Accepted Manuscript

Impact of opioid therapy on sleep and respiratory patterns in adults with advanced cancer receiving palliative care

A/Prof Phillip Good, Prof Ross Pinkerton, Dr Simon Bowler, Justin Craig, Prof Janet Hardy

PII: S0885-3924(17)30691-7

DOI: 10.1016/j.jpainsymman.2017.11.026

Reference: JPS 9654

To appear in: *Journal of Pain and Symptom Management*

Received Date: 16 August 2017

Revised Date: 22 November 2017

Accepted Date: 22 November 2017

Please cite this article as: Good P, Pinkerton R, Bowler S, Craig J, Hardy J, Impact of opioid therapy on sleep and respiratory patterns in adults with advanced cancer receiving palliative care, *Journal of Pain and Symptom Management* (2018), doi: 10.1016/j.jpainsymman.2017.11.026.

Title Page.

Title:
Impact of opioid therapy on sleep and respiratory patterns in adults with advanced cancer receiving palliative care

Running Title:
Sleep and palliative care

Authors:
1. A/Prof Phillip Good

Mater Health Services
Mater Research Institute-University of Queensland
St Vincent's Private Hospital, Brisbane, Australia

2. Prof Ross Pinkerton

Hummingbird House

3. Dr Simon Bowler

Mater Health Services

4. Justin Craig

Queensland Sleep

5. Prof Janet Hardy

Mater Health Services
Mater Research Institute-University of Queensland

Corresponding Author:
A/Prof Phillip Good
411 Main Street,
Kangaroo Point,
Brisbane, Qld, Australia, 4169

Phone: +61 732401111
Fax: +61 7 3240 1192
Email: Phillip.Good@svha.org.au

Tables: 1
References: 37
Words: 2499

Abstract

Context In advanced cancer, abnormal sleep patterns may contribute to poor quality of life but the impact of opioid related sleep disorders has not been explored in detail in these patients.

Objective To document sleep and respiratory patterns in patients with cancer, receiving a range of opioids, determine factors that contribute to severity of central or obstructive apnoea and to what extent these contribute to sleep disturbance.

Methods Adults with advanced cancer admitted to a palliative care service underwent a sleep analysis by an unattended polysomnograph. Total sleep time, apnea hypopnea index (AHI), central apnea index (CAI), obstructive apnoea hypopnea index OAHI), arousal index (AI) and oxygen desaturation were measured. Baseline assessment included body habitus, Mallampati score, comorbidity indices, concomitant medications and the Berlin questionnaire. Epworth sleepiness scale, Stanford Sleepiness scale and Wu cancer fatigue scales were documented

Results 28 patients were studied, including 25 receiving opioids. In the latter group, the AHI was mildly abnormal in 6 patients and severely abnormal in 10 patients. CAI and OAHI were abnormal in 9 and 17 patients respectively. There was no significant correlation between opioid dose and polysomnographic results. **Conclusion** In patients with advanced cancer receiving opioid analgesia, there was a high prevalence of respiratory disturbance, both central and obstructive, and deranged sleep patterns. Addressing sleep disordered breathing in cancer patients has the potential to improve day-time drowsiness and quality of life.

Keywords

Cancer, palliative care, respiratory disturbance, sleep apnea, quality of life

Introduction

Sleep disturbance in patients with advanced cancer has been identified as a significant contribution to symptom burden and is often poorly treated (1). The mechanisms are complex and include pain, anxiety, depression, medications, and gastrointestinal disorders. Sleep studies may be used to define the nature of disordered sleep in an attempt to identify aspects that are amenable to therapy.

Sleep disordered breathing (SDB) is the repeated interruption of ventilation during sleep leading to arousal or partial arousal and oxygen desaturation (2). Obstructive sleep apnoea is related to the repetitive or partial collapse of the pharyngeal airway leading to hypoxia, and has an incidence of 5-34% in the general population (3,4). Central sleep apnoea reflects a reduced response to hypercapnia in central chemoreceptors and is associated with a lack of rib cage and abdominal expansion. It is rare, with an incidence in the general population probably less than 1% (5).

The adverse impact of long term opioids on sleep patterns in adults without cancer has been well demonstrated (6,7), but little is known about shorter term use in the palliative care setting. Abnormal sleep/wake patterns have been documented in patients with advanced solid tumours with reduced quantity and quality of nocturnal sleep and episodes of sleep occurring during the day (8). Almost three-quarters of the patients were receiving opioid therapy but the effect on breathing patterns was not explored.

It is thought that respiratory depression secondary to opioid use is not a common problem encountered in palliative care clinical practice when opioids are carefully titrated to control pain (9). Whilst respiratory depression in patients on opioids is rarely seen during the day, concern has been expressed that it may be more common than previously recognised at night during sleep, with consequent adverse effects on quality of life. In a previous case series from this group, two of three women with metastatic breast cancer on high dose opioids who underwent sleep studies were shown to have severe central sleep apnoea (10).

The literature suggests that central apnoea is a common complication of chronic opioid therapy in adults without cancer, affecting between 30-90% of patients (11-13). Moreover, it can be reversed following opioid withdrawal (14). Most studies have been carried out in patients on methadone maintenance programs or from patients referred to sleep disorder clinics. The distinguishing sleep disordered features in patients receiving opioid medications include greater severity of disturbance during non REM compared to REM sleep and ineffectiveness of nasal CPAP (15). The effect may be dose related (13,16), but in the palliative care setting, opioid dose reduction may not be feasible.

In addition to central apnoea, opioids may cause or exacerbate obstructive sleep apnoea. This has been demonstrated in patients on methadone maintenance programmes where the effect was not clearly related to dose (17).

The present study was designed to assess the prevalence of sleep disordered breathing in a series of patients with malignant disease, the majority of whom were on chronic opioid therapy. Polysomnography was used to determine the frequency of central and obstructive sleep apnoea and any correlation with medications, diagnosis or co-morbid conditions.

Patient and Methods

Eligible patients were those with malignant disease admitted to Mater Health Services, Brisbane, known to the palliative care service, having no change in opioid dose during the preceding 48 hours, willingness to undergo a formal sleep study whilst an in-patient, and the ability to give fully informed written consent.

Exclusion criteria comprised; acutely unwell (eg sepsis, pulmonary embolus, myocardial infarction), unstable medical condition/symptoms that that would prevent compliance with all trial requirements, resting oxygen saturation levels <90% on room air, chest infection, acute exacerbation of COPD or asthma or other reversible pulmonary disease and any known sleep disordered breathing.

Baseline assessment

Participants provided a detailed medical history including respiratory illnesses, co-morbidities and sleep pattern followed by a physical examination. Demographics collected at baseline included; age, sex, malignant diagnosis, date of diagnosis, height and weight. Comorbidities were assessed using the Charlson Comorbidity index, the New York Heart Association (NYHA) Classification and the Australian – modified Karnofsky Performance Status (AKPS) (18,19). Also documented were: opioid dose (oral morphine equivalent (OME)) (20) and duration of use, concomitant medications such as benzodiazepines or other sleeping tablets, cigarette and alcohol use.

The anatomy of the oral cavity; specifically, the visibility of the base of uvula, faucial pillars (the arches in front of and behind the tonsils) and soft palate was examined pre-sleep test to determine a Mallampati score (21). A high Mallampati score (class 4) is associated with a higher incidence of obstructive sleep apnoea. Other factors that might predispose to sleep apnoea assessed included Body Mass Index (BMI), neck circumference and the Berlin Questionnaire (22). This 10-item questionnaire enquires about snoring behaviour, wake time sleepiness or fatigue, and the presence of obesity or hypertension in 3 categories. A positive result in 2 or more categories equates with a chance of apnoea.

A number of assessments were undertaken to measure the possible adverse effect of sleep disturbance on overall quality of life. The Epworth Sleepiness Scale (23) is a self- administered questionnaire that provides a measurement of the patients' general level of daytime sleepiness. It scores the chance of sleep in a number of situations (eg watching television) on a scale from 0-3. A total score of >10 is consistent with abnormal day-time sleepiness. The Stanford Sleepiness Scale (24) is a 7-point self-rating scale used to quantify progressive steps in sleepiness from "wide awake" to "sleep onset soon". The Wu Cancer Fatigue Scale (25) is a nine question, five point scale, with a range of possible scores from five to 45. The lower the score, the better the fatigue.

Participants completed the Hospital Anxiety and Depression Scale (HADS) (26) - a 14-item scale, with seven items measuring anxiety (HADS-A) and seven measuring depression (HADS-D). Scores range from 0 to 21 for each scale, higher numbers represent more distress.

Study procedure

A Somté (Compumedics, Melbourne, Australia) unattended polysomnogram was performed at the patient's ward bedside. The device was set up in the evening and taken down in the morning by a member of the Sleep Unit or the nurse who

was looking after the patient. Patient observations could be carried out during the night if required without interfering with data. A minimum of eight hours data collection was considered ideal for optimal data analysis. Overnight staff in the sleep disorders unit responded to any queries from the ward staff and a sleep physician was available on call.

The results were scored manually according to standard techniques (27). Of particular interest were: total sleep time, arousal index, total apnea hypopnea index (AHI), central apnoeic index (CAI), obstructive apnoeic hypnoea index (OAHI) and oxygen desaturation index (ie % time where Hb-O2 saturation is < 90%). The definition of central versus obstructive events and apnoea vs hypopnea were according to standard criteria (27). An AHI greater than 5 per hour was regarded as abnormal

Sample size and Analysis.
It was planned to include three groups of approximately ten patients participants per group:
- patients on high dose opioid >200mg/day OME
- patients on moderate dose opioid ≥40 - 200mg/day OME
- patients on low dose (<40mg OME/day)/no opioid therapy

Statistical analysis
Frequencies and descriptive statistics were determined for all variables based on the type of measure. The prevalence of sleep apnoea overall, and by group, was determined. Bivariate analyses (correlations or chi-square tests) was tested for associations between central sleep or obstructive apnoea and potential predictors. Simple logistic regression analyses was used to assess the relationship between sleep apnoea and each of the potential predictors, and also the opioid dose, for the entire sample.

Results

Sleep studies were performed on 28 patients (19 male), 25 of whom were receiving regular opioid medications. Of these, 14 were on fentanyl transdermal (1 plus methadone, 1 plus morphine), 9 on oxycodone (1 plus morphine), 1 on hydromorphone, 1 on methadone, morphine and oxycodone.

Participants had a range of malignancies, most commonly prostate (7), genitourinary (4) and lung (3). The median age and performance status was 72 years (range 43 -91) and 60 (range 40-90). The median BMI was within the healthy population BMI range at 24.5 (range 17.3 - 35.1).

Total sleep time ranged from 3.1 to 9.9 hrs (median 6.5 hr). Overall, 7 of 28 had no evidence of any sleep disturbance. Of the 3 participants not on opioids, 1 sleep study was normal and 2 were moderately abnormal (AHI 10 and 18). CAI was normal in all those not receiving opioids. The patterns of abnormalities are shown in Table 1.

In patients receiving opioids, two patients had an abnormal CAI only, 12 OHAI abnormalities and 7 demonstrated a mixed pattern. The severity of abnormalities in 9 patients with CAI >5 events /hr ranged from 7-126. In 8 of these the OAHI was also abnormal. OAHI was greater than 5 events/hr in 18 patients. Four were severe and exceeded 30 events/hr. Two of the latter had concurrent abnormalities in CAI. The total AHI ranged from 0-129 events/hr (median 16.5). Ten patients had an AHI >30 events/hr. Arousal index was outside the normal range of 10-25 in 11 cases and exceeded 50 in 6 patients. The percentage time that oxygen saturation fell below 90 ranged from 0-95% (median 8%). In 6 patients this was for more than 50% of the observation time.

When analysed with regard to OME in 24 hours grouped into low (0-40, medium (40-200 and high dose (>200,) there was no overall correlation with AHI, CAI or OAHI. The Arousal Index was not influenced by OME.

The Mallampatti score was 1 in most patients. The OAHI in 3 patients with scores over 3 were all high - 107, 23, and 22 events/hr respectively, however a low Mallampatti score did not exclude an abnormal result. Twelve participants had a high risk of apnoea from the Berlin questionnaire.

With regard to sleepiness and fatigue measures, the Epworth Sleepiness Score was abnormal (>10) in 10 patients, Stanford Sleep Scale was 2 or less (suggesting full alertness) in 6 patients. The Wu index was over 20, suggestive of considerable fatigue, in 12 patients. On HAD scoring, 7 participants demonstrated significant anxiety and 8 significant depression (scores>7). None of these outcomes appeared have a significant correlation with any of the polysomnographic data.

Similarly, there was no correlation with any of the other variables measured ie co-morbidities, concomitant medications or other sleeping tablets, cigarette and alcohol use.

Discussion

In this study the majority of patients with advanced cancer had evidence of sleep disordered breathing as reflected by an abnormally high AHI. The patterns observed were consistent with apnoea that was predominantly obstructive in nature, and less frequently central in origin or a mixture of the two. In the 3 cases previously reported by Hardy et al (10), one patient had severe central apnoea (121 episodes/hour) a level that was observed in only one participant in the present series. The second patient also had severe central apnoea, but this was combined with a moderate obstructive element.

Disturbed sleep in patients with cancer has been widely reported (28) and the adverse impact of sleep disturbance on the quality of life of patients receiving palliative care has been emphasised (29). In a recent study using ambulatory polysomnography in 114 patients with cancer (8), 17% achieved less than 5 hours sleep per night. A curvilinear relationship has been demonstrated between mortality and sleep in patients with advanced cancer (30). Seventy-three of the

sample population were receiving opioid medication and this was associated with a small but significant increase in Stage 2 REM sleep. No other specific sleep characteristics were noted with opioids whereas serotonin uptake inhibitors and beta blockers were both associated with reduced sleep time and beta blockers also increased daytime REM sleep. No attempt was made to evaluate the possible contribution of apnoea to sleep disturbance in this study.

Sleep disordered breathing associated with long term opioid therapy in adults without cancer has also been widely reported (11,13) although the precise nature of such disorders has not been clearly defined. A recent systematic review (31) suggested that opioids were associated with a moderately increased risk of central, but not obstructive, apnoea. In contrast, a study in adults receiving methadone, observed obstructive apnoea to be the dominant abnormality (17). In the 71 patients studied, 35% had OSA and 14% CSA.

There are fewer data on the acute or short term use of opioids, particularly in the palliative care setting, where formal evaluation using polysomnography is likely to be impractical and access to sleep laboratory expertise difficult. In a study of healthy volunteers, 42 subjects received either placebo, sustained release morphine (15mg) or methadone (5 mg). This was a double blind crossover study over three consecutive nights (32). Total sleep time was not altered. Both drugs reduced arousal index and to a significant extent with methadone. There was no difference in OAHI between the three groups. The adverse effects of oral and intravenous opioids on breathing during sleep and sleep architecture also has been demonstrated in healthy adults (33,34).

The influence of opioids on both breathing rhythm and control of ventilation may increase the risk of central sleep apnoea. Obstructive sleep apnoea may also be exacerbated by opioids due to relaxation of pharyngeal tone and increased airway collapsibility (35). In view of the potential impact of sleep disordered breathing on both physical and psychological morbidity, it would seem appropriate to consider whether, particularly in those patients under palliative care who are not at end of life and who may have a longer life expectancy, are screened to anticipate potential sleep problems. In the present study a number of possible predictive factors were evaluated, but none were associated with sleep disordered breathing, possibly because of the relatively small sample size.

Continuous Positive Airways Pressure (CPAP) has been shown to be of benefit in obstructive apnoea but may not assist central apnoea. A more complicated 'servo controlled 'technique has been recommended to assist ventilation in this condition (16,36). Simpler measures include oral appliances fitted by orthodontists and worn at night, that move the tongue and mandible forward thus enhancing airway patency (37).

The major limitation of this study was the small sample size. This meant there was potential for sample bias, selection bias, and limited ability to empirically evaluate covariates. It was also limited by the fact that polysomnography was not performed on a larger number of patients not receiving opioids. As baseline polysomnography data prior to initiation of opioid therapy was not available, it

is difficult to conclude unequivocally whether the findings are due to opioid therapy or other characteristics of these patients with advanced cancer.

In conclusion, this study has confirmed a high prevalence of sleep disturbance and sleep disordered breathing in this set of patients with advanced cancer. Further research is needed to define the effect of advanced cancer and opioid usage on sleep disorders. This will help to guide future interventional studies aimed at improving quality of life.

Disclosure/Conflict of Interest:
All of the authors have nothing to disclose.

Acknowledgements:
We would like to acknowledge Queensland Sleep for performing the sleep studies.

Funding:
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1) Yennurajalingam S, Tayjasanant S, Balachandran D, et al Association between daytime activity, fatigue, sleep, anxiety, depression, and symptom burden in advanced cancer patients: A preliminary report. J Palliat Med 2016 ;19:849-856.

2) Dempsey JA, Veasey SC, Morgan BJ,et al. Pathophysiology of sleep apnea. Physiol Rev.2010; 90:797-8.
3) Lee W, Nagubadi S, Kryger, MH et al. Epidemiology of obstructive sleep apnea: A population-based perspective. Expert Rev Respir Med 2008 ;2: 349-364

4) Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013;177(9):1006–14

5) Orr JE, Malhotra A, Sands SA. Pathogenesis of central and complex sleep apnoea. Respirology 2017 ;22:43-52.

6) Hassamal, S, Miotto K,, WangT,et al A narrative review: The effects of opioids on sleep disordered breathing in chronic pain patients and methadone maintained patients. Am J Addict, 2016; 25: 452-465

7) Panagiotou I, Mystakidou K. Non-analgesic effects of opioids: opioids' effects on sleep. Curr Pharm Des 2012;18:6025-6033

8) Parker KP, Bliwise DL, Ribeiro M, et al Sleep/Wake Patterns of Individuals with Advanced Cancer Measured by Ambulatory Polysomnography. J Clin Oncol 2008;26:2464-2472

9) Currow DC, Ward AM, Abernethy AP (2009). Advances in the pharmacological management of breathlessness. Curr Opin Support Palliat Care; 3: 103-106

10) Hardy J, Bowler S . Central sleep apnoea in cancer patients on opioids. J Pain Symptom Management 2010; 40: e3-e5

11) Farney RJ, Walker JM, Coward TV et al . Sleep-disordered breathing associated with long-term opioid therapy. Chest, 2003;123;632-639

12) Wang D Teichtahl H, Drummer O, et al. Central sleep apnea in stable methadone maintenance treatment patients. Chest 2005; 128:1348-1356

13) Walker JM, Farney RJ, Rhondeau S, et al . Chronic opioid use is a risk factor for the development of central sleep apnea and ataxic breathing. J Clin Sleep Med 2007; 3:455-461

14) Ramar K. Reversal of sleep disordered breathing with opioid withdrawal. Pain Pract 2009;9;394-398

15) Zutler M, Holty JE. Opioids, sleep, and sleep-disordered breathing. Curr Pharm Des.2011;17: 1443-1449

16) Javaheri, S, Athar Malik, Smith, J et l.. Adaptive pressure support servoventilation: a novel treatment for sleep apnea associated with use of opioids. J Clin Sleep Med 2008;4: 305-310

17) Sharkey, KM, Kurth, MD, Andersen, BJ et al Obstructive sleep apnea is more common than central sleep apnea in methadone maintenance patients with subjective sleep complaints. Drug Alcohol Depend 2010;108:77-83.

20) Australian College of Rural and Remote Medicine (2014) GP Pain Help. Centre for Palliative Care Research and Education. Available from http://www.gppainhelp.com/Dose_Conversion.html. (Accessed 20June 2017)

21) Nuckton TJ, Glidden DV, Browner et al. Physical examination: Mallampati score as an independent predictor of obstructive sleep apnea. Sleep 2006;29:903-908

22) Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome .Ann Intern Med 1999;131:485-91

18) Groot V, Beckerman H, Landhorst G, Bouter L. How to measure comorbidity: a critical review of available methods. J Chron Dis. 1987;40:373-83.

19) Abernethy, AP, Shelby-James T, Fazekas B, Woods D, Currow DC. The Australian-modified Karnofsky Performance Status (AKPS) scale: a revised scale for contemporary palliative care clinical practice. BMC Palliat Care 2005;4:7. doi:10.1186/1472-684X-4-7

23) Johns MW. A New Method for Measuring Daytime Sleepiness: Epworth Sleepiness Scale.. Sleep 1991; 14: 540-545.

24) Hoddes E, Zarcone V, Smythe H et al. Quantification of Sleepiness; a new approach. Psychophysiology 1973;10:431-436.

25) Wu H, Wyrwich K, McSweeney M. Assessing fatigue in persons with cancer: further validation of the Wu Cancer Fatigue Scale. J Pain Symptom Manage 2006;32:255-265.

26) Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-70

27) Iber C, Ancoli Israel S, Chesson Jr A, Quan S The AASM manual for the scoring of sleep and associated events. Westchester, IL: Am Acad Sleep Med. 2007.
28) Sheely LC. Sleep disturbances in hospitalized patients with Cancer. Oncology Nursing Forum 1996; 23: 109-111

29) Hajjar RR. Sleep disturbance in palliative care. Clinics in geriatric medicine. 2008 Feb 29;24(1):83-91.

30) Collins KP, Geller DA, Antoni M, Donnell DM et al. Sleep duration is associated with survival in advanced cancer patients Sleep Med. 2017;3:208-212

31) Filiatrault, ML, Chauny, JM, Daoust, R et al. Medium increased risk for central sleep apnea but not obstructive sleep apnea in long-term opioid users: A systematic review and meta-analysis. J Clin Sleep Med 2016; 12: 617-625

32) Drimsdale, JE. Norman, D. DeJaAHIn, D et al. The effect of opioids on sleep architecture. J Clin Sleep 2007 Med; 3 :33-36

33) Robinson RW, Zwillich CW, Bixler EO et al. Effects of oral narcotics on sleep-disordered breathing in healthy adults. Chest 1987;91:197-203.

34) Shaw IR, Lavigne G, Mayer, P et al. Acute intravenous administration of morphine perturbs sleep architecture in healthy pain-free young adults: a preliminary study. Sleep 2005 ;28:677-82

35) Pattinson, KTS. Opioids and the control of respiration. Br J Anaesth 2008; 100 :747-58

36) Reddy R, Adamo D, Kufel T et al . Treatment of opioid-related central sleep apnea with positive airway pressure: a systematic review. J Opioid Manag 2014; 10: 57-62

37) Norman D, Loredo JS. Obstructive sleep apnea in older adults. Clin Geriatr Med.2008;24:151-65

Table1. Results of Polysomnography

OME	Total Sleep Time	CAI Events/h	OAHI Events/h	AHI Events/h	AI Events/h	%Time $Sa0^2$<90%
270	7.4	9	1	9.5	11.4	0
135	6.9	1	1	2	1.2	0.2
270	9	0	1	1.8	16	5
135	6.2	1	**107**	**108**	**102**	37
160	6.1	**35**	**20**	**54**	29	27.2
80	8.9	0.3	0.5	2.5	4.4	0.2
877	9.7	1.4	**6.4**	7.9	19.7	0.2
510	6.8	0	**16.8**	**16.8**	19.6	11
1110	4.9	**25.9**	**22.9**	**48.8**	**59.7**	95.8
1150	6	0	0	1.5	11	0.1
180	8.5	**15.8**	**22.5**	**38.3**	**37.6**	-
40	9.8	0	0	0	**26.4**	8.4
135	7.8	0.5	**34.8**	**35.3**	**22.9**	0
1970	7.8	**42.9**	**28.9**	**71.7**	**51**	-
60	6.7	1	**11.6**	**12.7**	14.6	0
200	6.9	0	**16.4**	**16.6**	**26.2**	54.2
135	7.2	1.8	**52.8**	**55**	**53**	24
580	4.8	0	0	0	4.6	0
30	6.6	4.4	**13.55**	**18**	**21.6**	10
560	4.1	**8.6**	**5.2**	**13.8**	5.7	0.2
200	8.9	2.6	**113.28**	**115.9**	**107.1**	95
0	5.9	0	**17.56**	**17.56**	**24.7**	20
0	3.05	0	2.3	2.3	12.5	-
225	9.9	**126.3**	2.34	**128.6**	**44**	9
387	9	**26.8**	**11**	**37.8**	**39**	4
20	3.1	0	**15.36**	**15.36**	15	0.4
0	3.2	**7.2**	**9.6**	**116.8**	**56.9**	2.5
313	6.33	0	**6.95**	6.95	11.8	25

OME = Oral morphine equivalent mg/24 hours
CAI = Central Apnoea Index
OAHI = Obstructive Apnoea Hypopnoea Index
AHI = Apnea Hypopnea Index
AI = Arousal Index

Abnormal results in bold.