/13	ns
Preferred CPAP	7/13	6/13	ns

Table 4.17 Comparison of Baseline data based on ESS score

Parameter	**ESS < 12 (n=11)** (mean ± SD)	**ESS ≥ 12 (n=18)** (mean ± SD)	**p value**
AHI	16 ± 10	14 ± 7	ns
ESS	8 ± 2	15 ± 3	**0.002**
Sleep Efficiency	76 ± 10	81 ± 8	ns
Desaturation Index	18 ± 10	14 ± 9	ns
Fixed Pressure CPAP	8 ± 2	8 ± 2	ns
Median Pressure APAP	7 ± 1	6 ± 1	ns
Age	48 ± 8	56 ± 8	**0.15**
BMI	31.0 ±6.0	29.2±3.8	ns
Neck circumference	42.5±2.1	41.3±1.8	ns
Preferred APAP	2/9	11/17	ns
Preferred CPAP	7/9	6/17	ns

(ns = not significant)

Table 4.18 Comparison of Baseline data based on Fixed Pressure requirements

Parameter	< 8 cm H_2O (n=10) (mean ± SD)	≥ 8 cm H_2O (n=19) (mean ± SD)	p value
AHI	11 ± 8	17 ± 8	ns
ESS	11 ± 4	13 ± 4	ns
Sleep Efficiency	78 ± 7	80 ± 10	ns
Desaturation Index	11 ± 10	18 ± 8	ns
Fixed Pressure CPAP	6 ± 1	9 ± 1	**0.000**
Median Pressure APAP	5 ± 1	7 ± 1	**0.000**
Age	54 ± 8	52 ± 9	ns
BMI	26.5±4.2	31.7±4.0	**0.003**
Neck circumference	40.6±1.7	42.3±1.9	**0.02**
Preferred APAP	1/8	12/18	**0.03**
Preferred CPAP	7/8	6/18	**0.03**

(ns = not significant)

4.15 Follow up Questionnaire Survey

A short questionnaire was sent out to the twenty-nine patients eighteen months after this study was completed.

Table 4.19 Follow-up Questionnaire Survey

Question	Answer
Still on PAP treatment?	22/29 (76%)
Number APAP / CPAP in use	13/14 (APAP) 9/12 (CPAP)
Mean estimated nights used	99%
Mean estimated hours/night used	6.7 hrs/night
Problems with treatment?	52% (yes)
What types of problems?	50% nasal only, 25% mask leaking only, 9% machine noise, 16% more than one side effect
Mean Epworth Sleepiness Scale	6 ± 3 (baseline untreated value 12 ± 4)

From the results of the questionnaire we can see that more than three-quarters of the patients remained on positive airway treatment and that there were more patients on APAP therapy than on CPAP therapy, but this difference is not significant. Compliance figures were excellent, but these data were based on the patient's estimated subjective values rather than the objective machine data. Treatment appeared very effective as the mean Epworth Sleepiness Score (ESS) value remained within the normal limits (<11), which was significantly less than the original baseline (pre treated) value. However, more than half the patients still complained of some side effects with the treatment, in particular, nasal problems. This study compliments the findings of many previously published studies in that a significant number of patients will remain on effective treatment even in the presence of ongoing side effects. All the patients in this study continue to be followed up regularly in the out-patients clinic.

4.16 References

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5. DISCUSSION

5.1 Introduction

Although the relationship between breathing and sleep has only been "discovered" by the medical community, excellent literary descriptions of what we know to be the sleep apnoea syndrome were made long ago. The most important literary contributions in this area were by Charles Dickens. His description of Joe, the fat boy in the Pickwick Papers, about 140 years ago, is an example of his brilliant skills of observation and description. Respiratory failure in sleep, because of "failure of the chest and diaphragmatic movements" was defined as a specific sleep disorder by Silas Weir Mitchell in 1890. However, the two main reasons for overlooking the sleep apnoea syndrome for so long have been the misdiagnosis of patients with sleep apnoea as having narcolepsy and the scepticism regarding the validity of excessive daytime sleepiness as a clinical sign[1].

We now know that OSAHS is the most organic sleep disorder resulting in excessive daytime sleepiness. It is estimated to occur in 1 out of 20 adults and it is usually unrecognised, undiagnosed and results in behavioural and cardiovascular morbidity[2]. Studies have shown that OSAHS is associated with upper body obesity[3], age[4], alcohol consumption[5] and smoking[6] and that such individuals are sleepy[7], likely to take less exercise and drink about three times more caffeine than non OSAHS patients[8]. Also, most importantly, although mild and seemingly asymptomatic OSAHS occurs in only 20% of all patients with this condition, a small increase in the average blood pressure, cardiovascular disease incidence or attributable behavioural morbidity, even in this group, could lower the overall well being of a population. The impact therefore, with regard to this disease, from a public health standpoint is profound, in particular in relation to sleepy drivers and road traffic accidents.

5.2 Anthropometric and Social Data

The patients studied in this trial were comprised predominantly of middle aged, over-weight, hypertensive males, diagnosed with mild to moderate OSAHS, according to their apnoea hypopnoea index (AHI), which ranged between 5 and 30 events per hour of sleep. Six other studies[9-14] (Table 5.1) that looked at a similar patient population had comparable anthropometric data. In these studies, average ages ranged between 48-57 years compared to the 53 years in the current group. The mean body mass index (BMI) values ranged from 29–33.4 kg/m^2 versus the mean 29.9 kg/m^2 in the present patient group. Differences noted however, between the current and previous studies, included the fact that the other groups had a higher proportion of females 14-48% compared to only 10% in this present group. Also Engleman *et al*[10,11] set inclusion limits for the AHI of 5-15 and Monasterio *et al*[12] 10-30. Only Barnes[9], Randerath[13] and Redline *et al*[14] included patients with AHIs in the 5-30 range, as was used for the current study population. The mean AHI in these latter three studies[9,13,14] ranged from 13-18 per hour of sleep compared to 15 in the present group. However, in summary, for the above parameters of age, AHI, etc. this study is directly comparable with those cited[9-14].

The relationship between weight and OSAHS has been established. In one population-based observational study[15], six hundred and ninety men and women were examined over a four-year period. Based on logistic regression modelling, the authors suggested that a 10% weight gain increased six-fold the odds of developing moderate or worse OSAHS (i.e. AHI $\geq$ 15). That study also indicated that in persons with an existing degree of OSAHS, there was an approximate 3% increase (decrease) in the AHI expected for each 1% increase (decrease) in body weight after adjusting for sex, age and cigarette smoking. During the 17 weeks of this current trial there was no significant increase or decrease in the mean BMI of the group, so it was expected that the positive air pressure treatment

needs would not vary over the course of the study period due to changes in body weight. It should be noted that all patients attending the Respiratory Sleep Disorders Unit in St Vincent's University Hospital are strongly encouraged to reduce their weight and advised that weight reduction could improve their chances of not requiring life-long positive airway pressure therapy.

Table 5.1 Antrophmetric data in 7 studies of mild to moderate OSAHS patients
Age in years, Body mass index in kg/m^2 (BMI), Apnoeas & hypopnoeas per hour of sleep (AHI), Epworth Sleepiness Scale 0-24 (ESS), M/F = % Males & females in study population

	AGE	BMI	AHI	ESS	M/F%
Engleman *et al*[10] 1997 (n=16)	52±2	29.8±1	11±1	14±1	75/25
Redline *et al*[14] 1998 (n=97)	48±10	33.4±7	13±10	10±4	52/48
Engleman *et al*[11] 1999 (n=34)	44±8	30±5	10±3	13±3	62/38
Monasterio *et al*[12] 2001 (n=125)	54±9	29±4	20±6	12 ±4	86/14
Barnes *et al*[9] 2002 (n=42)	*	*	13±6	11±5	83/17
Randerath *et al*[13] 2002 (n=20)	57±10	31.2±6.4	18±8	*	80/20
Present Study 2004 (n=29)	53±8	29.9±4.7	15±8	12±4	90/10

*Data not available

Most [16-20] but not all[21,22] studies, in which defined quantities of alcohol were administered to healthy subjects or patients with OSAHS before bedtime, have demonstrated harmful effects on nocturnal respiration, including increased number and duration of hypopnoea and apnoea events. Five of the patients in this present study group consumed more than seventeen units (mean 24) of alcohol per week but this subgroup (n=6) did not have a significantly higher mean AHI (12 versus 16) or Epworth Sleepiness Scale (13 versus 12) than the rest of the group (n=23). The AHI values on both APAP and CPAP treatments in

these two subgroups groups did not differ significantly either, APAP, 3 (n=6) versus 3 (n=23) or CPAP, 6 (n=6) versus 3 (n=23).

5.3 Hypertension and Blood Pressure Data

Hypertension affects 20% of the overall adult population[23]. It is a major risk factor for the development of coronary artery disease, congestive heart failure and strokes.

OSAHS clearly causes night time rises in arterial blood pressure[24], because it is associated with chronic abnormalities of cardiovascular autonomic regulation, characterised by heart rate and blood pressure variability. The transition from wakefulness to non REM sleep is accompanied by marked alterations in respiratory and cardiovascular regulation. Heart rate, blood pressure, cardiac output, and systemic vascular resistance all decrease. However, surges in heart rate and blood pressure occur 5-7 seconds after apnoea termination, coincident with arousal from sleep. These repetitive surges counteract the usual fall in heart rate and blood pressure that accompany normal sleep and are thought to contribute to the adverse cardiovascular consequences of OSA. Also caffeine has been shown to have significant acute effects on blood pressure[25,26] (refer to section 1.5.1).

Methodologically rigorous population-based studies have yielded convincing evidence in favour of a modest but definite association between OSAHS and systemic hypertension, independent of age, obesity or other confounding factors[27-29]. For example Fletcher *et al*[30] found 30% of hypertensive subjects with an AHI ≥ 10 per hour and Worsnop *et al*[31] found 38% of hypertensive patients with an AHI > 5 compared to only 9% and 4% in normotensive subjects respectively. OSAHS is also more likely to be an independent risk factor for hypertension in younger (< 60 years) patients[32,33]

In a recent study by Peppard *et al*[34] patients with AHI in the range of 5-15 (n=132) had a mean blood pressure (BP) of 130/84 mmHg and those with AHI > 15 (n=67) had a mean BP of 135/88 mmHg. The prevalence rates in these two subgroups for hypertension was 48% and 60% respectively. Comparing the blood pressure and prevalence rates of this previous study to the current study group, six patients (20%) were already on hypertensive medications and another ten (34%) had either systolic BP >140 mmHg or diastolic BP > 90 mmHg. Therefore a prevalence rate of 55% for hypertension was found in the mild to moderate patient population of the current study. However, although the mean blood pressure appeared higher at baseline in the present study for the treated group (145 ± 81) compared to the non treated group (131 ± 84), neither group showed any significant improvement in blood pressure over the course of the sixteen weeks of positive airway treatment.

In summary, it appears that the obstructive sleep apnoea hypopnoea syndrome is a significant independent risk factor for daytime hypertension, with up to 50% of OSAHS patients hypertensive and even those at the lower end of the severity spectrum not exempt from this increased risk.

5.4 Sleep Quality

Patients with OSAHS have a typical disturbed sleep architecture with increased number of arousals and increased proportion of the NREM Stages 1 + 2 and depressed Stages 3 and 4 (SWS) and REM sleep as well.

In general the literature supports the idea that the improvement in sleep quality with APAP and CPAP is similar. Seventeen[35-51] randomised controlled trials comparing APAP and CPAP resulted in equivalent sleep quality, i.e. reduction in arousal index and increase in SWS and REM sleep. In Table 5.2, a sample of data from several of these

sixteen trials are listed and we can see for example, that d'Ortho[37], Ficker[38], Sharma[40] and Scarf *et al*[41] all found significant increases in SWS and REM when both APAP and CPAP were compared to a non-treatment diagnostic night. But no appreciable differences were demonstrated between the two modes of treatment. Respiratory arousals and awakenings per hour were also equally significantly reduced from baseline on both APAP and CPAP treatment. Only Konnerman *et al*[42] found APAP improved SWS more than CPAP, but this was a parallel trial not a cross-over one.

However, these previous studies included patients with severe OSAHS, and therefore some patients would have had more sleep disturbance, leading to a greater reduction in overall sleep quality at baseline assessment compared to this group which included those with mild to moderate OSAHS only. So, in contrast to the studies above there was no significant improvement in SWS or REM sleep between baseline and either of the two treatment modes in the group of patients studied in this current trial. Both treatments did however lead to an increase in sleep latency time and a reduction in Stage 1 as a percentage of total sleep time (% TST) as well as a reduction in the amount of time awake after sleep onset. In addition, patients on the CPAP leg of treatment also had a significant improvement in sleep efficiency, sleep maintenance and REM latency from their baseline untreated values.

Only one previous study to date has compared sleep quality between baseline and treatments (CPAP v mandibular advancement device) in a mild to moderate category of patients. This study by Randerath *et al*[13] did not demonstrate any significant difference between baseline and CPAP treatment for either SWS or REM, but did show a significant reduction in Stage 1 as a percentage of Total Sleep Time, snore events and respiratory arousals per hour. It would appear therefore that the results of the current trial are in close agreement with a similar patient population studied previously.

Table 5. 2 Sleep Quality data in 9 studies comparing APAP and CPAP Therapies
Stage 1 as % total sleep time (ST1 % TST), Stage 3+4 as % total sleep time (SWS % TST), Rem sleep as % total sleep time (REM % TST), Wake after sleep onset in minutes (WASO), (B=baseline, C=CPAP, A=APAP)

		ST1%TST	SWS%TST	REM%TST	WASO
Sharma *et al*[40]	B	**9.7±8.1**	**9.1±8.5**	**17.8±8.1**	*
1996 (n=20)	C	**6.2±5.8**	**16.7±9.8**	**22.7±7.9**	
	A	**6.1±4.**	**17.1±9.3**	**25.3±7.4**	*
Scarf *et al*[41]	B	*	*	*	*
1996 (n=12)	C	**5.4±2.7**	**4.6±6.0**	**22.6±8.0**	**8.0±10.0**
	A	**6.7±2.9**	**8.6±7.5**	**23.5±6.0**	**11.7±22.3**
Ficker *et al*[38]	B	*	**13.0±3.8**	**13.9±6.4**	*
1998 (n=16)	C	*	**16.8±7.1**	**17.0±8.3**	*
	A	*	**20.7±11.9**	**18.1±5.5**	*
Konnerman *et al*[42]	B	*	**11.4±10.4/13.2±12.2**	**5.4±6.0/8.2±8.1**	*
1998 (n=50)**	C	*	**17.6±18.4**	**10.2±7.7**	*
	A	*	**27.2±16.5**	**20.1±10.0**	*
Boudewyns *et al*[49]	B	*	*	**9.0**	*
1999 (n=15)	C	*	*	**24.2**	*
	A	*	*	**20.5**	*
d'Ortho *et al*[37]	B	**9.9**	**11.7**	**16±5**	*
2000 (n=25)	C	**5.6**	**25.7**	**22±5**	*
	A	**8.6**	**23.5**	**21±8**	*
Randerath *et al*[48]	B	**18.2±11.2**	**16.3±13.9**	**14.2±6.7**	**50.9±42.8**
2001 (n=25	C	**14.3±7.6**	**19.0±11.0**	**17.1±7.4**	**53.6±37.1**
	A	**12.5±5.2**	**21.6±10.9**	**20.3±7.3**	**60.2±39.9**
Randerath *et al*[13]	B	**15.2±9.5**	**14.2±10.6**	**15.1±5.9**	**35.9±26.4**
2002 (n=20)***	C	**12±7.2**	**16.2±9.1**	**15.3±6.8**	**39.4±24.9**
Present Study	B	**15.1±5.7**	**13.7±8.0**	**17.6±5.1**	**63.5±30.3**
2004 (n=29)	C	**14.7±8.4**	**14.7±8.4**	**19.6±6.8**	**47.1±30.5**
	A	**12.4±6.0**	**15.0±7.4**	**17.1±7.3**	**51.0±26.7**

*Data not available ** Parallel trial ***Comparison of CPAP and Mandibular advancement device (MAD)

5.4.1 Cognitive Function

Over the past 20 years it has become increasingly evident that sleep plays an important role in the efficiency of memory consolidation. Cognitive procedural tasks are vulnerable to REM sleep deprivation, while simple motor skill tasks are vulnerable to Stage 2 loss or interruption[52]. If sleep is interrupted, even by a brief EEG arousal, then the benefit of the period of sleep immediately prior to the arousal is lost. This notion is stated explicitly by Bonnet[53,54] as the sleep continuity hypothesis to explain the effects of sleep fragmentation on daytime function. Studies suggest that segments of sleep must be at least 10 minutes in duration to be restorative[55,56] but this view remains controversial. Other authors[57] suggest that an increase in daytime sleepiness following nights of sleep fragmentation is due to changes in total sleep time (TST) and or changes in sleep architecture, increased Stage 1 and reduced SWS and REM sleep. They point out that Stage 1 sleep may not be as restorative as other sleep stages and that an increase in Stage 1 and a reduction in total sleep time can lead to significant sleep debt, therefore increased daytime sleepiness can be explained as a consequence of partial sleep deprivation. Either way, what is clear from the literature is that fragmented sleep is less restorative than consolidated sleep and leads to sleepiness related daytime functional impairment.

The subjects in this current study of mild to moderate sufferers stated that they did feel less sleepy on positive airway treatment. They demonstrated a significant reduction in Stage 1 sleep and in the arousal/awakening index, but with no significant increase in SWS or REM sleep on either treatment leg when these studies were compared to the baseline untreated ones.

5.4.2 Subjective Sleepiness – Epworth Sleepiness Scale

Another method of assessing the effectiveness of positive airway treatment is to determine if subjective daytime sleepiness measures improved after treatment. The Epworth Sleepiness Scale (ESS) data from the current study group showed a significant reduction from the baseline pre-treated values of 12 (0-24), to 9 and 8 on APAP and CPAP respectively. This means baseline value was similar to values obtained by other groups[9-14] (range 10 –14) for patients with mild to moderate OSAHS (Table 5.1).

Table 5.3 Epworth Sleepiness Scores from 9 Studies Comparing CPAP and APAP Therapies

Epworth Sleepiness Scale 0-24, < 11 implies mild /no sleepiness, > 18 implies severe daytime sleepiness

	Baseline	APAP	CPAP
Meurice *et al*[50] 1996 (n=16)**	15 ± 4 / 14 ± 6	6 ± 4	9 ± 7
Ficker *et al*[38] 1998 (n=16)	14 ± 4	5 ± 4	7 ± 4
Boudewyns *et al*[49] 1999 (n=15)	6	4	4
d'Ortho *et al*[37] 2000 (n=25)	13 ± 5	9 ± 6	9 ± 5
Hudgel *et al*[43] 2000 (n=33)	16 ± 1	9 ± 1	8 ± 1
Senn *et al*[47] 2003 (n=29)	14 ± 1	9 ± 1	8 ± 1
Massie *et al*[45] 2003 (n=44)	*	8 ± 4	9 ± 4
Planès *et al*[51] 2003 (n=35)**	15 ± 4 / 16 ± 5	8 ± 3	8 ± 3
Present Study 2004 (n=29)	12 ± 4	9 ± 4	8 ± 5

*Data not available ** Parallel trial

The authors in those studies[9-14] also demonstrated the same significant decrease in ESS from baseline on both APAP and CPAP therapy, but with no difference in results between either mode of treatment. In addition other groups[37,38,43,45,47,49-51] have also demonstrated that different types of positive airway treatments do significantly improve daytime sleepiness in all categories of patients (Table 5.3). Only Boudewyns *et al*[49] failed to demonstrate a significant reduction in ESS after APAP treatment, but patients had been on nasal CPAP therapy for one year prior to the study and their baseline ESS of 6 was well within the normal range anyway.

5.5 Respiratory Data

In all studies to date[13,36-38,40,41,45,48-51] where respiratory data are compared between APAP and CPAP therapy there has been a consistent and significant difference between the baseline and treatment data values, but the treatments have not differed significantly from each other in any trial (Table 5.4). All studies have shown clearly that both treatments will reduce the AHI to normal levels (i.e. < 5 per hour), with the exception of d'Ortho[37] and Massie *et al*[45]. In both these studies the mean AHI did drop significantly from a baseline (in the case of d'Ortho 58, not available for Massie) to between 9 - 11 events per hour on either APAP or CPAP treatment. Similar significant differences were found between baseline and treatment AHI values in the current study group. The mean AHI baseline value was 15 per hour of sleep, which was reduced to 3 and 4 on APAP and CPAP therapy respectively.

Similarly, the data for arousals/awakenings in studies[13,36-38,40,41,45,48-51] that present these data, have all shown a significant difference between both treatments and non-treated values, but no significant difference between the modes of treatment (Table 5.4). For example Meurice *et al*[50] demonstrated that a mean baseline arousal index of 36 arousals

per hour reduced to 9/hour and 10/hour on CPAP and APAP respectively. Likewise in a recent study by Planés *et al*[51] in a multicenter prospective trial, the arousal index fell significantly from 49 arousals per hour at baseline to 15/hour on CPAP and 14/hour on APAP, but there was no significant difference demonstrated between the modes. Randerath *et al*[48] showed that the respiratory arousal index was significantly reduced on APAP (4/hour) and CPAP (5/hour) compared to the baseline value of 18 respiratory arousals per hour. The results from the current study follow the same pattern, with a mean respiratory arousal index at baseline of 16/hour, which fell significantly on treatment to 2/hour on APAP and 4/hour on CPAP. However neither treatment was more effective than the other in reducing this index.

Snoring is a major night-time symptom of OSAHS, which mostly affects the bed partner rather than the patient. Snoring can be recorded during a CRPSG study. The total number of snores or the number of epochs of snoring per hour can be calculated. Snoring data is presented in Table 5.4. Comparing the studies of Behbehani[36] and Randerath *et al*[48], we see that they demonstrated a significant reduction in the amount of snoring on either treatment, but that there was no difference between the modes of treatment. For example in the study by Randerath *et al*[48] the mean baseline of 35 epochs/hour of snoring was reduced to 4 epochs/hour on both APAP and CPAP treatments. Similarly, in the current study group of mild to moderate patients the mean number of epochs of snoring per hour at baseline was 61 epochs/hour, which reduced significantly to 4 on APAP and 3 on CPAP therapies.

Table 5.4 Respiratory data in 12 studies comparing APAP and CPAP Therapies
Apnoea hypopnoea index per hour of sleep (AHI), Epochs of snoring per hour of sleep (Snore), Respiratory arousal index per hour of sleep (Resp/Ar), Arousal Index (AR/In) (B=baseline, C=CPAP, A=APAP)

		AHI	SNORE	RESP/AR	AR/In
Meurice *et al*[50]	B	**41± 18 / 47 ± 22**	*	*	**36 ± 16 / 36 ± 17**
1996 (n=16)**	C	**3 ± 3**	*	*	**10 ± 3**
	A	**2 ± 1**	*	*	**9 ± 3**
Sharma *et al*[40]	B	**51 ± 29**	*	*	**34 ± 23**
1996 (n=20)	C	**4 ± 3**	*	*	**11 ± 5**
	A	**6 ± 5**	*	*	**11 ± 1**
Scarf *et al*[41]	B	**57 ± 31**	*	*	*
1996 (n=12)	C	**1 ± 1**	*	**2 ± 1**	*
	A	**1 ± 2**	*	**1 ± 2**	*
Ficker *et al*[38]	B	**54 ± 24**	*	*	**48 ± 20**
1998 (n=16)	C	**4 ± 4**	*	*	**2 ± 3**
	A	**4 ± 5**	*	*	**3 ± 5**
Behbehani *et al*[36]	B	**55 ± 34**	**22 ± 30**	*	*
1998 (n=31)	C	**4 ± 4**	**12 ± 28**	*	*
	A	**5 ± 5**	**9 ± 14**	*	*
Boudewyns *et al*[49]	B	**66**	**28**	*	**27**
1999 (n=15)	C	**2**	**4**	*	**9**
	A	**3**	**4**	*	**10**
d'Ortho *et al*[37]	B	**58 ± 6**	*	*	**46 ± 26**
2000 (n=25)	C	**10 ± 2**	*	*	**14 ± 8**
	A	**11 ± 9**	*	*	**16 ± 9**
Randerath *et al*[48]	B	**32 ± 18**	**35 ± 37**	**18 ± 16**	**29 ± 9**
2001 (n=25	C	**7 ± 9**	**4 ± 7**	**5 ± 8**	**18 ± 10**
	A	**6 ± 4**	**4 ± 6**	**4 ± 4**	**17 ± 9**
Randerath *et al*[13]	B	**18 ± 8**	**55 ± 26**	**9 ± 6**	**22 ± 10**
2002 (n=20)***	C	**3 ± 3**	**10 ± 5**	**2 ± 4**	**14 ± 5**
Massie *et al*[45]	B	*	*	*	*
2003 (n=44)	C	**11 ± 7**	*	*	*
	A	**10 ± 5**	*	*	*
Planès *et al*[51]	B	**61 ± 17 / 58 ± 17**	*	*	**49 ± 14 / 44 ± 19**
2003 (n=35)**	C	**10 ± 13**	*	*	**15 ± 9**
	A	**8 ± 7**	*	*	**14 ± 8**
Present Study	B	**15 ± 8**	**61**	**16 ± 14**	
2004 (n=29)	C	**4 ± 4**	**4**	**4 ± 6**	
	A	**3 ± 3**	**3**	**2 ± 3**	

*Data not available ** Parallel trial *** Comparison of CPAP & Mandibular advancement device

5.5.1 Oximetry Data – Blood Oxygen Levels

All studies[37,40,41,42,44,47,48,50,51] where results of oximetry data were discussed (Table 5.5) showed significant improvements in mean oxygen saturation (SaO_2), minimum SaO_2 values and the percentage of total sleep time where SaO_2 was greater than 90% between both treatments and baseline, but with no significant difference between APAP and CPAP treatments except the studies by Sharma *et al*[40].

D' Ortho *et al*[37] found the number of minutes (mins) that $SaO_2 < 90\%$ to be 8.8 mins on APAP and 3.6 mins on CPAP in a crossover trial. Scharf *et al*[41] demonstrated no differences in the number of oxygen desaturation events per hour on either APAP (9/hour) or CPAP (11/hour). Meurice *et al*[50] found mean sleeping oxygen saturation levels not to differ between APAP and CPAP. While Konnerman *et al*[42] found CPAP and APAP not to differ with respect to the percentage of time the oxygen saturation levels were above 90%, which were 97.2% on CPAP and 99% APAP therapy. Juhász[44], Scarf[41], Konnerman[42] and d'Ortho *et al*[37] all found that the minimum oxygen saturation on APAP was not different from that on CPAP, but was significantly improved from the baseline untreated value. Only Sharma *et al*[40] found significantly lower oxygen saturation on APAP (79.9%) compared to CPAP (84.4%). The APAP device used in this trial was a prototype whose algorithm was based on airway vibrations not on flow limitation.

In the current study group there was a mean oxygen saturation of 93.2% (APAP), 93.2% (CPAP), which improved significantly from the baseline value of 92%. The minimum SaO_2 values of 87.5% (APAP) and 82.7% (CPAP) versus 78% (baseline) were significantly improved on both treatments, but there was no significant difference between the two modes.

Table 5.5 Oximetry data in 10 studies comparing APAP and CPAP Therapies
Mean oxygen saturation (SaO_2%), Minimum oxygen saturation (Min SaO_2), Percentage of sleep time where oxygen saturation < 90% saturation (% TST SaO_2 < 90%)
(B=baseline, C=CPAP, A=APAP)

		SaO_2%	Min SaO_2 %	% TST SaO_2< 90%
Meurice *et al*[50]	B	**92.9± 3.4 / 91.5± 4**	*	*
1996 (n=16)**	C	**96±3**	*	*
	A	**96±2**	*	*
Sharma *et al*[40]	B	*	**66.3±16.5**	**27.8±27.1**
1996 (n=20)	C	*	**84.4±4.3**	**11.9±23.5**
	A	*	**79.9±9.7**	**13.9±25.6**
Scarf *et al*[41]	B	*	*	*
1996 (n=12)	C	*	**84.2±3.0**	*
	A	*	**82.6±3.4**	*
Konnerman *et al*[42]	B	**91.9± 2.6 / 90.5±2.6**	**74.5±10.7 / 76.5±12.4**	*
1998 (n=50)**	C	**94.3±2.4**	**87.2±9.2**	*
	A	**94.7±1.4**	**90.3±3.6**	*
d'Ortho *et al*[37]	B	**93±3**	**66.5±13.6**	**82.0±80.5**
2000 (n=25)	C	**95.9±1.5**	**86.6±7.7**	**3.8±10.3**
	A	**95.6±1.6**	**85.2±9.0**	**8.8±20.5**
Randerath *et al*[48]	B	*	**81.6±6.1**	*
2001 (n=25)	C	*	**87.0±4.2**	*
	A	*	**87.9±4.5**	*
Juhász *et al*[44]	B	*	**82.8±6.5**	*
2001 (n=12)	C	*	**93.4±1.7**	*
	A	*	**93.2±1.6**	*
Senn *et al*[47]	B	*	*	**12.6±3.4**
2003 (n=29)	C	*	*	**1.1±0.7**
	A	*	*	**0.9±0.7**
Planès *et al*[51]	B	*	*	**12.7±12.8 / 24.9±21.6**
2003 (n=35)**	C	*	*	**1.9±5.0**
	A	*	*	**0.3±0.6**
Present Study	B	**92.0±2.1**	**78.0±11.5**	*
2004 (n=29)	C	**93.2±1.8**	**82.7±11.0**	*
	A	**93.3±1.7**	**87.5±3.5**	*

*Data not available **Parallel trial

5.6 Auto-adjusting to Determine a Fixed CPAP Pressure

In most studies where APAP was selected to determine a fixed CPAP pressure, a single pressure was selected only after a detailed review of the auto-titrating night data. That is, periods with high mask leak were often eliminated after consideration by manual review. A single number calculated by the computer from the overnight data was not simply accepted as the prescribed level of fixed home pressure. For example, in the present trial, the mean 95th Centile, this is the pressure exceeded only 5% of the night, calculated during lab night 2 (auto-titration) was 10 cm H_2O, whereas the mean prescribed fixed pressure, chosen after inspecting the data the following morning, was significantly lower at 8 cm H_2O. In four randomised controlled trials [58-61] and three clinical series[44,62,63] it was found that APAP could be used to select a fixed CPAP pressure that reduced the AHI < 10 per hour in 80-95% of the OSAHS patients studied. Therefore a single night of auto-adjusting positive airway pressure to determine long term fixed pressure therapy has been shown to be as reliable as the traditional manual CPAP titration studies carried out during Cardiorespiratory Polysomnography (CRPSG) testing. In fact automatic titration studies have been the standard and successful method employed in this Respiratory Sleep Disorders Unit for the past decade to determine fixed CPAP pressure for long-term home treatment.

5.7 Positive Airway Pressure Therapy

Nasal CPAP has been demonstrated to effectively reduce both subjective and objective measures of daytime sleepiness in randomised placebo controlled trials[7,64]. In general, higher pressures are needed in the supine position and during REM sleep[65]. Higher pressures are also needed to eliminate residual snoring and respiratory effort related arousals associated with airflow limitation than to prevent apnoea and hypopnoea[66]. The

optimal pressure therefore is the lowest pressure needed to eliminate all respiratory events, in all sleep positions and sleep stages. However, this optimal pressure may change over time, secondary to many factors including weight gain, nasal congestion, sleeping posture and sleep stage[67]. Also the use of a single high pressure for the entire night could potentially increase mask leaks, mouth leaks, pressure intolerance and this might theoretically reduce acceptance and adherence with CPAP therapy in some patients[68].

APAP devices, on the other hand, are designed to increase pressure only as needed to maintain airway patency on a continuous basis and then to decrease pressure if no events are detected over a set period of time. This allows the minimum effective pressure to be delivered in any given circumstance at all times and therefore the mean pressure delivered over the night is often lower than the fixed optimal CPAP pressure. As a result of this lower mean pressure, it has been hypothesised that APAP therapy could increase acceptance and adherence to treatment in the long term[69,70]. However, mask and mouth leaks tend to raise the baseline flow delivered by APAP units and can therefore diminish the variations in airflow during inspiration and expiration. The resulting airflow signal may then be interpreted as an apnoea or hypopnoea, which prompts an inappropriate increase in pressure that may further increase leak. To control for this problem of leak many APAP units have algorithms that limit pressure increases when mask leak exceeds certain values. Another advantage of APAP devices is that they allow transfer of pressure over time information to a computer for analysis. This information can provide not just usage data but also mask leak data, which can help to pinpoint mask fitting problems that may be affecting long term acceptance and compliance with treatment. Table 5.6 presents the mean pressure levels on APAP and CPAP in ten trials including the current one.

Table 5.6 Compliance & Pressure data in 10 studies Comparing APAP & CPAP Therapies

Median pressure APAP cm H_2O (APAP P), Mean fixed pressure CPAP cm H_2O (CPAP P), Percentage of nights used (% nights), Median hours used per night (hrs/night)

	APAP P	CPAP P	% nights	hrs/night
Meurice *et al*[50] 1996 (n=16)**	*	*	*	**5.1 ± 1.1 (CPAP)**
			*	**6.5 ± 1.0 (APAP)**
Konnerman *et al*[42] 1998 (n=50)**	**7 ± 2**	**8 ± 2**	**81 ± 1 (CPAP)**	**5.6 ± 2.5 (CPAP)**
			93 ± 1 (APAP)	**5.9 ± 1.6 (APAP)**
d'Ortho *et al*[37] 2000 (n=25)	**9 ± 2**	**10 ± 3**	*	**4.7 ± 1.8 (CPAP)**
			*	**4.1 ± 1.8 (APAP)**
Hudgel *et al*[43] 2000 (n=33)	**11± 1**	**6 ± 1**	**82 ± 4 (CPAP)**	**5.5 ± 0.3 (CPAP)**
			84 ± 4 (APAP)	**6.0 ± 0.3 (APAP)**
Teschler *et al*[46] 2000 (n=10)	**7 ± 1**	**9 ± 1**	*	**6.1 ± 0.5 (CPAP)**
			*	**6.3 ± 0.4 (APAP)**
Randerath *et al*[48] 2001 (n=25)	**6 ± 2**	**8 ± 2**	*	*
Senn *et al*[47] 2003 (n=29)	**7 ± 1**	**8 ± 1**	*	**5.5 ± 0.2 (CPAP)**
			*	**5.6 ± 0.2 (APAP)**
Planès *et al*[51] 2003 (n=35)**	**9 ± 2**	**12 ± 3**	*	**5.3 ± 1.4 (CPAP)**
			*	**4.5 ± 1.7 (APAP)**
Massie *et al*[45] 2003 (n=44)	**7 ± 2**	**11 ± 2**	**81 ± 15 (CPAP)**	**4.6 ± 1.9 (CPAP)**
			92 ± 11 (APAP)	**5.1 ± 1.9 (APAP)**
Present Study 2004 (n=29)	**6 ± 1**	**8 ± 2**	**81 ± 25 (CPAP)**	**4.9 ± 1.9 (CPAP)**
			79 ± 29 (APAP)	**4.9 ± 2.1 (APAP)**

*Data not available **Parallel trial

All but one[43] of these trials demonstrated lower mean pressure on APAP compared to CPAP. CPAP therapy is a highly effective treatment for OSAHS, but a major challenge facing clinicians is the low levels of CPAP acceptance and compliance over time[71-73]. APAP devices, on the other hand, irrespective of mode of operation, deliver a

significantly lower pressure throughout the night than the traditional fixed pressure systems (CPAP) and therefore this may be beneficial for compliance in the long-term.

5.8 Compliance with APAP and CPAP Therapy

Internationally some 5-50% of SAHS patients recommended for CPAP either reject this treatment option or discontinue within the 1st week and 12-35% of the remaining patients can be expected to have discontinued CPAP by 3 years[74]. Studies have shown that the best predictor of long term compliance with positive airway pressure treatment is the subjective symptomatic benefits of treatment[75,76].

Nine previous studies[37,42,43,45-48,50,51] in which acceptance or compliance to CPAP and APAP therapy are compared in Table 5.6. Meurice *et al*[50] in a parallel trial, after 3 weeks on both CPAP and APAP showed an increase in mean nightly time, at pressure, on APAP of 6.5 hours, per night compared to 5.1 hours per night on CPAP. However the short treatment period may have limited the validity of these results for the long term.

Konnerman *et al*[42] in a parallel design trial, over a 3-6 month treatment period, found the number of nights per week, greater in the APAP group (7 (93%) nights per week v 6 (81%) nights per week) than in the CPAP group. But there was no significant difference in the mean nightly duration, 5.6 hours per night (CPAP) versus 5.9 hours per night (APAP).

Hudgel and Fung[43] found increases in the mean hours per night on APAP, 6 hours compared to 5.5 hours on CPAP using a randomised controlled trial in large group of patients. However, no statistical test of the effect of order was performed and the improvement in ESS was similar for both treatments.

d'Ortho *et al*[37] found similar adherence in a randomised controlled trial but the analysis of order effect was not significant. There was however only a difference in mean pressure

of 1cm H_2O between the two modes of treatment and this may explain the lack of difference in compliance. On the other hand Teschler *et al*[46] found no evidence for increased compliance on APAP v CPAP even though the median pressure was about 2cm H_2O lower on APAP than on CPAP.

Planés[51] and Senn *et al*[47] also demonstrated findings similar to the two latter studies[37,46]. In the most recent study by Massie *et al*[45] percentage of nights used (92%) on APAP were not significantly more than the 88% nights on CPAP therapy. But the hours used per night on APAP (5.1 hours/night) were significantly longer than the 4.5 hours per night on CPAP. The findings of the current study showed percentage of nights of APAP usage of 79%, and CPAP 81%, with hours used per night of 4.9 hours for both devices, which indicates that there was no significant differences in compliance in this particular patient population.

5.8.1 End Preference

Seven studies[37,38,40,44,45,47] including the current one looked at patient preference at the end of the study (Table 5.7). Three of these studies[38,40,44] were based on one night of treatment with each device and they all demonstrated that more patients preferred APAP than CPAP, Ficker *et al*[38] 10/16 (63%) versus 6/16 (37%), Sharma *et al*[40] 11/18 (61%) versus 7/18 (39%) and Juhász *et al*[44] 6/12 (50%) versus 2/12 (17%), 4/12 (33%) no choice). The study by Senn *et al*[47] gave patients four weeks treatment on both APAP and CPAP, but only after they had completed one month on CPAP therapy first. Four patients each preferred APAP and CPAP devices, but 21/29 patients did not have a preference. There was no order effect seen. Only the study by d'Ortho *et al.*[37] employed a similar method to the current trial, where CPAP-naive patients received eight weeks on each treatment device. The results of that study showed that the choice of mode was

independent from the order of mode, with fifteen out of the twentyfive (60%) patients preferring APAP at the end of the study.

Table 5.7 Patient Preference data from 7 Studies Comparing APAP and CPAP Therapies

Patient preference for APAP (Pref. APAP) and CPAP (Pref. CPAP),

	Pref. APAP	Pref. CPAP	Comment
Sharma *et al*[40] 1996 (n=20)	**11/20****	**9/20**	1 night randomised CPAP + APAP
Ficker *et al*[38] 1998 (n=16)	**10/16****	**6/16**	1 night randomised CPAP + APAP
d'Ortho *et al*[37] 2000 (n=25)	**15/23**	**8/23**	8 weeks randomised CPAP + APAP Choice of mode independent from order of mode Rem + auto (Nellcor Puritan –Bennett)
Juhász *et al*[44] 2001 (n=12)	**6/12**	**2/12**	1 night randomised CPAP+APAP
Senn *et al*[47] 2003 (n=29)	**4/29****	**4/29**	1 month randomised CPAP + 2 APAP devices 21/29 no preference at end of study No order effect DeVilbiss (Sunrise) Autoset T (ResMed)
Massie *et al*[45] 2003 (n=44)	*	*	Patients CPAP pressure >10cm H20 6 weeks randomised CPAP + APAP APAP tolerated better than CPAP Autoset T (ResMed)
Present Study 2004 (n=29)	**13/26****	**13/26**	8 weeks randomised CPAP + APAP Choice of mode dependent on order of mode – strong order effect Autoset T (ResMed)

* Data not available **Not significant

In contrast to previous studies, twenty-six out of twenty-nine patients in this current study expressed a definite preference, but with equal selection of devices (50% APAP and 50% CPAP). Also the current study demonstrated a strong order effect that was dependent on the order of mode. One reason for the strong order effect may be the fact that two separate devices were used in this study. The devices differ in both their

physical appearances (Fig 3.4 & 3.5, section 1.7) as well as in their modes of operation. Instructions for machine use were also different. Therefore many patients may have become biased to the device they first used and found that the changing physical features and operational instructions of the second device were not to their liking. Secondly, all of the previous studies included patients with severe OSAHS whereas the patient population in the current study was a selected subgroup of mild to moderate sufferers and this factor too may have had an impact on the end preference.

5.8.2 Side Effects with Positive Airway Pressure Therapy

In summary there seems to be conflicting evidence about whether chronic treatment with APAP improves acceptance or compliance over CPAP therapy, although some studies did find evidence of an increased patient preference for and usage of APAP devices. Overall it would appear however, that mean lower overnight pressures do not significantly increase the compliance on APAP therapy compared to CPAP therapy. One reason may be that patients do not find pressure intolerance to be the major discomfort with CPAP treatment. Nasal mask interface, nasal congestion and dryness still remain the major side effects with both types of treatment and these factors may be the main reasons affecting patient acceptance and compliance with treatment[71].

The literature clearly supports this theory (Table 5.8). As far back as 1989 Nino-Murcia *et al*[77] found that over 65% of patients using CPAP reported significant side effects such as nasal congestion, dry nose or throat and discomfort with the device. Engleman *et al*[79] in 1996 reported that nasal stuffiness, followed by the sensation of cold air, noise, and mask pressure were the most common side effects experienced by patients. They also found that CPAP noise and nocturnal awakenings due to CPAP therapy, correlated negatively with CPAP use and with benefits from CPAP therapy indicating that these

were the problems that the patients blamed for lack of CPAP use. Ninety percent of patients in a study by Marque-Baez *et al*[84] complained of side effects or problems with the equipment. The commonest complaints were again related to nasal problems (dryness, congestion rhinorrhea, etc), which affected 61.5%. The main complaint about the equipment was the noise it made (46%). Similar findings by Berry *et al*[68] in 2000 found that patients frequently stopped using CPAP therapy due to the discomfort with the treatment. Feelings of claustrophobia and nasal congestion, nasal mask interface problems relating to pressure sores or persistent air leakage were the reasons that appeared to lead to lack of compliance.

The present study confirms the findings of these previous authors. On the first night of treatment over 65% of patients complained about some aspect of the treatment. Although issues with the nasal mask, machine noise and feelings of claustrophobia all reduced after 8 weeks on each treatment, nasal side effects continued to be a significant problem on treatment, with more patients on APAP (44%) affected than on CPAP (35%).

Table 5.8 Side Effects with Positive Airway Therapies in Eleven Studies
% Nasal side effects stuffy/dry (Nasal), % Mask problems (Mask), % Noisy machine (Noise), % Claustrophobic (Claus.), % Any side effect (Any)
(B=Baseline, C=CPAP, A=APAP, T = Both APAP + CPAP)

		Nasal	Mask	Noise	Claus	Any
Nino-Murcia *et al*[77] 1989 (n=90)		69	6	23	*	>69
Waldhorn *et al*[78] 1990 (n=96)		38	54	15	*	88
Hoffstein *et al*[76] 1992 (N=96)		42	66	68	>10	>66
Rauscher *et al*[80] 1993 (n=63)		30	48	*	*	>48
Kribbs *et al*[81] 1993 (n=32)		47	28	54	28	>54
Engleman *et al*[74] 1994 (n=32)		28	*	*	*	41
Meurice *et al*[82] 1994 (n=44)		*	51	19	*	>51
Pepin *et al*[75] 1995 (n=96)		*	50	34	*	>50
Engleman *et al*[79] 1996 (n=204)		64	63	41	*	>64
Kalan *et al*[83] 1999 (n=300)		*	45	*	*	96
Present study 2004 (n=29)	B	55	65	45	37	>65
	C	35	24	21	14	>35
	A	44	22	15	22	>44
Present study (n=22) Follow-up @ 18months	T	36	23	9	*	52
	C	50	12	*	*	
	A	21	18	9	*	

* Data not available

In a follow-up survey 18 months after the patients completed the study 52% of patients still complained of difficulties with treatment, with more than 50% complaining of nasal problems and 25% of mask leaking. However, only 9% complained that the noise of the machine was a problem. Twenty-two out of the original twenty-nine patients had

remained on treatment, 13 on APAP therapy and 9 on CPAP therapy. Although there was no significant difference between the numbers who had remained on APAP compared to those on CPAP it would appear that APAP might be tolerated better in the long-term. Most of the problems with CPAP therapy related to nasal difficulties (50%) but only 12% complained of mask leaking. With APAP therapy the problems were more evenly divided between mask leaking (18%) and nasal side effects (21%). No patient on CPAP therapy complained of noise problems, whereas 9% of those on APAP found the machine noise a problem. However, all previous studies, including this current one, have demonstrated that positive airway pressure therapy in general remains effective and acceptable to most patients even in the presence of a high incidence of adverse effects.

5.9 References

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6. CONCLUSIONS

The patients studied in this trial were comprised predominantly of middle aged, over weight, hypertensive (55%), males (90%), diagnosed with mild to moderate OSAHS, according to their apnoea hypopnoea index (AHI), which ranged between 5 and 30 events per hour of sleep. Six of the twenty-nine patients were already on hypertension medication, but there was no significant difference in the mean blood pressure, between the treated (hypertensive medications) and untreated groups, on any of the three nights blood pressure was recorded in the sleep laboratory. When the above parameters were compared to those in the literature, the results drawn from this study fall within the limits of previously published reports.

Twenty-five (86%) of the group drank alcohol, all within acceptable limits, except one male patient who drank more than twenty-one units per week. 35% were smokers with an average caffeine (tea, coffee, cola) consumption in the whole group, of six cups per day, although one subject drank twice this amount. 90% of these patients worked outside the home, with (7/29) 24% of them doing some type of shift hours. There was no significant change over the course of the seventeen weeks of the trial in BMI, blood pressure, units of alcohol consumed, hours worked, cigarettes or caffeine consumed in this particular group of patients.

In terms of subjective daytime sleepiness, this particular group of patients demonstrated a mild to moderate degree (ESS =12) on the baseline, untreated night, with both APAP and CPAP treatments significantly reducing this effect. In terms of objective sleep assessment, the sleep pattern and sleep quality of the patients in the current study were not significantly different from the "normal" population, but both APAP and CPAP therapies appeared to improve some aspects of sleep. The treatments resulted in a

significant reduction in Stage 1 sleep and in the amount of wake time after sleep onset, although there was no significant difference between the two modes of treatment. These findings are consistent with previous studies, which have demonstrated that different types of positive airway treatments do significantly improve perceived daytime sleepiness levels and overnight sleep quality in all categories of patients, including those in the mild to moderate range. However, patients in the current study still experienced difficulty staying asleep at night, even on treatment. This may be due to the normal effect of increasing age on sleep patterns, rather than the result of the OSAHS condition.

With regard to the respiratory assessment carried out in the study, our findings were consistent with those of similar published ones. Both APAP and CPAP therapies equally reduced the number of respiratory abnormalities, apnoeas, hypopnoeas, and associated arousals and awakenings during sleep. This resulted in fewer arterial blood oxygen desaturations and led to a higher overall mean oxygen saturation during the night.

In the literature there appears to be differing evidence about whether chronic treatment with APAP improves acceptance or compliance over CPAP therapy. Some studies, but not this one, did find evidence of an increased patient preference for and /or usage of APAP devices. Compliance data from the current study did not demonstrate any significant difference in terms of compliance between the two treatments. However, we did find that patients used their preferred device longer than the non-preferred one and that patients who used APAP on the second leg of the trial, but preferred CPAP, did not meet the minimum compliance targets of 70% nights and more than four hours per night of use.

Also in a follow-up survey 18 months after the trial ended we found more patients had remained on APAP therapy, but this was not statistically significant. There also appeared to be a strong order effect in the current study, which was contrary to the results from

previous studies, however two different devices were used in this trial which may explain the difference. Major side effects remain a common problem for all patients on positive airway therapy and these issues rather than pressure intolerance may be the factors that affect patient acceptance and compliance with treatment. In particular nasal problems, stuffy nose, dry mouth etc. accounted for over 40% of all complaints, which affected patients in both the short term and the long term. The findings of this current study are consistent with those in the literature in regard to side effects of treatment.

When patients were subdivided based on their fixed pressure requirements and the baseline data of these subgroups compared, no differences were noted between the two groups in terms of disease severity (AHI), perception of daytime sleepiness (ESS), sleep characteristics (REM, NREM, and sleep efficiency), or social and anthropometric characteristics.

The only parameter that showed significant difference related to fixed pressure requirement, when end preference was taken into account. It was noted that patients requiring higher pressures preferred APAP and those requiring lower pressures preferred CPAP. Also patients requiring higher pressures appeared to be more compliant than those requiring lower pressures and this finding is consistent with a recently published work. The indirect post hoc inference therefore might be that end preference is related to fixed pressure.

In conclusion, based on the results of this study, it would appear that APAP and CPAP are equally effective in resolving sleep-related breathing disturbances and improving daytime sleepiness in patients with mild to moderate OSAHS, but fixed pressure requirements may have an impact on long-term compliance with the two treatments.

Furthermore, the design of future studies, based on the research presented here, should include a patient study group that focuses on high and low fixed pressure requirements,

rather than the metric of disease severity used in this current study. This would enable future research to determine if there were any significant differences between CPAP and APAP therapies. From the follow-on questionnaire data, looking at compliance with treatment after the study period was completed, it would appear that APAP therapy was better tolerated in the longer term. Any future study design therefore, should focus on the long-term impact of both CPAP and APAP therapy, rather than on the relatively short-term period used in this study.

In addition to the results presented and discussed in this thesis a number of abstracts have been submitted which include a poster presentation to the European Respiratory Society meeting held in Vienna in September 2003, oral presentation read at the Association of respiratory Technologists and Physiologists meeting held in Telford, UK in January 2004 and a refereed publication is currently in preparation for probable submission to the European respiratory Journal (ERJ) in early 2005. Copies of the abstracts for these publications are included in Appendix O.

Appendix A

The differential diagnoses of dyssomnias of intrinsic origin according to the International Classification of Sleep Disorders (American Sleep Disorders Association 1990)

Dyssomnias

Intrinsic Sleep disorders:

- Psychophysiological insomnia
- Sleep state misperception
- Idiopathic insomnia
- Narcolepsy
- Recurrent hypersomnia
- Idiopathic insomnia
- Posttraumatic hypersomnia
- Obstructive sleep apnoea syndrome
- Central sleep apnoea syndrome
- Central alveolar hypoventilation syndrome
- Periodic limb movement disorder
- Restless leg syndrome

Appendix B

EPWORTH SLEEPINESS SCALE

NAME: DOB:

HOSP NO. DATE:

HOW LIKELY ARE YOU TO DOZE OFF OR FALL ASLEEP IN THE FOLLOWING SITUATIONS?

USE THE FOLLOWING SCALE TO RATE YOUR SCORE:

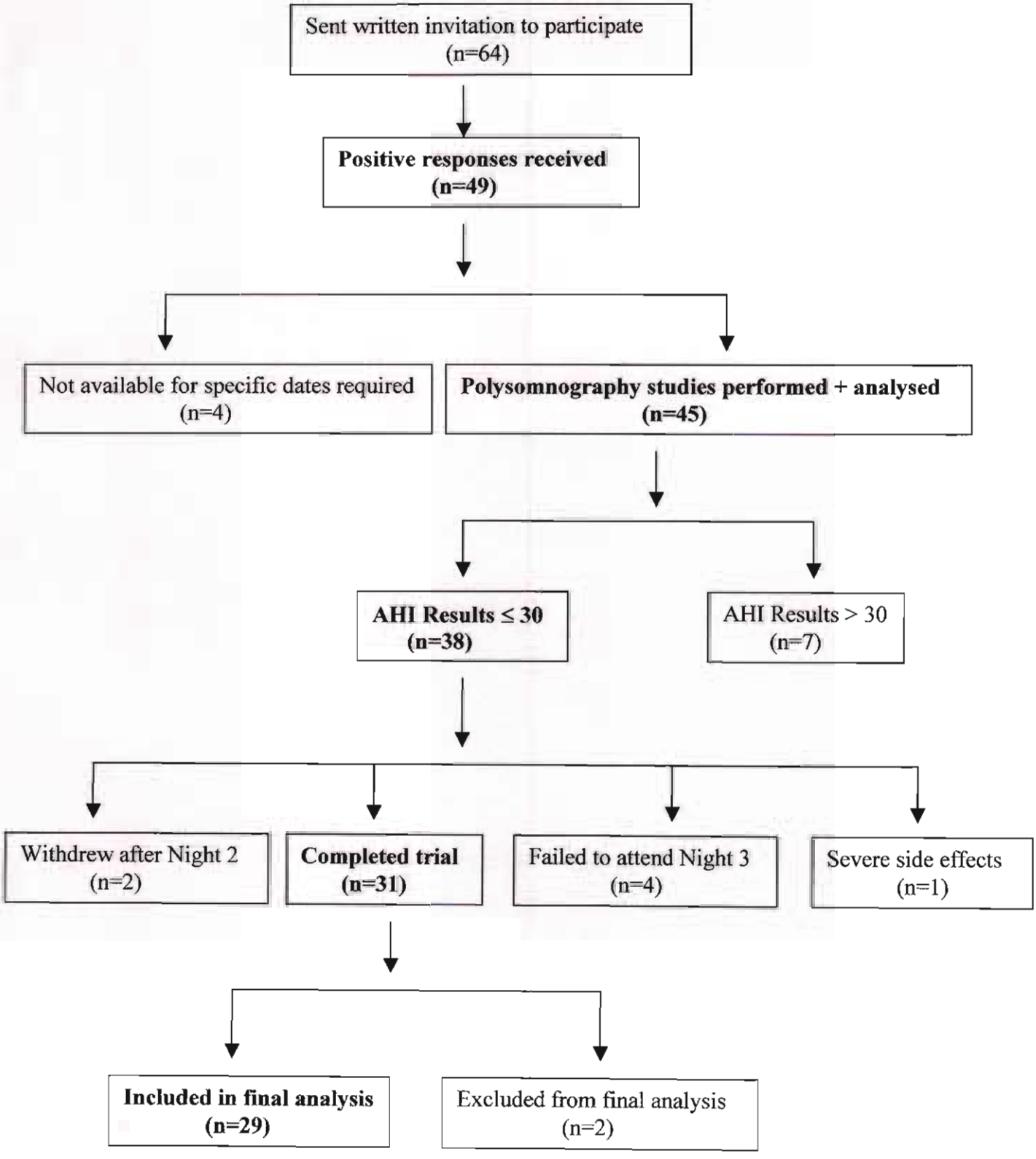
0 = WOULD NEVER DOZE
1 = SLIGHT CHANCE OF DOZING
2 = MODERATE CHANCE OF DOZING
3 = HIGH CHANCE OF DOZING

SITUATION	**CHANCE OF DOZING**
SITTING AND READING	_____
WATCHING TV	_____
SITTING INACTIVE IN A PUBLIC PLACE (e.g. WAITING ROOM, MEETING)	_____
AS A PASSENGER IN A CAR FOR AN HOUR WITHOUT A BREAK	_____
LYING DOWN TO REST IN THE AFTERNOON WHEN CIRCUMSTANCES PERMIT	_____
SITTING AND TALKING TO SOMEONE	_____
SITTING QUIETLY AFTER LUNCH WITHOUT ALCOHOL	_____
IN A CAR, WHILE STOPPED IN TRAFFIC	_____

TOTAL EPWORTH SCORE: =

Appendix C

FLOW CHART - SUBJECT RECRUITMENT



Appendix D

DIARY CARD QUESTIONS

Did you wake refreshed?	0 = good night 1 = slept well, woke once 2 = woke 2-3 times 3 = bad night, awake most of time
Was your nose congested last night?	0 = not at all 1 = slight problem during the night 2 = blocked in the early morning only 3 = blocked all night
Was your throat dry during the night?	0 = not at all 1 = slight problem during the night 2 = slight dryness in the am 3 = very dry all night
Was the mask comfortable during the night?	0 = very comfortable all night 1 = slight problem during the night 2 = uncomfortable in early am only 3 = uncomfortable all night

Appendix E

JAEGER SLEEP LAB 1000e - SPECIFICATIONS

POWER SUPPLY

Input range 110-240V, 50-60 Hz, 200VA

ENVIRONMENTAL CONDITIONS

Operating temperature: +10° C to +40° C

Barometric presssure: 700 to 1060 mBar

Storage and transport temperature: -30° C to +50° C

Humidity: 30% - 75% non-condensing

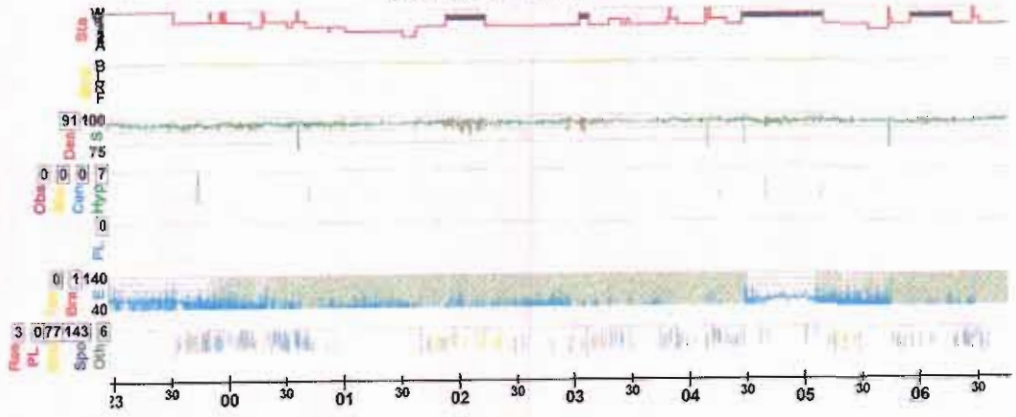
OXIMETER

The accuracy of the system is ± 3% (± 1Standard deviation) in the range 70-100%

Appendix F

CARDIORESPIRATORY POLYSOMNOGRAPHY REPORT

GRAPHIC SUMMARY



SLEEP STAGING

Total recording time (hr) :	7.8	Total sleep time (hr) :	7.1
Sleep Efficiency (%):	91.1	Sleep Maintenance Effic(%):	98.4
Sleep onset latency (min) :	35.0	Stage REM latency (min) :	142.0

Sleep Stage	Latency (mins) Absolute	Latency (mins) Relative	Duration (mins)	%TIB	%Sleep Time
Stage REM	177.0	142.0	89.5	19.1	20.9
Stage 3	116.0	81.0	42.0	8.9	9.8
Stage 4	154.5	119.5	6.5	1.4	1.5

HEART RATE

Basal heart rate during sleep (bpm)	60.7
Slowest heart rate (bpm)	46.8
Fastest heart rate (bpm)	94.4
Brady/Tachy Index (/hr)	0.1

SATURATION

Percent desaturation required	4
Total number of desaturations	91
Desaturation Index (/hr)	13
Basal O2 during sleep	95.2
Average low O2 for desaturations < 90	87.5
Average low O2 for desaturations < 88	86.0
Minimum O2 value	58.4

RESPIRATORY EVALUATION

	Obstructive	Mixed	Central	Hypopnea
Event Totals	0	0	0	7
Index Totals	0.0	0.0	0.0	1.0

Apnea (O+M+C) Index = 0.0 Apnea + Hypopnea Index (RDI) = 1.0

PLM

	Number of Movements	Index/hr
Sleep	0	0.0
Wake	0	0.0

AROUSAL

	Number of Arousals	Index/hr
Total	229	32.1

Appendix G

BCI PULSE OXIMETER SPECIFICATIONS

PARAMETERS RECORDED

SpO_2

Pulse Rate

Pulse Strength

PERFORMANCE SpO_2

Range: 100%

Accuracy: ± 2% at 70-100%

± 3% at 50-69%

Alarm Limits: High 100-50% and off in 1% steps

Low 50-99% and off in 1% steps

Averaging: 4, 8, or 16 pulse beat average

SENSORS Red: 660nm, 2mW (typical)

Infrared: 905nm, 2 –2.4mW (typical)

DIMENSIONS (H x W x D)

82 x 216 x 140 mm

WEIGHT 850gr

POWER SUPPLY

Input range 105-125V, 60 Hz,

ENVIRONMENTAL CONDITIONS

Operating temperature: 0 to 40° C

Storage temperature: -4° to +75° C

Relative Humidity: Operating 15% -95% non-condensing

Relative Humidity: Storage 10-95%

Appendix H

AUTOSET® PORTABLE II PLUS SPECIFICATIONS

PERFORMANCE

Settling time range: 3 to 20 minutes

Operating pressure range: minimum 4 to 20 cm H_2O

Maximum 4-20cm H_2O

(Note: Minimum pressure is always less than or equal to maximum pressure)

DIMENSIONS (H x W x D)

190 x 240 x 350 mm

WEIGHT 5.7 kg

POWER SUPPLY

Input range 110-240V, 50-60 Hz, 200VA

HOUSING CONSTRUCTION

Injected moulded plastic

ENVIRONMENTAL CONDITIONS

Operating temperature: +5° C to +40° C

Storage and transport temperature: -20° C to + 60° C

Humidity: 15% -95% non-condensing

AIR FILTER STRIPS

Outer Filter Strip – Polyester fibre

Inner Filter Strip – Open cell polyester-urethane foam

AIR TUBING

Flexible plastic, 2.0 m length

OXIMETER

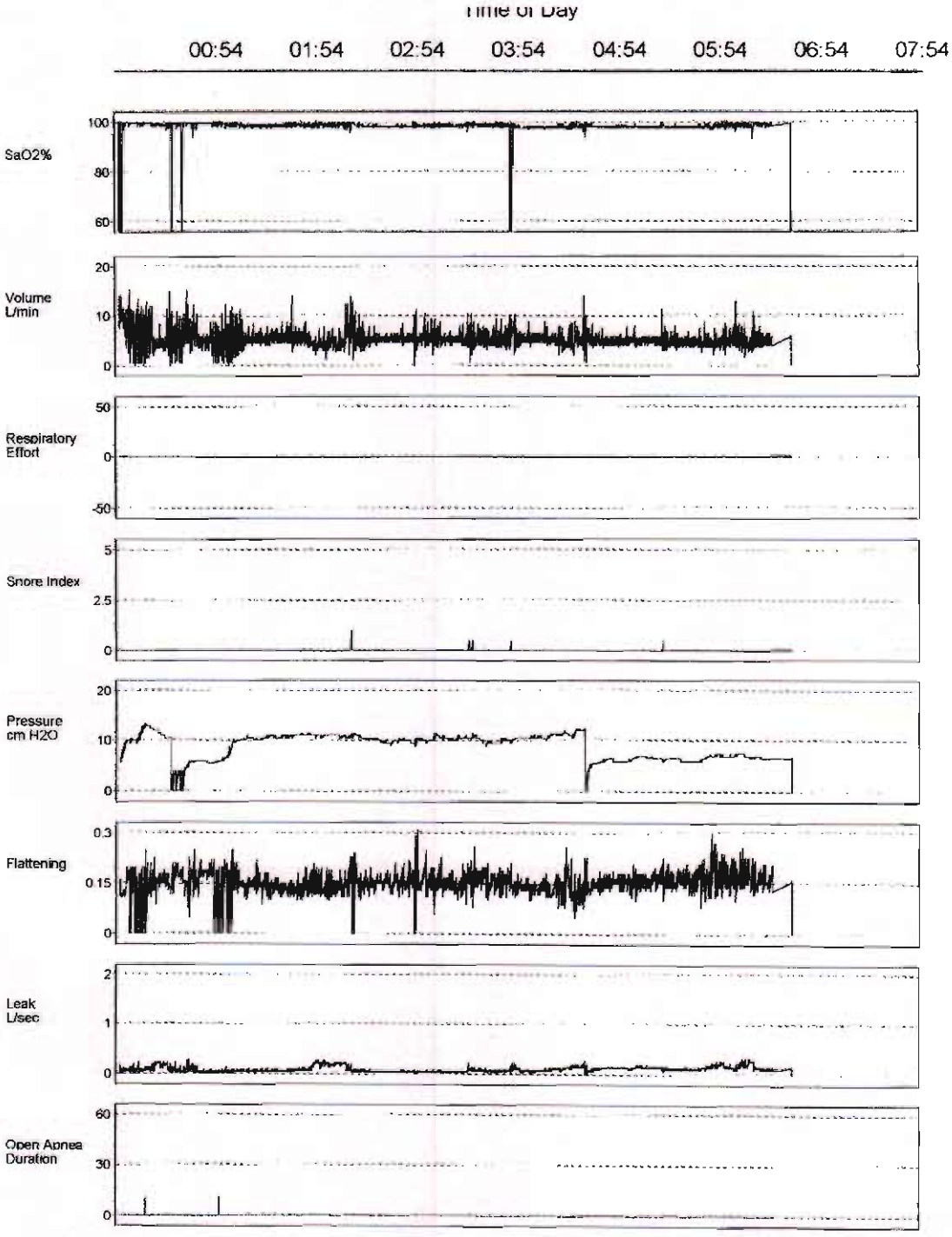
The accuracy of the system is ± 3% (±1Standard deviation) in the range 70-100%

IEC 601 – 1 CLASSIFICATIONS

Class I, Type B

Appendix I

AUTOSET PORTABLE 11 PLUS REPORT (PAGE 1)



Appendix J

AUTOSET PORTABLE 11 PLUS REPORT (PAGE 2)

Patient: ,

ID:

Physician :

Date of Birth:		Study Date:	8/23/2004
Address:			
		Weight:	0.0
		Height:	0.0
		Sex :	Male
Telephone (Home):		Ethnic Category:	
Telephone (Work):		Neck Circumference:	0.0
Sleep Lab:		BMI:	0.0
Equipment Provider:			
Insurance Company:		Systolic:	0.0
SSN:		Diastolic:	0.0

Automatic Session

Pressures (low leak)

median	10.0
90th centile	11.0
95th centile	11.5
highest	13.5

FLATTENING INDEX

% time less than index

35	0.15
5	0.10

LEAK

% time less than leak, l/sec

100	0.40

Average leak = 0.10

BODY POSITION

Position	*% time*
back	100
right	0
left	0
front	0

OXIMETRY

% time less than %SaO2

4	95
3	85
3	75
3	65

Minimum SaO2 % = 0

APNEA INDICES

Type	*Events/hr*
open	0
closed	2
total	2

APNEAS & HYPOPNEAS

Position	*AHI/hr*	*Apnea/hr*
back	8	
right	0	
left	0	
front	0	
total	8	2

Respiratory Irreg Index /hr: 24

Appendix K

AUTOSET T SPECIFICATIONS

PERFORMANCE

Settling time range: 1 to 30 minutes

Operating pressure range: 4 to 20 cm H_2O

Mask pressure: +/- 0.5 cm H_2O

Leak: +/- 0.2l /sec or +/- 20% whichever is greater

DIMENSIONS (H x W x D)

145 x 260 x 315 mm

WEIGHT 3.5 kg

POWER SUPPLY

Input range 110-240V, 50-60 Hz, 120VA

HOUSING CONSTRUCTION

Injected moulded Noryl® plastic

ENVIRONMENTAL CONDITIONS

Operating temperature: +5° C to +40° C

Storage and transport temperature: -20° C to + 60° C

Humidity: 15% -95% non-condensing

AIR FILTER STRIPS

Two layered, powder bonded, polyester open cell foam

AIR TUBING

Flexible Hytrel plastic, 2.0 m length

IEC 601 – 1 CLASSIFICATIONS

Class II,

Type CF

Appendix L

RESMED S6 ELITE CPAP SPECIFICATIONS

PERFORMANCE

Operating pressure range: 4 to 20 cm H_2O

DIMENSIONS (H x W x D)

110 x 240 x 290 mm

WEIGHT 1.77 kg

POWER SUPPLY

Input range 110-240V, 50-60 Hz, 200VA

HOUSING CONSTRUCTION

Injected moulded plastic

ENVIRONMENTAL CONDITIONS

Temperature limits: Operating +5°C to +40° C

Storage -20°C to + 60°C

Humidity: 15% -95% RH (non-condensing); storage, up to 95% RH (non- condensing)

AIR FILTER STRIPS

Filter strip: Progressively structured synthetic fleece, resin bonded: each fibre adhesive coated, with scrim on leaving air side

AIR TUBING

Flexible Hytrel plastic, 2.0 m length

IEC 601 – 1 CLASSIFICATIONS

Class II, (double insulated/double isolated)

Type CF (Applied Part)

Appendix M

CPAP DEVICE COMPLIANCE REPORT

Date : 01/08/01

Statistical Summary - 18 April 2001 to 12 June 2001

Device :	CPAP S6 ELIT
Device Mode :	CPAP
Total Days :	56
Median Usage :	04:54 hours:minutes
Usage Days :	98.2%
Median Usage :	04:54 hours:minutes

Appendix N

APAP DEVICE COMPLIANCE REPORT

Date : 11/22/04

Statistical Summary - Friday, May 08, 1998 to Thursday, May 21, 1998

Device :	AutoSet T
Device Mode :	Autoset
Total Days :	14
Median Usage :	04:55 hours:minutes
Usage Days :	100.0%
Median Usage :	04:55 hours:minutes

Median Treatment Values

Minimum Pressure Setting :	4.0 cm H2O
Maximum Pressure Setting :	20.0 cm H2O
Time in Apnea :	0.2 % Mask On Time
Apnea Index :	0.5 events per hour
AHI :	3.7 events per hour
Median Pressure :	4.4 cm H2O
Pressure 95th centile :	7.2 cm H2O
Maximum Pressure :	9.3 cm H2O
Median Leak :	0.02 litres/sec
Leak 95th centile :	0.11 litres/sec
Maximum Leak :	0.24 litres/sec

Appendix O

European Respiratory society Poster:

http://www.ersnet.org/er/Ir/

Association of Respiratory Technologists and Phyiologists:

Comparison of auto-adjusting and fixed positive airway pressure therapy in patients with mild to moderate obstructive sleep apnoea syndrome (OSAS)

G. Nolan, L. Doherty, P. Goodman, W.T. Mc Nicholas. Respiratory Sleep disorders Unit, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland.

Background: Continuous positive airway pressure (CPAP) is the therapy of choice for many patients with OSAS, but may be poorly tolerated in patients with mild to moderate disease. Auto-adjusting positive airway pressure (APAP) has been developed to constantly adapt the positive pressure to the optimal level and might be better tolerated. The aim of this study was to compare APAP and CPAP with regard to effects, patient preference and compliance in this category of disease.

Methods: 29 patients (mean age 53yrs) with polysomnography confirmed mild to moderate OSAS (apnoea/hypopnoea freq/hr [AHI] 5-30) were given 8 weeks of laboratory determined fixed level CPAP and 8 weeks of APAP in a randomised blinded, crossover trial. Data are given as, mean ± SD, APAP *v* CPAP.

Results: No differences were observed in the AHI (2.8 ± 3 *v* 3.5 ± 3.5), or subjective daytime sleepiness as measured by the Epworth score (ESS; 8.6 ± 4 *v* 7.7 ± 4.6) between the two modes, all values were significantly improved from baseline (AHI 14.7 ± 8, ESS 12.3 ± 4; $p<0.001$). Patient compliance and duration of use were similar with both treatments. However, mean APAP pressure was significantly lower than CPAP pressure (6.2 ± 1.4 *v* 8.4 ± 1.7 cmH_2O, $p<0.001$). There was a trend for patients requiring higher fixed pressures (> $8cmH_20$) to prefer APAP and those n lower pressures (< 8cm H_20) to prefer CPAP after trial completion.

Conclusion: APAP and APAP are equally effective in improving sleep-related breathing disturbances and daytime sleepiness in patients with mild to moderate OSAS.