Anaesthetists' Knowledge of Appropriate Adrenaline Administration in Three Clinical Scenarios

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DECLARATION

I, Prodromos Christopher Anamourlis declare that this research report is my own work. It is submitted for the admission to the degree of Master of Medicine in Anaesthesiology by the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

…………………………………….. (Signature of candidate)

27th day of February, 2015

ABSTRACT

Lack of knowledge and clinical experience in the event of an emergency are a lethal combination. Adrenaline is the drug of choice for resuscitation during cardiovascular collapse. Incorrectly dosing patients with adrenaline can lead to death by overdose or by undertreating the emergent condition. This highlights the importance, not only of resuscitation protocols but also the physician's knowledge of and adherence to such guidelines. Research has consistently shown that physicians commonly make dosing mistakes during emergencies concerning adrenaline. Identifying whether or not this is due to a deficit in knowledge is important in understanding how to improve the outcomes of patients in such emergencies.

The aim of this study was to determine the knowledge of anaesthetists working in the Department of Anaesthesiology at the University of the Witwatersrand regarding the appropriate administration of adrenaline for anaphylaxis, cardiac arrest and inotropic infusions.

This was a prospective, contextual, descriptive study on a sample of anaesthetists working in the Department of Anaesthesiology at the University of the Witwatersrand. Anaesthetists who were willing to participate in the study were given a brief introduction to the study and a questionnaire to complete regarding adrenaline doses in three different clinical scenarios. Data collection took place during February 2014 and June 2014. Anaesthetists' knowledge of adrenaline was analysed using descriptive and inferential statistics.

The knowledge of Wits anaesthetists regarding adrenaline use in cardiac arrest, anaphylaxis and as an infusion, is inadequate. A total of 104 anaesthetists answered the questionnaire (n=104). The pass rate for the questionnaire was 14% (n=15). The median score for the questionnaire was 50%. A statistically significant difference was found between the pass rates of those anaesthetists who had attained an ACLS course and those who had not (p=0.0339). A weak correlation was found between anaesthetists knowledge and years of anaesthetic experience (r=0.2460). When comparing the knowledge of anaesthetists between different professional designations, a statistically significant difference was found between the intern groups' knowledge and the consultants (33% vs 67%: p=0.0013).

The study questionnaire uncovered major knowledge deficits in Wits anaesthetists, and revealed that ACLS certification improved knowledge in anaesthetists. This study warrants educational intervention and future investigation into knowledge improvement.

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ABBREVIATIONS

HPCSA: Health Practitioner's Council of South Africa

Wits: The University of the Witwatersrand

ANS: Autonomic nervous system

SNS: Sympathetic nervous system

PNS: Parasympathetic nervous system

ENS: Enteric nervous system

NTS: Nucleus tractus solitaries

VMC: Vasomotor centre

COMT: catechol-O-methyltransferase

MAO: monoamine-oxidase

cAMP: cyclic adenosine monophosphate

ACLS: Advanced cardiac life support

CPR: Cardiopulmonary resuscitation

ROSC: Return of spontaneous circulation

CHAPTER 1: Overview of study

1.1 Introduction

In this chapter an overview of the study is given and will include the background to the study, the problem statement, aim and objectives, demarcation of the study field, ethical considerations, research methodology, significance of the study, research report outline and a summary.

1.2 Background

Providing healthcare is both a science and an art. The science driving this process is often revisited for the benefit of maintaining or improving knowledge. The implementation of such knowledge is the licence we work under and the art that we so intimately engage with. As anaesthetists, an in-depth understanding of pharmacology is required to make informed decisions about patient care.

It is increasingly difficult to stay up to date with the breadth of knowledge in the field of anaesthesiology and related pharmacological practice, as it grows daily. Drug doses, effects, side-effects and interactions are crucial to the correct practice of anaesthesia, and especially relevant in the event of an emergency. Lack of knowledge and clinical experience in the event of an emergency, are a lethal combination. Adrenaline is the drug of choice for resuscitation during cardiovascular collapse, the dose of which should be tailored to the profile of the patient and clinical emergency. Incorrectly dosing patients with adrenaline can lead to death by overdose or by undertreating the emergent condition. To improve the quality of care and decrease the variation in practice (1), standard practice guidelines are endorsed by medical councils the world over. (2-4)

In the anaesthetic setting, cardiac emergencies are relatively common, with international management protocols in place for the correct guidance of such situations (5). Although the causes of cardiovascular collapse may be numerous, treatment often involves the use of adrenaline, whether in incremental doses or as an infusion. Doses and modes of administration can be confusing (6) and hence the use of protocols to drive successful resuscitation and ameliorate variation in treatment (1). Despite guidelines, clinical case studies are reported regularly, highlighting the shortcomings in physicians' knowledge on the correct dosing of adrenaline (7-15). Commonly reported scenarios involve emergencies relating to anaphylactic events and cardiac arrest, where a standard initial adrenaline dose is required with or without subsequent doses or infusions, depending on the emergency (3, 5).

Cases of anaphylactic shock being administered cardiac arrest doses of adrenaline have been reported (6). Reports of cardiac arrest patients being overdosed with adrenaline, leading to severe and near fatal cardiomyopathies or cardiac dysfunction, have also been documented (7-15). Regarding inotropic infusions, significant drug dosing errors can be made when preparing infusions, regardless of clinical experience (16). No studies were identified with regard to inadequate doses being given as infusions. This highlights the importance, not only of resuscitation protocols but also the physician's knowledge of and adherence to such guidelines.

Cabana et al. (17) have shown that the implementation of emergency protocols and standard practice guidelines has had a limited effect on the behavioural change of physicians (18-20), identifying attitude as the major barrier to physician's adherence to protocol based practice (17). Other barriers include physician knowledge and behaviour, which affect the ability of the physician to successfully execute emergency protocols (17).

1.3. Problem statement

Doctors specialising in anaesthesiology are expected to know the appropriate resuscitation guidelines regarding the use of adrenaline for anaphylaxis, cardiac arrest and inotropic infusion. In each scenario specific doses and routes of administration are recommended (3, 4). It was not known if anaesthetists working in the Department of Anaesthesiology, at the University of the Witwatersrand (Wits) knew how to appropriately administer adrenaline in an emergency.

1.4. Aim and objectives

1.4.1 Aim

The aim of this study was to determine the knowledge of anaesthetists working in the Department of Anaesthesiology at Wits regarding the appropriate administration of adrenaline for anaphylaxis, cardiac arrest and inotropic infusions.

1.4.2 Objectives

The primary objectives of this study were to:

- describe the knowledge of anaesthetists regarding adrenaline doses in three different clinical scenarios
- compare whether the overall knowledge of anaesthetists, with and without ACLS certification, regarding adrenaline was adequate
- compare whether the knowledge of anaesthetists, with and without ACLS certification, regarding each scenario was adequate
- correlate knowledge of adrenaline with years of anaesthetic experience

The secondary objective was to:

- compare the knowledge of anaesthetists between different professional designations.

1.5. Research assumptions

The following definitions were used in the study:

Anaesthetist: in this study, an anaesthetist refers to all doctors (interns, medical officers, registrars, and consultants) who were working in the Department of Anaesthesiology.

Professional designation: in this study, the anaesthetist's rank in the department e.g. intern, is defined as the professional designation.

Intern: a qualified doctor who has not yet completed their internship, and who was busy completing the required training in the Department of Anaesthesiology.

Medical officers: a qualified doctor who was registered with the Health Practitioners Council of South Africa (HPCSA) as an independent practitioner practicing anaesthesia under specialist supervision. A distinction was made between junior medical officers and career medical officers. Career medical officers were considered as consultants.

Registrars: a qualified medical doctor who was registered with the HPCSA as a registrar in the specialty of anaesthesiology.

Consultants: any anaesthetist who has completed the required South African College of Medicine examinations and who is registered with the HPCSA. Career medical officers were included in this category.

Knowledge: in this study, knowledge refers to the medical knowledge that a physician possesses regarding standard practice guidelines, protocols and algorithms relating to adrenaline.

Adequate knowledge: in this study an overall score of 80% and above is considered adequate knowledge (pass mark). Adrenaline is a drug often used in emergencies. Adequate knowledge in emergencies has previously been defined as 80% and above (21).

1.6 Demarcation of study field

This study was conducted in the Wits Department of Anaesthesiology. Wits Medical School is affiliated with: Chris Hani Baragwanath Academic Hospital, Charlotte Maxeke Johannesburg Academic Hospital, Helen Joseph Hospital, Rahima Moosa Mother and Child Hospital and The Wits Donald Gordon Medical Centre.

The level of doctors within this department ranges from interns to senior consultants. The department has approximately 15 to 20 interns, 24 medical officers, 107 registrars, and 74 consultants.

1.7 Ethical considerations

Permission to conduct the study was obtained from the relevant authorities. This study was knowledge-based, using an anonymous self-administered questionnaire (Appendix

4). The questionnaires were voluntary and consent was implied on completion of the questionnaire. Care was taken to maintain anonymity and confidentiality of the anaesthetists involved.

The study was conducted in accordance with the Declaration of Helsinki (22) and the South African Good Clinical Practice Guidelines (23).

1.8 Research methodology

1.8.1 Research design

This study was prospective, contextual and descriptive.

1.8.2 Study population

The study population consisted of anaesthetists working in the Department of Anaesthesiology at Wits.

1.8.3 Study sample

In consultation with a bio-statistician a sample of 85 anaesthetists was estimated and a convenience sampling method was used.

1.8.4 Inclusion and exclusion criteria

All anaesthetists who attended the weekly academic meetings and who were willing to participate in the study were included. Incomplete questionnaires returned were included and a score of zero was allocated to unanswered questions.

Blank questionnaires returned were excluded.

1.8.5 Data collection

Development of questionnaire

No questionnaires pertaining to the appropriate administration of adrenaline were identified in the literature. A draft questionnaire based on a review of the literature was developed.

The self-administered questionnaire (Appendix 4) consisted of two sections. Section 1 included the demographic data. Section 2 consisted of questions regarding the knowledge that anaesthetists have on the dose and route of administration of adrenaline in the three scenarios.

Data collection process

Data was collected during February and June 2014.

Before distribution of the questionnaires, all sheets were numbered so as to keep track of questionnaires completed.

Questionnaires were distributed and anaesthetists decided whether to participate or not, following a brief introduction to the study aim and objectives. Those who agreed to participate received an information letter (Appendix 3) along with the questionnaire (Appendix 4).

After completion of the questionnaire, the participant placed the questionnaire into an envelope, sealed it and dropped it into a collection box. This ensured anonymity and confidentiality of the anaesthetists participating in the study.

1.8.6 Data analysis

Using Microsoft Excel 2010, data was captured onto spreadsheets. The statistical program, GraphPad InStat, was used to analyse data.

1.9. Significance of the study

Adrenaline is the most commonly used emergency drug. The incorrect dose of adrenaline may cause the death of the patient, an inadequate dose may not correct the cardiovascular collapse and an overdose may lead to myocardial infarction, lethal dysrhythmias and cerebrovascular accidents (6, 8-10, 14, 24-26). Therefore, it is detrimental to patient safety if adrenaline doses are not known.

Case studies, the world over, have documented incidents of inappropriate adrenaline doses in situations ranging from anaphylaxis to cardiac arrest (6-11, 14, 15, 27). The cause of this is thought to be deficits in doctors' knowledge of adrenaline (17, 25). For this reason it was imperative that the current knowledge of anaesthetists working in the Department of Anaesthesiology at Wits was determined. The results from this study may contribute to the awareness of anaesthetists' correct use of adrenaline, which may influence patient safety.

1.10. Validity and reliability of the study

Measures were put into place to ensure the validity and reliability of this study.

1.11. Research report outline

The report will be discussed as follows:

Chapter 1: Overview of study

Chapter 2: Literature review

Chapter 3: Methodology

Chapter 4: Results and discussion

Chapter 5: Summary, limitations, recommendations and conclusion

1.12. Summary

This chapter gave an overview of the study background, the problem statement, aim and objectives, demarcation of the study field, ethical considerations, research methodology, significance of the study, and a research report outline. Chapter 2 follows with the literature review.

CHAPTER 2: Literature Review

2.1 Introduction

In this chapter, the literature regarding adrenaline knowledge of anaesthetists will be discussed. The literature review will give background to the problem at hand, and then discusses the anatomy and physiology of adrenaline as well as the pharmacology important to understanding adrenaline. To contextualise adrenaline use in anaphylaxis, cardiac arrest and as an infusion, the importance of adrenaline will be deliberated, with reference to the significance of knowing the correct doses and an attempt at explaining the possible reasons for dosing mistakes in each context. A brief discussion on the way that knowledge and attitude affects behaviour will also be explored.

2.2 Background

Anaesthetists need to have an in-depth understanding of pharmacology to make informed decisions about patient care. This has become increasingly difficult as the breadth of knowledge in anaesthesia and related pharmacological practice grows daily. Drug doses, effects, side-effects and interactions are crucial to the correct practice of anaesthesia, and especially relevant in the event of an emergency. During the management of an emergency situation, lack of knowledge and clinical experience are a lethal combination. Adrenaline is often the drug of choice for resuscitation during cardiovascular collapse. Anaesthetists, however, use exogenous adrenaline in everyday clinical practice for vasoconstriction and inotropic support during cardiac arrest and anaphylaxis. Although these life threatening emergencies are infrequent, the correct management using adrenaline needs to be known. The incorrect dose of adrenaline may cause the death of a patient. An inadequate dose may not correct the cardiovascular collapse, and an overdose may lead to myocardial infarction, lethal dysrhythmias and cerebrovascular accidents. (28)

For this reason, under standard practice guidelines, many international institutions use algorithmic protocols for the specified emergency. Training of anaesthetists in South

Africa is less protocolled and therefore the extent of the anaesthetists' knowledge of the doses of adrenaline in emergencies is not known.

Clinical practice guidelines are defined as, "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" (24). Knowledge of standard practice guidelines is extremely important. In emergencies, practical implementation of the guideline not only prompts efficient treatment of the patient, but also improves the quality of care and decreases the variation in practice so often seen with doctors (1, 29). For the anaesthetist, this means that in the event of an emergency, one is able to reliably treat patients where a reversible cause exists. However, despite clinical practice guidelines, case reports document the inappropriate use of adrenaline in various circumstances, often with detrimental effects (6, 8-11, 14, 15, 25).

In order to use adrenaline safely it is important to understand the relevant anatomy and physiology of endogenous adrenaline.

2.3 Anatomy and physiology of adrenaline

Adrenaline is a naturally occurring catecholamine. It is actively secreted by the adrenal glands in response to splanchnic nerve stimulation during times of stress. There are two adrenal glands, each situated on top of a kidney. They comprise two main endocrine organs, the adrenal medulla, which secretes catecholamines and the adrenal cortex, which secretes mineralocorticoids. For the purpose of this literature review, only the adrenal medulla will be discussed. (30)

The adrenal medullas originate from neural crest cells and essentially consist of modified nervous tissue. This collection of postganglionic sympathetic neurones does not have axons and comprise of two types of chromaffin cells, which secrete adrenaline and noradrenaline respectively. Chromaffin cells are responsible for the production and release of the catecholamines, which includes noradrenaline. In addition to adrenaline release, the adrenal medulla is also responsible for the conversion of noradrenaline to adrenaline. The medulla receives blood from the adrenal cortex, already rich in corticosteroids, thus enhancing the production of the enzyme responsible for the conversion process. Within the medulla up to 80% of circulating noradrenaline is converted to adrenaline. However, noradrenaline is also released locally at tissue level. (30)

The mechanisms of action of catecholamines are complex, and depend on what receptors are found on target organs and what the affinity the receptor has for adrenaline or noradrenaline (31). To explain this, a brief overview of the autonomic nervous system (ANS) is required.

2.3.1 The Autonomic Nervous System

The ANS (Figure 2.1) is part of the peripheral nervous system and therefore acts below ones level of consciousness to control visceral function and maintain cardiovascular homeostasis. Classically the ANS is divided into the parasympathetic nervous system (PNS), sympathetic nervous system (SNS) and enteric nervous system (ENS). The medulla oblongata in the brainstem is responsible for the control of this system, specifically the nucleus tractus solitarius (NTS), the vasomotor centre (VMC), and the cranial origin of the vagus nerve (31). For the purpose of this study the SNS will be discussed.

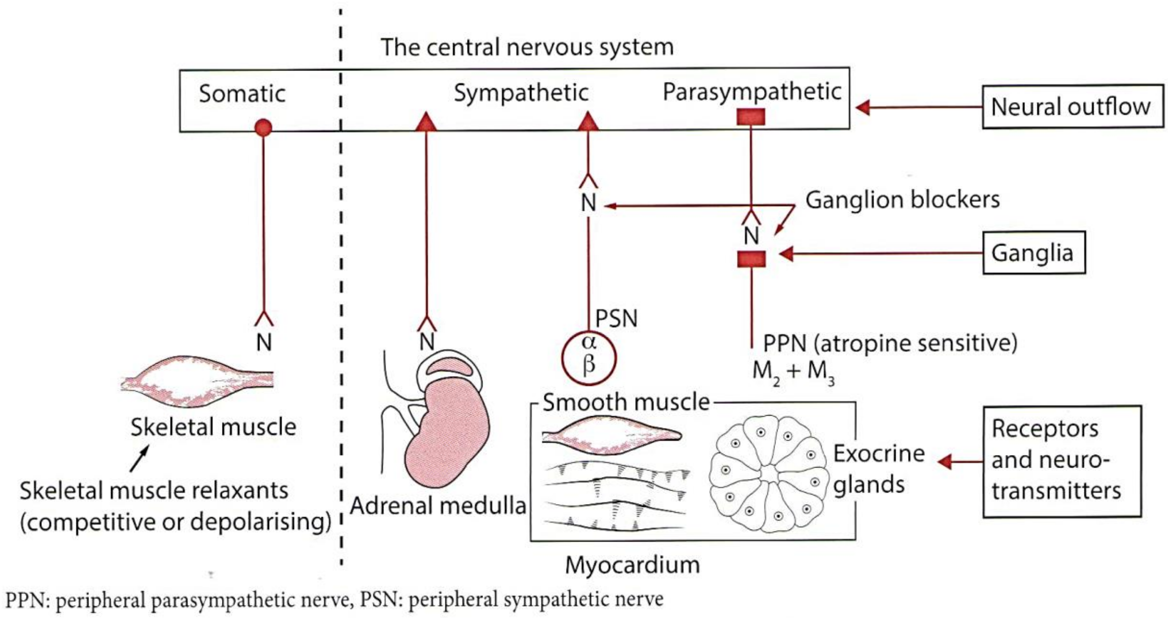


Figure 2.1 Schematic overview of the autonomic nervous system (31)

2.3.2 The SNS: Neural output

Control of the SNS is mediated by aortic and carotid sinus baroreceptors, which form part of a reflex connecting to the NTS. The NTS is rich in noradrenergic cell bodies and nerve endings and hence stimulation of the reflex affects blood pressure, heart rate, blood vessels and the renin-angiotensin aldosterone system (RAAS). The vagus nerve and VMC are controlled by the NTS to affect blood pressure in the following ways. If a normotensive individual has raised blood pressure, the vagus nerve is stimulated to cause bradycardia. This is initiated by a feedback mechanism via aortic mechanoreceptors that respond to stretch when blood pressure rises. Furthermore, the VMC, which is constitutively active, is inhibited to decrease sympathetic output to peripheral blood vessels. During hypotension, the opposite occurs. (30)

2.3.3 The SNS: Neurotransmitters

Noradrenaline, adrenaline and dopamine are involved in controlling the SNS.

Nerve terminal endings of adrenergic nerve fibres produce local noradrenaline in their axoplasm. This is the main neurotransmitter at postsynaptic nerve endings. This process is completed inside the secretory vesicles of the same cell. Its production begins with tyrosine's hydroxylation to dihydroxyphenylalanine, which is then decarboxylated to dopamine. Dopamine is then transported into the vesicles of nerve terminals where it is further hydroxylated to noradrenaline. These vesicles are bubble shaped granules and arise from the Golgi apparatus near the nucleus of the cell. (30, 32)

The methylation of noradrenaline, by phenylethanolamine N-methyltransferase, is responsible for the production of adrenaline, which occurs in the medulla of the adrenal glands. When splanchnic nerves are stimulated, acetylcholine is released from the sympathetic fibres that terminate in the adrenal medulla. This stimulates the release of catecholamines from membrane bound vesicles in the adrenal glands, into the bloodstream, and henceforth exerts their action. (30-32)

Catecholamines have a very short half-life in blood, about 10 to 20 minutes. Catecholamines are metabolised in the following ways; degradation by catechol-O-methyltransferase (COMT) in extra-neuronal tissue, reuptake into the nerve terminal or degradation by monoamine-oxidase (MAO) in nerve endings. MAO's are bound to the mitochondria of cells and are found in abundance at noradrenergic nerve terminals, liver cells and intestinal epithelium. This explains why exogenous catecholamines are not active if taken orally, as deamination would occur before allowed to circulate systemically. The by-products of catecholamines are metanephrines and vanillyl mandelic acid, all of which are renally excreted. (30)

2.3.4 Receptors

Two main groups of receptors exist in the ANS, cholinergic and adrenergic receptors. For the purpose of this review, only adrenergic receptors will be discussed as these are of significance to the mechanism of action of adrenaline. (30, 31)

Adrenergic receptors

This is the main group of receptors through which adrenaline exerts its action. They are divided into two major groups, alpha (α) and beta (β). (31)

The α-receptors comprise two groups, the α_1 and α_2 subtypes, which are post-junctional and pre-junctional respectively.

The α_1-receptors are found on heart muscle and blood vessels coupled to G stimulatory proteins (Gs). Since this G protein-coupled receptor is coupled to the inositol triphosphate (IP) second messenger system, it will activate phospholipase C, thus increasing the production of IP that causes increased calcium levels. It is the binding of calcium to calmodulin that leads to actin-myosin coupling and therefore contraction. The overall cardiovascular effect is through increasing total systemic vascular resistance, which in turn assists in the venous return of blood. This increases the preload to the right side of the heart raising the blood pressure. (31)

The α_2-receptors are found pre-synaptically and post-synaptically. They occur in the central nervous system, nerve terminals, pancreatic islets, platelets and vascular smooth muscle. There are three major effects of α_2-receptor agonism. They act as auto-receptors on presynaptic nerve terminals to decrease noradrenaline release, this works through negative feedback. In the brain, α_2–receptors are associated with reduced sympathetic outflow and are found post-junctionally. Stimulation of α_2-receptors causes decreases in cyclic adenosine monophosphate (cAMP) production with effects that may differ in the central versus the peripheral nervous system. (31)

In the central nervous system stimulation of the receptors causes vasodilation by decreasing outflow from the sympathetic tract. Additionally, they promote sedation, hypnosis, analgesia and neuroprotection, while modulating cognition, mood, sensory processing and locomotor activity. Stimulation of α_2-receptors centrally will also supress shivering. (31)

Peripherally, α_2-receptors cause vasoconstriction, and are found on arteries and veins. In pancreatic cells they inhibit insulin secretion and on lipocytes they inhibit lipolysis. In the gastrointestinal system, the receptors' stimulation results in sphincter contraction, glucagon release and decreases intestinal motility. (31)

The effects described are important as they summate the fight or flight response associated with surges in adrenaline and noradrenaline during a stress response (32).

β -cells are divided into three groups:

- β_1 in cardiac muscle
- β_2 in peripheral receptors
- β_3 in lipocytes. (31)

The β_1-receptors are coupled with G-stimulatory proteins (Gs). Gs protein-coupled receptors use cAMP as their second messenger system. Stimulation of these receptors therefore results in the conversion of adenosine triphosphate (ATP) into cAMP by activation of adenyl cyclase. This activates protein kinase A, which in turn phosphorylates a series of cascade proteins that activate a cellular reaction depending on the type of cell stimulated. Of importance are cardiomyocytes where cAMP activation will result in a positive inotropic effect because of the influx of calcium into the cell. In addition to this action the renin-angiotensin-aldosterone system is also activated to increase the absorption of sodium and therefore water by the kidneys. This assists in increasing the blood volume and hence blood pressure. (31)

The β_2-receptors are also coupled to the cAMP-dependant pathways but through a G-inhibitory (Gi) receptor. Thus the downstream effects here are seen to be a reduction in cytosol Ca^{2+} found in smooth muscle and thus an overall vasodilator effect. In addition to the vascular effect they are also important in the lungs where they act again on smooth muscle of the bronchial tree, therefore mediating a bronchodilator effect when stimulated. (31)

2.4 Pharmacology of adrenaline

The structure of adrenaline (Figure 2.2) is important as the activity of the molecule is rendered by specific chemical moieties. This dictates the clinical effect on target organs. All catecholamines are β phenylethylamines, meaning that they have sympathomimetic activity. The hydroxyl groups found at positions three and four of the phenyl ring is important because:

- they confer maximum intrinsic activity at α and β receptors;
- it makes the molecule more water soluble and hence cannot cross the blood: brain barrier;
- it allows breakdown by COMT and MAO. (31)

Adrenaline differs from the other catecholamines in that it has an additional methyl substitution on nitrogen, increasing its affinity for α-receptors. The aliphatic side chain (hydroxyl group) renders adequate β-adrenergic affinity as well, thus making it a better stimulant of both α and β-adrenergic receptors than noradrenaline. Adrenaline has a greater affinity for α and β-receptors than that of noradrenaline. Furthermore, β-carbon substitutions reduce the central stimulant effect and increase its potency. (31)

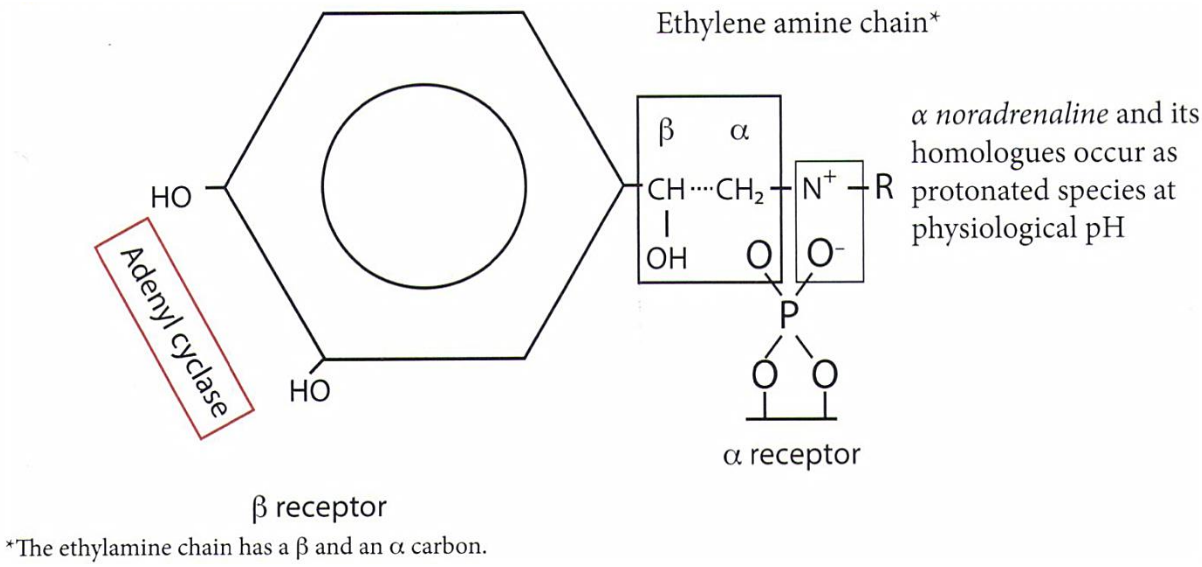


Figure 2.2 The Adrenaline Molecule (31)

Adrenaline's half-life is merely 18 minutes and duration of action no longer than two minutes. Therefore an infusion is imperative if a prolonged duration of action is required. (31)

Adrenaline is indicated for the use as an exogenous agent when cardiovascular support is needed i.e. during shock, arrest, anaphylaxis and cardiac bypass. This is because α and β effects are such that they provide positive inotropy, dromotropy and bathmotropy in the heart. Also, the vasopressor and vasoconstrictor effects assist in cardiac support. In the lungs β_2-receptor stimulation relieves severe bronchospasm and α-receptor mediated vasoconstriction helps reduce oedematous tissues of the upper airway. (31)

Some acute indications for use are thus as follows:

- anaphylactic shock
- cardiac arrest
- vasopressor
- inotropic infusion
- laryngeal oedema
- asthma. (4, 31)

The use of adrenaline in anaphylactic shock, cardiac arrest and inotropic infusions will be the only topics expanded on, as they are clinically relevant to this discussion.

2.5 Anaphylaxis

2.5.1 Overview

Anaphylactic reactions are relatively common medical emergencies, with an estimated world incidence rate of 0.5-2%. In South Africa, the incidence is not known, as there are limited allergy specialists to service a population over 47 million and limited data collection. (33-36)

Anaphylaxis is an acute systemic immune hyper-reaction that may present with a multitude of life threatening signs and symptoms. Clinically, anaphylaxis causes vasodilation, fluid extravasation, smooth muscle contraction and increased mucosal secretions. Cardiovascularly, this results in hypotension from massive vasodilatation, fluid shifts and myocardial depression. In the lungs and respiratory system, upper airway angioedema, bronchospasm and mucous plugging all lead to hypoxemia. (37)

2.5.2 Anaphylaxis in anaesthesiology

In anaesthesiology, anaphylactic reactions are common because many drugs causing allergies are given by anaesthetists. These include neuromuscular blocking agents (suxamethonium and rocuronium), β-lactam antibiotics, opiates (morphine), non-steroidal anti-inflammatories and intravenous fluids (e.g. Gelofusine® and Hartmann's solution). Therefore, the anaesthetist needs to be alert to the possibility of anaphylactic reactions on the operating table, especially since it is more difficult to recognise while under the influence of anaesthetic volatile agents. Early recognition and the prompt initiation of life saving adrenaline are crucial in the acute treatment of anaphylaxis. (38)

The time from exposure to collapse is variable, with life threatening symptoms occurring as quickly as five minutes. Therefore, prompt diagnosis and emergency medical treatment is required, often with the use of particular modes of administration and specific doses of adrenaline. (38)

2.5.3 Treatment of anaphylaxis

Adrenaline is the first line of treatment in severe anaphylaxis, and is the only drug with proven lifesaving properties (39). Adrenaline is used for treating cardiopulmonary collapse, caused by anaphylactic reactions, by acting on adrenoreceptors to cause:

- vasoconstriction, decreased mediator release and decreased mucosal oedema (α_1-adrenergic receptor);
- bronchodilation (α_1 and β_2-adrenergic receptors);
- positive inotropic and chronotropic effects on the heart (β_1-adrenergic receptor). (37, 38)

The Allergy Association of South Africa (ALLSA) and the Resuscitation Council of Southern Africa recommend the general management of 0.3-0.5 mg of adrenaline, given intramuscularly in the anterolateral aspect of the thigh (vastus lateralis) in the event of an acute unstable anaphylactic reaction in patients above six years of age. For children aged between two and five, 0.2 mg of adrenaline should be administered as above, and for infants aged less than two years, 0.1 mg is appropriate. The above-mentioned doses of adrenaline should never be given intravascularly for anaphylaxis as they may lead to angina, ischaemia and even cardiac arrest. Adrenaline should also never be given subcutaneously as its absorption is delayed and unpredictable. (2, 3)

In anaesthesiology, the preferred route is intravenous and doses of all drugs are administered based on calculating the unit of drug needed per kilogram body weight. In the context of adrenaline, this is particularly important as adrenaline acts differently at different doses. As mentioned under adrenergic receptors, lower doses (≤0.05 µg/kg/min) of adrenaline favour β-receptors in a ratio of β_2:β_1 of 10:1. This effector response will cause unfavourable vasodilation worsening hypotension and provoking cardiac arrest. Higher doses (≥0.1 µg/kg/min) favour α-receptor activation and thus provide vasoconstriction needed to support venous return and hence cardiac output. Therefore, for anaphylactic shock, a weight specific dose of 0.03-0.2 µg/kg is given as boluses, to titrate the drug to its clinical effect, and with subsequently larger doses on consecutive boluses. Should a patient require inotropic infusion doses, a rate of 0.05

μg/kg/min is appropriate as an intravenous infusion through a central venous catheter. (31)

2.6 Cardiac arrest

Cardiac arrest refers to the cessation of mechanical activity in the heart because of dysrhythmias in the heart or electromechanical dissociation (28). An arrest situation has numerous causes, of which, some are reversible. These include:

- hypovolaemia
- hypoxaemia
- acidosis
- hypo/hyperkalaemia
- hypothermia
- tension pneumothorax
- cardiac tamponade
- toxin ingestion
- pulmonary and cardiac thrombosis. (4, 5)

The dose of adrenaline in cardiac arrest, stipulated by Advanced Cardiac Life Support (ACLS) guideline, is a 1 mg bolus (7.5-15 μg/kg), in an adult, administered intravascularly every 3-5 minutes from the onset of cardiopulmonary resuscitation (CPR). (5)

Management of cardiac arrest with the rapid onset of CPR and adrenaline has been proven to facilitate the return of spontaneous circulation (ROSC) and thus improve short term survival (5). Adrenaline assists in the ROSC by augmenting coronary blood flow that CPR generates. By increasing peripheral vascular tone through α_1-adrenergic receptor stimulation, adrenaline assists with the venous return of blood to the right side of the heart while increasing aortic pressure and therefore coronary blood flow is facilitated. Without adequate coronary perfusion pressures, i.e. 15-20 mmHg, ROSC is not possible (28).

2.6.1 Overdosing in cardiac arrest

During a resuscitation attempt, it is easy to lose track of the timing between adrenaline doses thus leading to the overdosing of adrenaline i.e. giving more than the recommended dose of adrenaline (7.5-15 μg/kg). While this may augment ROSC, the long term detrimental effects have been well described (5, 40).

Adrenaline stimulates tachycardia, increases myocardial oxygen demand and stimulates the formation of tachyarrhythmias (28, 41). Furthermore, adrenaline activates platelet activity and promotes thrombogenesis (42). In the patients suffering from arrest situations due to acute coronary syndromes, this may cause coronary ischaemia to worsen (28). Overall, adrenaline may cause myocardial dysfunction by depleting myocardial ATP stores and increasing lactate accumulation (43). In addition to contributing to myocardial dysfunction in the recovery phase post-arrest, adrenaline also prolongs ischaemia peripherally, thereby causing persistent reductions in micro vascular flow (44). This has implications for the perfusion of vital organs and explains why adrenaline does not improve survival to hospital discharge and neurological status at discharge (45).

Persistent signs of hypo-perfusion post-ROSC in cardiac arrest patients are associated with the total dose of adrenaline administered during CPR. Therefore, overdosing of adrenaline in cardiac arrest has clinically relevant implications post-arrest, and ultimately impacts on survival despite successful resuscitation. (28, 40, 46)

2.7 Inotropic infusions

Infusions of adrenaline are sometimes necessitated by persistently low blood pressures. This may be in the context of post arrest-ROSC, for refractory hypotension in anaphylaxis or as a part of an anaesthetic plan for the critically ill patient.

Regardless of the circumstances, adrenaline infusions are prescribed at a rate, in weight dependant doses. An infusion of adrenaline required to support mean arterial pressures needs to be administered at a rate of at least 0.05 μg/kg/min and can be titrated upward to effect. Infusions lower than the recommended rate will tend to favour more β-adrenergic receptors and thus favouring unwanted peripheral vasodilation. Using doses above 0.5 µg/kg/min is not recommended as it may cause myocardial ischaemia, ventricular dysfunction, dysrhythmias or reductions in renal perfusion. (4, 31)

2.8 The importance of doses

Anaesthetists practice under the premise that they are familiar with the resuscitation algorithms presented by the American Heart Association and endorsed by the Resuscitation Council of Southern Africa (4, 47). This ensures that in the event of cardiac arrest a rapid resuscitation response ensues. This requires the anaesthetist to be astute and confidently apply the knowledge required to save a life. It is in the emergency scenario that a doctor's knowledge and ability is truly tested, unfortunately not always successfully.

The correct doses and modes of administration of adrenaline are often contested amongst doctors, leading to "judgement calls" being made by the doctor in charge of the resuscitation. This may be due to the lack of knowledge, lack of agreement concerning that knowledge or inexperience with the pending emergency. It is therefore important to understand why the correct doses are administered during anaphylactic reactions, cardiac arrest and inotropic infusions. These will now be discussed.

2.8.1 In anaphylactic reactions

The incorrect administration of adrenaline doses in anaphylaxis has been documented by many case reports (8-13, 15). Mistakes are usually as a result of overdosing of adrenaline and have led to cases of cardiogenic shock, myocardial infarction and ventricular tachyarrhythmia's (6).

In 2010 Kanwar et al (6) reported on three cases of inadvertent overdose with adrenaline, at a hospital in Detroit, due to confusion over the dose and route of administration (6). The three cases involved anaphylactic emergencies where all cases were given intravenous adrenaline at inappropriate doses i.e. the doses were too high. In two cases 0.3 mg of adrenaline was correctly prescribed, but were administered intravenously. Both of the patients subsequently developed acute ST segment elevation myocardial infarction for which they were successfully treated. In the third case, a man was given the cardiac arrest dose of adrenaline (1 mg) intravenously instead of the anaphylactic intravenous dose of 0.1 mg. He developed hypotensive shock secondary to ventricular tachycardia that was self-limiting and he recovered within a night in the intensive care unit. (6)

In 2010, Droste and Narayan (25) describe a near fatal event involving adrenaline. Again, 1 mg of adrenaline was administered intravenously by a junior doctor, under senior instruction, to a man suffering from anaphylaxis subsequent to receiving intravenous antibiotics. He suffered acute coronary vasospasm.

A short survey, by Droste and Narayan (48), was conducted in 2012 on hospital doctors, in a large district hospital in the north of England to determine their knowledge of adrenaline administration during anaphylaxis. The study was conducted on both junior and senior level doctors, working in General Medicine, General Surgery, Emergency Medicine, and Orthopaedics. It was found that only 15.5% of doctors would administer adrenaline correctly (dose and route) as recommended by the guidelines. Therefore, doctors of all grades and specialties were deficient in knowledge regarding the administration of adrenaline for acute anaphylaxis.

The detrimental effect of adrenaline overdose highlights the significance of knowing the correct doses of adrenaline in emergency situations such as anaphylaxis and cardiac arrest. This is supported by the evidence showing that half of all fatal anaphylactic reactions are iatrogenic and that the mean time to cardio-pulmonary arrest is less than five minutes in iatrogenic anaphylactic reactions (49).

2.8.2 In cardiac arrest

There is little literature around cases of inappropriate dosing in cardiac arrest, although there is literature showing the detrimental effects of overdosing with adrenaline in cardiac arrest, as highlighted in section 2.6.1 (28, 40-43, 45).

It is unequivocal that understanding adrenaline doses requires doctors to be able to correctly dilute their own syringes of adrenaline for administration in anaphylactic and cardiac resuscitation as well as for patients requiring inotropic support.

2.8.3 Dosing in infusions

Dosing errors regarding infusions are common. The incorrect concentration of adrenaline can easily be administered simply by making a dilution error. In 2012, Adapa et al (16) investigated variability in the preparation of infusions in the intensive care unit in Cambridge and found that adrenaline infusions prepared *de novo* were done so with much less precision. Importantly, doctors who are inexperienced in diluting drugs may not know how to correctly do so and therefore unintentionally give an incorrect infusion dose. (16)

In the intensive care unit, where drugs are mainly given as infusion, drug dosing errors are common. Patients in intensive care are at an estimated risk of 10% per day regarding dosing errors (50, 51). This has been attributed to mistakes made through preparation of drugs, inadequate mixing, fatigue, excessive workload and inexperience among staff (50, 52-54).

Rolfe and Harper (13) showed, in 1995, that junior doctors were unable to make simple drug dose calculations regarding lignocaine. Doctors were asked to convert between mass concentration, dilutions and percentage concentration, with 50% failing to do so. This highlights the shortcoming of some junior doctors and reiterates the possibility that drug infusion doses, such as adrenaline, are incorrectly prepared. (13)

Incorrect adrenaline dosing by doctors appears to be an international problem. Surveys regarding South African doctors' and anaesthetists' knowledge on the doses of adrenaline in the acute emergency scenario have not been identified, necessitating investigation.

2.9 The reasons for dosing errors

The contributions to dosing errors are multifactorial. Anaesthetists make drug calculations daily for a variety of patients dependent on their weights (neonates to obese adults). Inadequate knowledge of adrenaline dosing, route of administration and calculation errors appears to be the most frequently encountered problems (6, 25). However, studies have also shown that doctors are unable to identify dilutions of adrenaline preparations and/or prepare the dilutions themselves (13, 55). This might be due to confusing pharmacological labelling (56), a lack of formal training in serial dilution, and inexperience in the regular use of emergency adrenaline (50, 52, 54, 57).

In a randomised controlled trial in 2008, Wheeler et al (56) investigated the effect that pharmacological labelling might have on the clinical performance of physicians when faced with simulated emergencies. In the study, physicians had to prepare an appropriate dilution of adrenaline for a child with anaphylaxis secondary to a peanut allergy. Results of this study showed that physicians are more likely to make dosing errors when the adrenaline vials used to prepare the dilutions were expressed as a ratio i.e. as 1 ml of 1:1000 (56). Moreover, when physicians were asked to give the dose in milligrams of the dilutions of adrenaline they had prepared, they did not know how to do this. This is despite their knowledge of anaphylactic doses e.g. an adult should receive 0.5 ml of 1:1000 adrenaline (26).

It is an unspoken assumption that anaesthetists are able to correctly dilute drugs. This is done on a daily basis. In a 2013 study by Stucki et al (58) assessing the accuracy of intravenous drug preparations by anaesthetists, the investigators analysed the contents of unused syringes. Their findings showed that only two thirds of the total syringes sampled were within the dose accuracy range, allowing for variation up to 10% outside the concentration specified. Imprecise preparation practices and dilution errors were identified as the causes of the drug dose discrepancies.

Dosing errors are common amongst doctors and have significant consequences for the practice of anaesthesiology. The emergency scenarios, cardiac arrest and anaphylaxis, are not common occurrences and therefore the knowledge doctors acquire to treat these conditions are subject to fade (59). Although the focus of this topic is to discuss the knowledge that anaesthetists have about the use of emergency adrenaline, one cannot dismiss the contributing factors that either deter knowledgeable decision making or affect it indirectly. The affect that incorrect knowledge of adrenaline dosing has on patient outcomes has been discussed above. The knowledge that anaesthetists have to properly manage specific emergencies, also mentioned above, can essentially be described as a function of the known doses, preparation and routes of administration of adrenaline in the three scenarios outlined before. However, it has consistently been shown that despite standard practice guidelines and algorithms, clinical skills and medical knowledge should continuously be refreshed and evaluated because of the effect of memory fade and the growing body of evidence-based medical knowledge (4, 59).

The successful implementation of clinical practice guidelines, however, is not only dependant on the medical knowledge, but on how the physician engages with this knowledge. Clinical practice guidelines alone have been shown to have a very limited effect on the behavioural change of the practicing physician (18-20). The factors responsible for this are unclear, but suggestions have been made. Cabana et al (17) identified influences that restrict a physician from complying with guidelines and has termed them adherence barriers. By systematically reviewing the literature on knowledge, attitude and behaviour, these adherence barriers are investigated by Cabana et al (17).

2.10 Adherence barriers

Cabana et al (17) propose that in order to affect the outcomes of patients based on practice guidelines, the guideline has to first affect the knowledge of the physician. Knowledge has an effect on the attitude that the physician adopts regarding the proposed guideline and ultimately dictates the behavioural outcome. Any one of these factors may restrict the adherence of the physician to a guideline and is thus termed a barrier. (17)

2.10.1 Knowledge

Knowledge adherence barriers are cognitive factors that limit the physician from adequately treating patients (17). The two main cognitive factors identified by Cabana et al (17) are the lack of awareness of the knowledge material or protocols (60-66) and the lack of familiarity with knowledge (17, 60, 61, 65-67). Interestingly, of the articles that Cabana et al (17) reviewed on knowledge barriers, up to 10% of the doctors were not even aware that any guideline existed (17).

Considering the expanding scope of knowledge that physicians must stay aware of, the difficulty in achieving this can be appreciated (19). Also, worldwide awareness of certain guidelines (e.g. immunisation guidelines) does not guarantee the familiarity with the knowledge material and the application thereof. Additionally, the volumes of information that account for some guidelines are vast, requiring time to process the information that cannot be afforded to all doctors. Staying abreast with medical knowledge is also under the proviso that one has complete access to the information at all times, which is not the case when dealing with doctors working in developing countries, where resources are limited, if available at all (17).

This does not explain, however, why doctors who are up to date with specialist field guidelines still deter from protocol despite their academic soundness. It is proposed that physician attitude to protocols are a major determinant of the behavioural outcome (17).

2.10.2 Attitude

The physician's attitude towards practice guidelines is complex, as it involves not only a psychosocial aspect but is also driven by academic pride (17). Identifying attitudes that resist adherence has prompted much literature on resistance to adopting standard practice guidelines. By reviewing studies on adherence to protocols, researchers have attempted to identify the causes of attitude barriers.

Lack of agreement

Several studies have investigated the possibility that lack of agreement in the medical community may be an important explanation for physician non-adherence to practice guidelines (61, 68-71). One could argue that the lack of agreement is yet another form of lack of knowledge through insight, and thus not different from a knowledge barrier. Often the reasons for lack of agreement were shown to be due to differences in the interpretation of the guideline's evidence. Also, the applicability of the guidelines to specific populations and the cost implications are not always practical options. Furthermore, it was shown that the credibility of the guideline authors was also under contention by some physicians. This may explain, in part, why physicians choose to exert their autonomy when treating patients for problems where practice guidelines exist. The lack of agreement as an attitude barrier, however, is less commonly shown to be a cause of non-adherence to guidelines (17).

Lack of self-efficacy

Other attitude-related adherence barriers include the physician's belief that one cannot perform the expected behaviour necessary to implement the practice guideline and belief that the expected outcome of the guideline will not initiate change. The belief that one can actually perform behaviour is known as self-efficacy and is dependent on the physician's confidence in executing the skills required to deliver the practice guidelines adequately. (72)

Self-efficacy influences the initiation and sustainability of behaviour despite poor outcomes (72). Regarding expectations of behaviour leading to a particular consequence, if the physician has no expectation of the guideline improving the outcome, they are less likely to adhere to the guideline (17).

It is true for most that "old habits die hard"; implying that changing practice habits is a difficult hurdle to overcome. The practicing physician needs to be amenable to the changing face of medicine, but it is not easy to stay motivated to do so. This appears to be a problem that many physicians experience, but has not been investigated as widely as other attitude barriers.

2.10.5 Behaviour

Although attitudes are shown to affect behaviour significantly (69), it is sometimes external barriers that pose great implications for instituting practice guidelines. Barriers outside the control of the practicing physician can be an unconquerable hurdle, leading to non-adherence to guidelines (17).

External barriers include:

- guideline-related barriers
- patient-related barriers

- environmental-related barriers. (17)

Guideline-related barriers refer to the difficulty or inconvenience that the institution of the guideline would impose, thus rendering non-adherence (17). However, when guidelines prompt adding a behaviour it is shown that the guideline may be more easily instituted than eliminating or replacing an established behaviour (73), as this then relates back to the inertia of previous practice as an additional barrier to adherence (17).

Patient related barriers pose great implications, as reconciling the patient preference for a practice guideline may not be possible (74). Even with complete physician knowledge, agreement with guidelines and self-efficacy of the implementation thereof, without patient agreement of the need for guideline recommendations, adherence is impossible (17).

Barriers regarding resource or facility deficits are referred to as environmental-related factors and are beyond the physicians control (75). Additionally, physician environments lacking a reminder system, insufficient staff, increased practice costs and poor reimbursement may also be factors beyond physical control. The lack of a reminder system is an important barrier because managing emergencies involving adrenaline is subject to the constant update in current literature and algorithmic protocols (4).

Compensation for external barriers may be possible when adequate resources or referral systems are in place, however this does not ensure adherence to guidelines as discussed above. Few studies have been able to show variety in the barriers that need to be overcome to achieve adherence. This is because most studies are only looking at one barrier to adherence, therefore restricting interventions to improve adherence. (17)

In summary, in order to improve adherence to practice guidelines one needs to understand the factors influencing the desire to deviate from the recommendations. Cabana et al (17) have successfully highlighted the barriers that restrict physician behaviour in implementing practice guidelines (17). This is congruent with other research by Phipps et al (69, 70, 76) emphasising that attitudes and belief systems are a major influence on the behavioural outcome. This is explained again by the theory of planned behaviour (77).

2.11 Theory of Planned Behaviour

The Theory of Planned Behaviour (TPB) holds the belief that three main factors are responsible for a person's intention to engage in a specific behaviour (77). The first is the perceived outcome of the behaviour or attitude towards the behaviour. Secondly, the subject norm refers to the perceived expectations of others regarding the behaviour. Lastly, perceived behavioural control is the degree of volitional control that a person has over their behaviour. Interestingly, Phipps et al (76) applied this behavioural model to anaesthesiology consultants to identify factors that predict their intention to deviate from standard anaesthetic practice guidelines (76) . It was shown that attitude to behaviour was the most persistent influence over behaviour. Phipps et al (70) go on to re-examine their findings in detail in a 2010 study, expanding on how individual beliefs may influence the anaesthetist's behaviour in each composite TPB measure. Their findings were consistent with their previous work in that the results suggested that anaesthetists' intention to deviate from guidelines was not an absolute, but rather a case of clinical judgement (69). This reflects a previous qualitative study by Phipps (76), showing that there is a discrepancy between what should be done in "the ideal world" versus what is really done in anaesthetic practice. Importantly, the behavioural intentions of the anaesthetist can now be predicted by the parameters discussed above. What is unclear however, is how far the behaviour extends. If clinicians can deviate from practice guidelines based on their attitude and knowledge towards the guideline, then how do intentions deviate when the guideline is pertaining to an emergency?

2.12 Conclusion

The knowledge of anaesthetists in the management of emergencies involving adrenaline is of critical importance, as emphasised by the above discussion. The medical knowledge pertaining to adrenaline starts with a basic physiological understanding of why adrenaline would help in the event of anaphylaxis, cardiac arrest, or as an inotropic infusion. These clinical scenarios are all familiar to the practicing anaesthetist. Furthermore, all scenarios have algorithms that are internationally recognised and implemented to standardise the treatment of patients and conform management to a best possible outcome. Despite guidelines, doctors the world over are still getting it wrong when it comes to adrenaline dosing in emergencies. Understanding why this happens is multifactorial and involves the interaction between knowledge and behavioural attitudes.

In order to maximise the therapeutic benefits of adrenaline-based protocols, anaesthetists need to be able to conform to them in the event of an emergency. Familiarity with the correct adrenaline doses, routes of administration and dilutions is also of grave importance, as it will assist in efficiently executing the implementation of these protocols when an emergency arises. The current knowledge of anaesthetists on this topic, however, is not known in South Africa.

2.13 Summary

Chapter two has summarised the importance of understanding adrenaline by anaesthetists by giving the background to the problem as well as the anatomy, physiology and pharmacology. Adrenaline's importance is then highlighted in the context of three specific emergency scenarios, with emphasis on why giving the correct drug dose is of grave importance. By exploring the topics of adherence barriers and planned behaviour, the reasoning behind differing practices is better understood. Chapter three will now explain the methodology behind the study design.

CHAPTER 3: Research methodology

3.1. Introduction

In this chapter the problem statement, aim and objectives, ethical considerations, research methodology and the validity and reliability of the study are discussed.

3.2. Problem statement

Doctors specialising in anaesthesia are expected to know the appropriate resuscitation guidelines regarding the use of adrenaline for anaphylaxis, cardiac arrest and inotropic infusion. In each scenario specific doses and routes of administration are recommended (3, 4). It was not known if anaesthetists working in the Department of Anaesthesiology, at Wits know how to appropriately administer adrenaline in an emergency.

3.3. Aim and Objectives

3.3.1 Aim

The aim of this study was to determine the knowledge of anaesthetists working in the Department of Anaesthesiology, at Wits, regarding the appropriate administration of adrenaline for anaphylaxis, cardiac arrest and inotropic infusions.

3.3.2. Objectives

The primary objectives of this study were to:

- describe the knowledge of anaesthetists regarding adrenaline doses in three different clinical scenarios
- compare whether the overall knowledge of anaesthetists, with and without ACLS certification, regarding adrenaline was adequate
- compare whether the knowledge of anaesthetists, with and without ACLS certification, regarding each scenario was adequate
- correlate knowledge of adrenaline with years of anaesthetic experience

The secondary objective was to:

- compare the knowledge of anaesthetists between different professional designations.

3.4. Ethical considerations

Application to the Postgraduate office (Appendix 1) and to Human Research Ethics Committee (Appendix 2) of the Faculty of Health Science, Wits was approved.

This study was knowledge-based using a self-administered questionnaire (Appendix 4). The researcher invited participants to take part in the research. Those who agreed received an information letter (Appendix 3) and questionnaire (Appendix 4).The questionnaires were voluntary and consent was implied on the completion of the questionnaire. Care was taken to maintain anonymity and confidentiality of the anaesthetists involved. A study number was allocated to each questionnaire and placed in a sealed box with no identifying information being requested from the participants. Only the researcher and the supervisors had access to the raw data. Data will be stored securely for six years, following completion of the study. Based on the results of the study, an update on the appropriate use of adrenaline will be presented at a departmental academic meeting.

The study was conducted in accordance with the Declaration of Helsinki (22) and the South African Good Clinical Practice Guidelines (23).

3.5. Research methodology

3.5.1. Research design

Burns and Grove (78) describe a research design as the blueprint for a study. According to Brink (79), a research design determines the methods by which the researcher obtains subjects, collects data and interprets results.

This was a prospective, contextual, descriptive study.

A prospective study is one in which a specific population is followed over time to observe an outcome (79). This was a prospective study as data was collected at departmental academic meetings.

A contextual study is one which refers to a specific group or population, defined by De Vos (80) as a "small-scale world". The "small-scale world" can be a ward, an intensive care unit or a clinic. This study was contextual because research was conducted in the Department of Anaesthesiology, Wits.

According to Brink (79), a descriptive study is one in which a population's characteristics are being described, so as to answer a specific question about the population, without attempting to establish a causal link (79). The knowledge that anaesthetists have about the appropriate administration of adrenaline in emergencies was described in this study.

3.5.2. Study population

The study population consisted of anaesthetists working in the Department of Anaesthesiology.

3.5.3. Study sample

Sample Size

In consultation with a bio-statistician a sample of 85 Wits anaesthetists was estimated. This was based on the assumption that 67% of anaesthetists in the Wits Department of Anaesthesiology would have adequate knowledge of adrenaline to an accuracy of within 10%, with 95% confidence.

Sampling method

This study used a convenience sampling method, as is appropriate for a descriptive study (78).

Convenience sampling involves the sampling of participants who are readily available to the researcher (79). Importantly, for the purpose of this study, a sample of anaesthetists who were in the same place at the same time was required in order to distribute a “surprise” questionnaire, thus eliminating the possibility of pre-empting answers to questions. This was done on two occasions several weeks apart at different hospital meetings, sampling from different members of the Department of Anaesthesiology.

Inclusion and exclusion criteria

All anaesthetists who attended the weekly academic meetings and who were willing to partake in the study were included. Incomplete questionnaires returned were included and a score of zero was allocated to unanswered questions.

Blank questionnaires returned were excluded.

3.5.4. Data collection

Development of questionnaire

Self-report techniques are used when the objective of the researcher are to determine what a population believes, thinks, or knows (79). An easy method to collect this data is by means of questionnaires

No questionnaires pertaining to the appropriate administration of adrenaline were identified in the literature. To ensure content validity the draft questionnaire was based on a review of the literature. To further achieve face and content validity, three anaesthesiologists were consulted. Following consultation minor corrections were made.

The self-administered questionnaire (Appendix 4) consisted of two sections. Section 1 included the following demographic data:

- years of experience in anaesthesiology
- professional designation e.g. registrar, consultant
- ACLS certification and date attained.

Section 2 consisted of questions regarding the knowledge that anaesthetists have on the dose and route of administration of adrenaline in the following three scenarios:

- anaphylaxis
- cardiac arrest
- inotropic infusions.

Data collection process

Before distribution of the questionnaires, all sheets were numbered so as to keep track of the number of questionnaires completed. Numbering the questionnaires also helped prevent reproduction of results. Furthermore, a response rate could then be calculated.

Data was collected during February 2014 and June 2014 at departmental academic meetings. The researcher and two assistants were present during completion of the questionnaires to assist with queries and prevent data contamination. To further prevent data contamination, the researcher collected data at non-consecutive departmental meetings.

At the start of the meeting the researcher addressed anaesthetists, giving them a brief introduction to the study and inviting them to participate. Information letters and questionnaires were distributed allowing 10 to 15 minutes to complete the questionnaire.

All the questionnaires, complete and incomplete, were placed in an unmarked envelope, sealed and dropped into a collection box. This ensured anonymity and confidentiality of the anaesthetists participating in the study.

Based on the results of the study, an update on the appropriate use of adrenaline will be presented at a future departmental academic meeting.

A post-test often follows an educational lecture. It was decided not to do a post-test in this study, as attendance at departmental meetings cannot be guaranteed as anaesthetists have service commitments that influence meeting attendance. The anaesthetists completed the questionnaire anonymously, therefore it was not possible to organise a post-test at an alternative time. Furthermore, Cabana et al (17) highlighted that knowledge alone does not change behaviour, but it is also influenced by the doctors attitude.

3.6. Data analysis

Using Microsoft Excel 2010, data was captured onto spreadsheets. The statistical program, GraphPad InStat, was used to analyse data.

The knowledge regarding doses and route of administration of adrenaline was described using frequencies and percentages. Knowledge of adrenaline and years of experience was correlated with a Spearman Rank Correlation test, and knowledge between professional designations was compared using the Kruskal-Wallis test, as data was not normally distributed. Categorical variables were compared using the Fisher's exact test.

A 0.05 level of significance was used.

3.7. Validity and reliability of the study

According to Botma (81), "Validity indicates whether the conclusions of the study are justified based on the design and interpretation".

Reliability refers to how consistent the measurements have been (81).

The validity and reliability of this study was maintained by:

- using a standard questionnaire with face and content validity
- using an appropriate study design
- the sample size being calculated in consultation with a biostatistician
- a researcher and two assistants being present on completion of the questionnaires to answer any queries and prevent data contamination
- questionnaires being completed at non-consecutive academic meetings, to prevent data contamination
- questionnaires being placed anonymously into an envelope, thereby facilitating a non-threatening environment

- data being analysed with the assistance of a biostatistician.

3.8. Summary

In this chapter the problem statement, aim and objectives, ethical considerations, research methodology, data analysis and validity and reliability were discussed. In the next chapter the results of the study are reported and discussed.

CHAPTER 4: Results and discussion

4.1 Introduction

The sample realisation, results of the study according to the objectives and the discussion are presented in this chapter. The objectives of this study are therefore repeated.

The primary objectives of this study were to:

- describe the knowledge of anaesthetists regarding adrenaline doses in three different clinical scenarios
- compare whether the overall knowledge of anaesthetists, with and without ACLS certification, regarding adrenaline was adequate
- compare whether the knowledge of anaesthetists, with and without ACLS certification, regarding each scenario was adequate
- correlate knowledge of adrenaline with years of anaesthetic experience

The secondary objective was to:

- compare the knowledge of anaesthetists between different professional designations

4.2 Results

The findings here are described and analysed using descriptive and inferential statistics. Descriptive tables are used to report objectives where appropriate. Spearman's Rank correlation, Fisher's exact test and Kruskal-Wallis test are the inferential stats used to compare group results. P-values of <0.05 are considered statistically significant. Each objective is discussed separately.

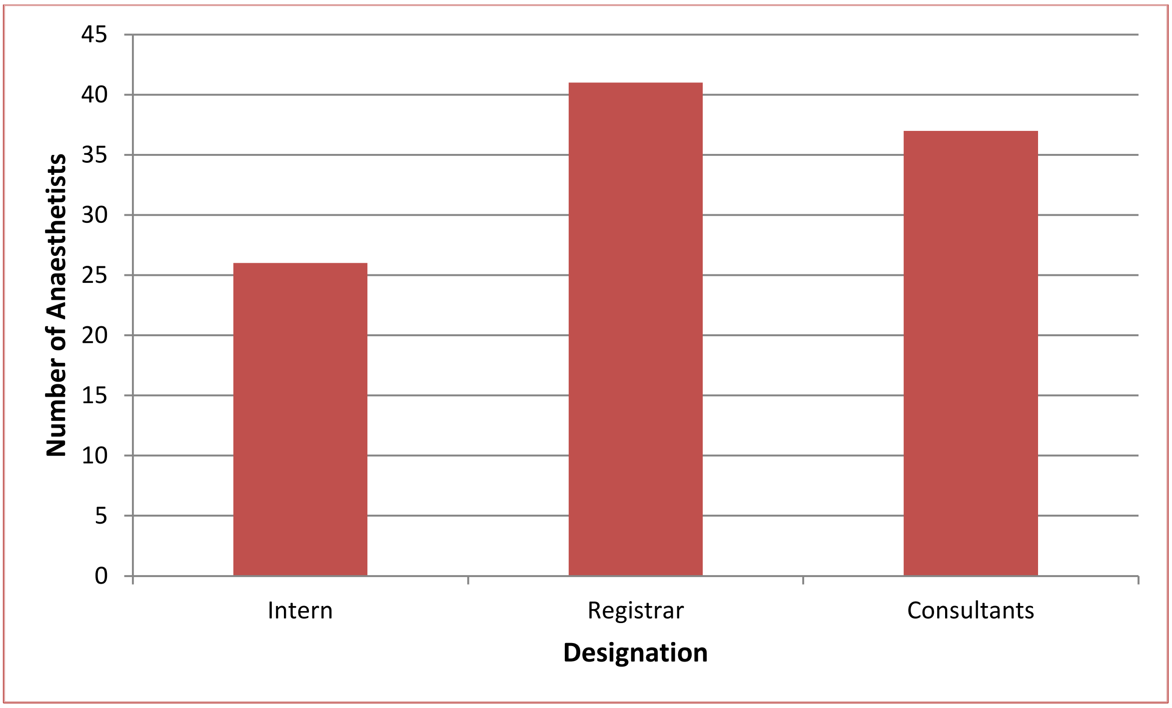
4.2.1 Demographics

Sample Realisation

A total number of 105 questionnaires were distributed between the four hospitals during February 2014 and June 2014. Only one questionnaire was excluded as it was returned blank. Therefore a total of 104 questionnaires were included in the statistical analysis (n=104). This sample size is well above the estimated sample size of 85 needed to power the study with a p-value of < 0.05.

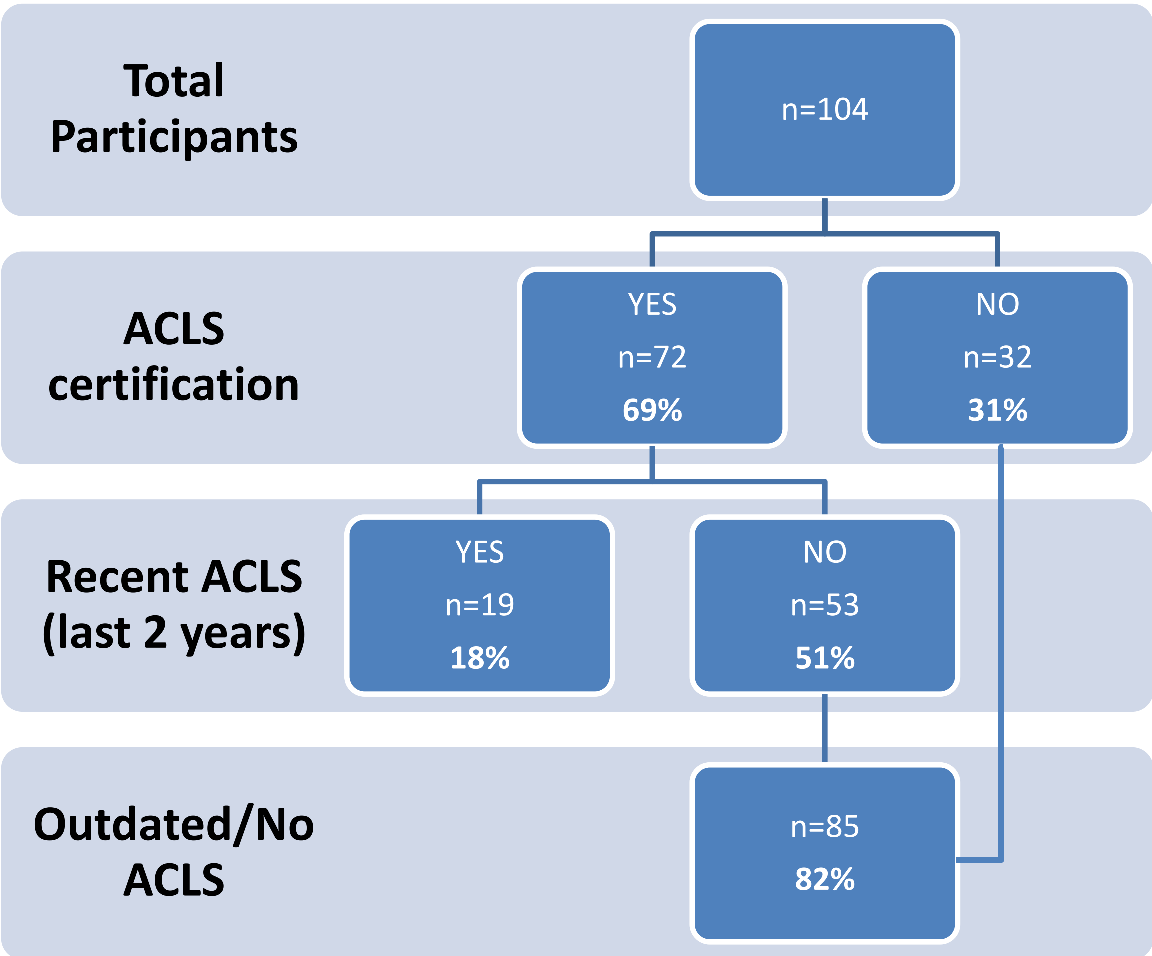
The sample of anaesthetists consisted of 21 interns (20%), 9 medical officers (9%), 37 registrars (35%), one career medical officer (1%) and 36 consultants (35%) In order to fulfil the objectives of this research report, the designated groups were re-grouped into three comparative groups. Interns and medical officers, with less than one year experience, are pooled together to comprise the first group, interns (n=26). Registrars and medical officers with more than one year experience comprise the second, registrars (n=41), and the third group is made up by adding the only career medical officer to the consultant group (n=37) (Figure 4.1).

Figure 4.1 Bar graph showing the designation of anaesthetists



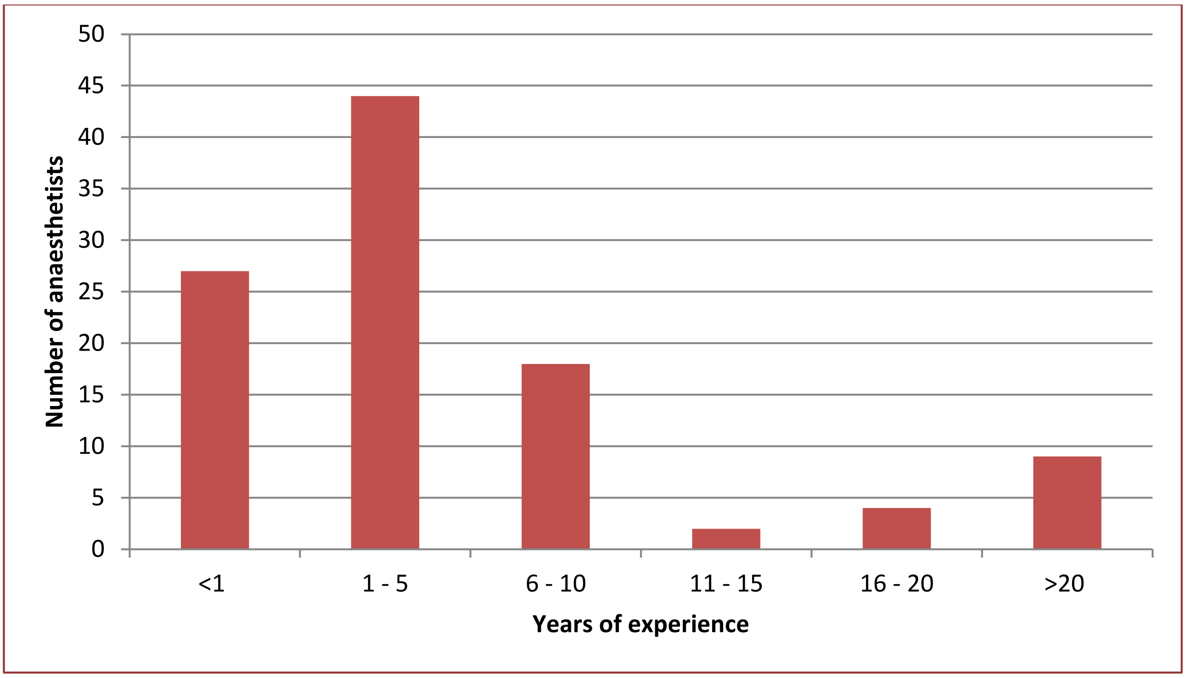
Of the 104 participants, 72 (69%) had completed an ACLS course, and 32 (31%) had never completed the course. Of all the participants only 19 (18%) had completed the ACLS course in the last two years (and were therefore certified), with 53 (51%) of participants having completed ACLS more than two years ago. Overall 85 (82%) anaesthetists had outdated ACLS course knowledge or had never attended an ACLS course (Figure 4.2).

Figure 4.2 Flow diagram showing proportions of anaesthetists who have ACLS and are certified



Participant information is also expressed as years of anaesthetic experience, showing that 71 anaesthetists (68%) who took part in the study were junior anaesthetists, having less than five years of anaesthetic experience (Figure 4.3).

Figure 4.3 Bar graph showing participants' years of anaesthetic experience



4.2.2 Objective: to describe the knowledge of anaesthetists regarding adrenaline doses in three different clinical scenarios

Of the 104 participants, no anaesthetists answered all six questions correctly. Only 15 of the 104 participants achieved over 80%. The pass rate was therefore 14% (n=15).

Overall, the participants answered 50.3% of the questions correctly. The median score for the 104 anaesthetists who completed the questionnaire was 50%.

The pass rate for each scenario is given in Table 4.1. The highest pass rate was for the cardiac arrest scenario, scenario 1, with 46% of anaesthetists correctly answering the questions. This was followed by scenario 2, the anaphylaxis scenario, with only 14% of the sample of anaesthetists answering correctly. Only 7% of anaesthetists correctly knew how to manage adrenaline infusions in scenario 3.

The results of each question are summarised in the Table 4.1. The highest score was for question 1, with 89 (86%) participants correctly answering the cardiac arrest dose of adrenaline (1 mg). The lowest score in the questionnaire was for question six, with 9 (9%) participants knowing the correct ceiling dose (0.5 mcg/kg/min) of adrenaline when used as an infusion. Question 2 shows that 50 (48%) participants know the cardiac arrest dose of adrenaline as a per kilogram dose (7.5-20 mcg/kg). In answering question 3, 63 (60.6%) anaesthetists knew how to correctly manage anaphylactic shock with intravenous adrenaline (0.03-10 mcg/kg). Question four resulted in 21 (20.2%) anaesthetists correctly answering an alternative route and dose for adrenaline administration in anaphylaxis (0.5 mg IM). Question five showed that 82 (79%) participants knew how to correctly start an adrenaline infusion at an appropriate dose (0.05 mcg/kg/min).

Table 4.1 Summary of the results for each scenario and question

Scenario	Scenario Pass Rate (%)	Scenario Mean (%)	Question	Correct	Incorrect
1	46	67	1	89 (86%)	15 (14%)
			2	50 (48%)	54 (52%)
2	14	4	3	63 (60%)	41 (40%)
			4	21 (20%)	83 (80%)
3	7	44	5	82 (79%)	22 (21%)
			6	9 (9%)	95 (91%)
Total				314 (50.3%)	310 (49.7%)

4.2.3 Objective: to compare whether the overall knowledge of anaesthetists, with and without ACLS certification, regarding adrenaline was adequate

To compare whether or not having ever done an ACLS course would make a difference to the overall knowledge of anaesthetists, a Fisher's exact test was used (Table 4.2). Of the 72 anaesthetists who had ever completed an ACLS course 14 (19%) passed the questionnaire and 58 (81%) failed. Of the 32 anaesthetists who had never completed an ACLS course only 1 (3%) participant passed and 31 (97%) failed the questionnaire. A statistically significant difference was found between these two groups (p=0.0339) with a greater proportion of anaesthetists passing if they had completed an ACLS course previously, whether their ACLS certification was current or not. Therefore, having an ACLS, made a difference to the overall questionnaire score the participants achieved (Table 4.2).

Table 4.2 Contingency table comparing overall knowledge of adrenaline, with and without an ACLS certification, with pass rate

	ACLS	No ACLS	Total
Pass	14	1	15 (14%)
Fail	58	31	89 (86%)
Total	72 (69%)	32 (31%)	104 (100%)

p=0.0339

Although not an objective, further Fisher's exact analysis (Table 4.3) was done to determine whether having a current ACLS certification, as opposed to a lapsed ACLS certification, had an effect on the pass rate of anaesthetists regarding the adrenaline knowledge questionnaire.

Of the 72 anaesthetists who had ever acquired ACLS certification 19 (26%) were currently certified and 53 (74%) had allowed their certification to lapse. Of the 19 anaesthetists currently certified with ACLS, 5 (26%) passed the questionnaire and 14 (74%) failed. Of the 53 anaesthetists whose ACLS had lapsed 9 (17%) passed the questionnaire and 44 (83%) failed. No difference was found between these groups (p=0.4999).

Table 4.3 Contingency table comparing overall knowledge of adrenaline, with and without a recent ACLS certification, with pass rate

	ACLS updated	ACLS not Updated	Total
Pass	5	9	14 (19%)
Fail	14	44	58 (81%)

Total	19 (26%)	53 (74%)	72 (100%)

P=0.4999

4.2.4 Objective: to compare whether the knowledge of anaesthetists, with and without ACLS certification, regarding each scenario was adequate

Scenario 1: cardiac arrest

Of the 104 anaesthetists, 48 (46%) participants passed the scenario and 56 (54%) failed (Table 4.4). Of the 72 anaesthetists who had ever completed an ACLS course 39 (54%) participants passed and 33 (46%) participants failed to answer correctly. Of the 32 anaesthetists who had never completed an ACLS course 9 (28%) participants passed and 23 (72%) failed. Using a Fisher's exact test a significant difference was found between the groups (p=0.0118). Therefore, having an ACLS course improved knowledge of anaesthetists regarding the correct doses of adrenaline in cardiac arrest.

Table 4.4 Contingency table comparing ACLS certified anaesthetists' knowledge of cardiac arrest with those who are not certified

	ACLS	No ACLS	Total
Pass	39	9	48 (46%)
Fail	33	23	56 (54%)
Total	72 (69%)	32 (31%)	104 (100%)

P=0.0118

Scenario 2: anaphylaxis

Of the 104 anaesthetists, 15 (14%) participants passed the scenario and 89 (86%) participants did not know the correct doses and route of administration of adrenaline in anaphylaxis (Table 4.5). Of the 72 anaesthetists who had ever completed an ACLS course 14 (19%) answered the question correctly and 58 (81%) participant answered incorrectly. Of the 32 anaesthetists who had never completed an ACLS course 1 (3%) participant answered correctly and 31 (97%) answered incorrectly. Using a Fisher's exact test a significant difference was found between the groups (p=0.0339). Therefore, having an ACLS course improved knowledge of the route and dose of administration of adrenaline during an anaphylactic reaction.

Table 4.5 Contingency table comparing the knowledge of the anaphylaxis scenario route and dose of adrenaline administration with ACLS certification

	ACLS	No ACLS	Total
Pass	14	1	15 (14%)
Fail	58	31	89 (86%)
Total	72 (69%)	32 (31%)	104 (100%)

P=0.0339

Scenario 3: adrenaline infusions

Of the 104 anaesthetists, 7 (7%) participants passed the scenario and 97 (86%) failed (Table 4.7). Of the 72 anaesthetists who had ever completed an ACLS course 6 (8%) participants passed and 66 (92%) participants failed to answer correctly. Of the 32 anaesthetists who had never completed an ACLS course 1 (3%) participant passed and 31 (97%) failed. No difference was found between these groups (p=0.4331). Therefore, having an ACLS course did not improve anaesthetists' knowledge of adrenaline infusions.

Table 4.6 Contingency table comparing the knowledge of adrenaline infusion scenario with ACLS certification

	ACLS	No ACLS	Total
Pass	6	1	7 (7%)
Fail	66	31	97 (86%)
Total	72 (69%)	32 (31%)	104 (100%)

P=0.4331

Although not an objective, analysis of each question was performed using Fisher's exact tests to show where the differences in knowledge are and whether or not having an ACLS course improved knowledge of that question. As summarised by Table 4.7, below, differences were found between the ACLS and No ACLS groups for questions 1, 4 and 5. Therefore having an ACLS certification made answering those questions more likely, whereas no differences were found between the groups for the remaining questions.

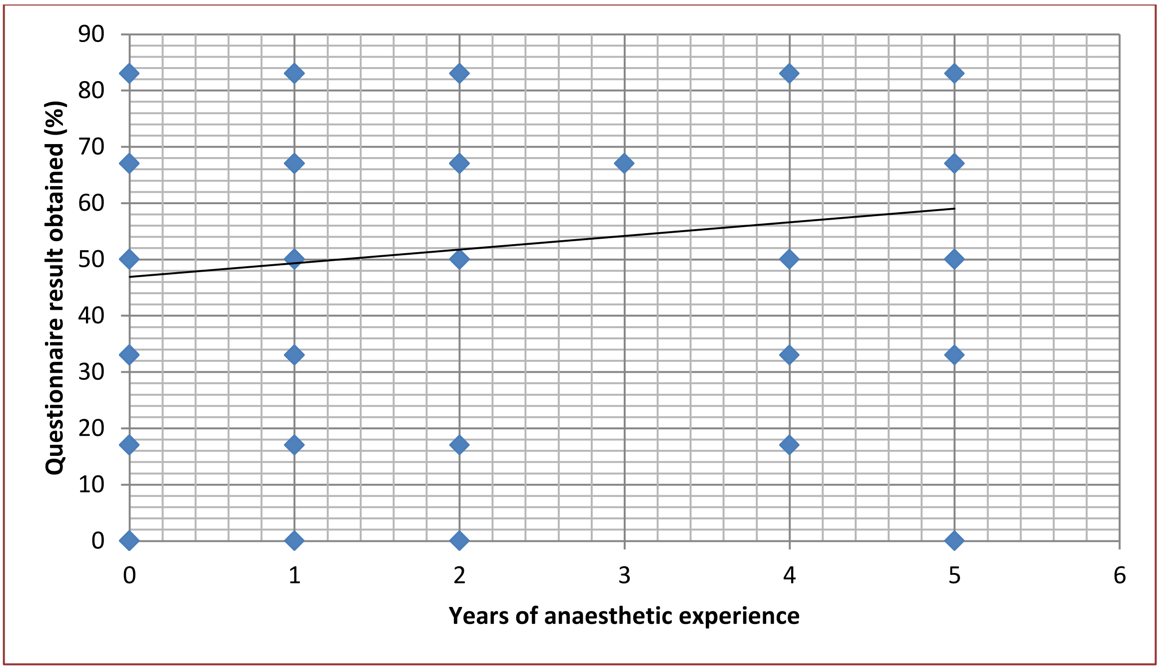
Table 4.7 Table showing the results of Fisher's exact tests performed on each question from the three adrenaline scenarios

Question	ACLS Yes/No	No ACLS Yes/No	P-value
1	69/3	20/12	p<0.0001
2	38/34	12/20	p=0.2023
3	46/26	17/15	p=0.3851
4	20/52	1/31	p=0.0031
5	63/9	19/13	p=0.0033
6	7/65	2/30	p=0.7179

4.2.5 Objective: to correlate the knowledge of adrenaline with years of anaesthetic experience

To identify whether there was a correlation between anaesthetists' knowledge of adrenaline and the number of years spent in anaesthetic practice a Spearman's Rank correlation test was used. The participants' years of anaesthetic experience are plotted on the x-axis in categories and are as follows: 1= <1 year experience, 2=1-5 years experience, 3=6-10 years experience, 4=11-15 years experience, 5=16-20 years experience and 6= >20 years experience (as per Appendix 4). Spearman's r= 0.2460 (95% CI 0.05031 to 0.4236), showing a weak positive correlation (Figure 4.4), meaning that the greater the number of years spent in anaesthetic practice, the greater the knowledge that anaesthetists have regarding adrenaline doses in different clinical scenarios. This finding was statistically significant (p=0.0118).

Figure 4.4 Scatter plot showing the relationship between anaesthetists' years of experience and their knowledge of adrenaline



Categories: 1= <1 year experience, 2=1-5 years experience, 3=6-10 years experience, 4=11-15 years experience, 5=16-20 years experience and 6= >20 years experience

4.2.6 Secondary objective: to compare the knowledge of anaesthetists between different professional designations

The three groups were compared using inferential statistics, namely a Kruskal-Wallis test with Dunn's multiple comparisons test post-hoc. The data was not normally distributed, so the medians of each group were compared. Of the three groups only the intern sample group passed the normality Kolmogorov-Smirnov test with a p-value of 0.0567 (Table 4.8).

Interns obtained a median score of 33 % (range: 0-83%). The registrars obtained a median score of 50% (range: 0-87%). The consultants obtained a median score of 67% (range: 17-87%). Of the three groups only the scores of the interns were normally distributed, therefore when comparing the groups a Kruskal-Wallis test was used. A statistically significant difference was found (p=0.0013) and was confirmed to be between the intern and consultant groups following a Dunn's multiple comparison test (p<0.001) (Table 4.9).

Table 4.8 Summary of the results for the comparison of knowledge between groups of anaesthetists according to professional designation using the Kruskal-Wallis Test

Group	Interns	Registrars	Consultants
Sample Size	26	41	37
Mean (%)	36.54	50	60.43
Standard Deviation	26.68	23.87	16.76
SEM	5.232	3.728	2.755
Median (%)	33	50	67*
Min (%)	0	0	17
Max (%)	83	83	83
Normality Test KS#	0.1681	0.1764	0.2200
Normality Test P value	0.0567	0.0025	<0.0001
Passed Normality Test	Yes	No	No

*significantly different from the intern group (p<0.001)
KS: Kolmogorov-Smirnov

Table 4.9 Dunn's Multiple Comparisons test table for group test result differences

Comparison	Mean Rank Difference	P-Value
Interns vs. Reg's	-14.896	ns P>0.05
Interns vs. Cons	-27.386	P<0.001
Reg's vs. Cons	-12.490	ns P>0.05

4.3 Discussion

Wits anaesthetists' knowledge on the use of adrenaline in different clinical scenarios is not adequate, since only 14% of anaesthetists who participated in the study passed the questionnaire. The results reflect findings by institutions worldwide who have similarly attempted to determine the knowledge that doctors have on the use of adrenaline in different emergency scenarios (25, 48, 82-84). A study by Jose et al (82) showed that in 2007, doctors in Wales and England were not only using the incorrect doses of adrenaline in anaphylaxis, but also the incorrect route of administration. Further studies by Droste et al (25, 48) showed that in 2010 and 2012 junior doctors in England were using inadequate doses of adrenaline in anaphylaxis.

The average score of the adrenaline questionnaire across all groups of anaesthetists was 50%, which is less than adequate in the treatment of patients in the emergency scenario. Discussing where the shortcomings of this knowledge are might explain why the overall test questionnaire scores are so poor. Therefore, it is important to discuss the results with regard to each question within the different clinical scenarios.

Clinical scenario one

In the first clinical scenario (Questions 1 and 2), cardiac arrest doses of adrenaline were required to correctly answer the questions. Only 46% of anaesthetists were able to answer both questions in the scenario and thus more than half the participants failed the scenario. Of the anaesthetists who passed the scenario, a significantly greater proportion of them were ACLS certified ($p=0.0118$) and therefore the likelihood of passing the scenario was dependant on the acquisition of knowledge from having completed an ACLS course. This seems obvious and yet not all ACLS certified anaesthetists passed the scenario.

It was shown that for question 1, 86% of anaesthetists knew that the cardiac arrest dose of adrenaline is 1 mg intravenously, given as a bolus dose (4, 47). It is interesting that this question was not answered with a 100% pass rate since it is common knowledge amongst anaesthetists and most doctors (4). Possibly, the lack of knowledge regarding question 1 has to do with the effect of memory fade suggested by Heard et al (59). Cardiac emergencies are also not that common and therefore, the need for constant updating of knowledge regarding ACLS algorithms is probably underestimated. This is supported by Ragavan et al (21), suggesting that emergency care knowledge should be updated every two years . Since 82% of the participants (Figure 4.2) did not have an ACLS certification or had not updated their certification (within the last two years), their lack of knowledge might be attributed, in part, to memory fade. It is important to mention that physicians attitudes towards protocols and resuscitation knowledge also affects the dose they would administer in such situations (17). Reasons for this have been described by Cabana et al (17), and include the lack of agreement and self-efficacy, meaning it is plausible that incorrect answers were provided because of disagreement with the guideline's recommendation.

It is unlikely that there are anaesthetists that have not been faced with a cardiac arrest situation at some point in their medical careers. One could argue that, although medical students are trained regarding cardiac arrest scenarios, there is no exit level exam testing cardiac arrest doses of adrenaline at medical school, hence, room for error when faced with the life saving scenarios. It is important to note that ACLS is not a compulsory course.

Furthermore, not all specialties require an ACLS certificate in order to become a specialist in training. In the Department of Anaesthesiology at Wits the questionnaire showed that only 69% of participants had ever completed an ACLS course. One possible reason for this could be that ACLS courses were not a pre-requisite for registrar posts when the more experienced anaesthetists began their training. Another reason could be that there were no consensus guidelines regarding cardiac support and thus some participants' training predated the integration of such protocols (ACLS). ACLS was first developed after discussions held at the Third National Conference on CPR in 1979 for the first time.

These reasons, however, do not negate the fact that there are anaesthetists who do not know, or are deterring from, the cardiac arrest dose of adrenaline recommended by the ACLS guidelines, which are an international standard.

The fact that an ACLS course was completed should not be interpreted as having acquired the knowledge indefinitely, as most of the participants who acquired an ACLS certificate had done so more than two years prior to the answering of this research report's questionnaire, and thus many of the details regarding the protocols may have been forgotten. This is corroborated by knowledge studies showing that the retention of knowledge is only reliable if done so repeatedly throughout ones career (21, 85). Some recommendations include three monthly updates of vital information, in order to remember such protocols, and to therefore be considered up to date with current information. Considering that only 18% of the sample of anaesthetists had completed the ACLS course in the last two years may also be suggestive of the poor knowledge outcomes regarding cardiac arrest doses.

In the second question, a more detailed dosing of adrenaline was required to correctly answer the question. For this question, the dose, per kilogram of body weight, of adrenaline was required to correctly answer the question (7.5-20mcg/kg). Only 48% of the participants correctly answered this question, indicating that there is a lack of understanding regarding the basis for using a single milligram bolus dose of adrenaline in cardiac arrest. Acquiring ACLS certification made no difference to the anaesthetists' pass rate regarding this question, which is explained by the fact that ACLS does not teach the cardiac arrest dose of adrenaline as a body weight adjusted dose, but as a bolus dose. This question, however, has relevant clinical applications due to the fact that during non-cardiac arrest scenarios, using doses in these ranges may be detrimental to patients, because doses as high as this may induce cardiac ischaemia and thus precipitate cardiac failure or even death (6, 28, 40, 43, 45).

Clinical scenario two

Only 14% of anaesthetists passed the anaphylaxis scenario. During anaphylactic shock, intravenous adrenaline administration is necessary in the range of 0.02 mcg/kg to 10 mcg/kg (31). The results of question 3 in the knowledge study show that 60% of anaesthetists know how much adrenaline to administer during such an emergency. Results of this question ranged greatly, with some participants under-dosing, but with the majority overdosing adrenaline boluses up to the cardiac arrest dose range, i.e. up to 20 mcg/kg. The medical implications of these high doses have already been discussed in the literature review and above (scenario one).

A potential reason for the lack of knowledge of intravenous adrenaline during anaphylaxis might be that in ACLS courses an intramuscular injection (IMI) dose of adrenaline is recommended, followed by an intravenous infusion of adrenaline if hypotension persists. This notion however, is not supported by the results of question four, which follows the recommendation by the ACLS guidelines for anaphylaxis. That is, question four asks the participant to recommend an alternate route and dose of adrenaline during anaphylaxis (0.5 mg IMI). This question was poorly answered, with only 20% correctly answering. Therefore it cannot be assumed that the ACLS recommendation is the reason for question 3 being answered poorly as well.

Interestingly, it was shown that there was a significant difference between those anaesthetists who answered question 4 correctly and had acquired an ACLS course, and those who had not. Of the anaesthetists who answered question 4 correctly 95% of them were ACLS certified. However, most of the ACLS certified anaesthetists failed the question. Therefore acquiring an ACLS certification made it more likely to answer questions about adrenaline in anaphylaxis correctly.

Jose et al (82, 83), showed with the use of a survey, that junior doctors in medical institutes in the United Kingdom had knowledge deficits in resuscitation guidelines pertaining specifically to the use of adrenaline in anaphylaxis. Only 44.5% of junior doctors knew the correct dose of adrenaline in anaphylaxis, and only 16.8% would administer the adrenaline as per United Kingdom resuscitation council guidelines (82, 83). These findings were congruent with those by Gompels et al (86), who investigated the knowledge of senior house officers in Accident and Emergency posts in the United Kingdom by means of an adrenaline questionnaire relating to scenarios of anaphylaxis. It would appear that problems relating to the poor knowledge of doctors regarding the dose and route of adrenaline administration in anaphylaxis are not unique to our study.

Clinical scenario 3

In this scenario participants had to know the recommended starting and ceiling doses of an adrenaline infusion. Only 7% were able to answer both questions correctly, therefore passing the scenario. It was shown in question five that while 79% of the anaesthetists knew how to safely start an infusion, at approximately 0.05 mcg/kg/min, only 9% knew that the recommended safe ceiling dose is 0.5 mcg/kg/min (4, 31, 47). As shown by Table

4.7, question 5's results also showed a statistically significant difference (p=0.0033) between answers given by anaesthetists who had completed ACLS and those who had not providing evidence that ACLS improved the knowledge of anaesthetists regarding adrenaline doses. It is of concern that question six's most frequent answer was in fact 1 mcg/kg/min, double the recommended dose. The implications of this are the possibility of myocardial ischaemia, renal failure, cerebrovascular insult, cardiac injury and death (6, 28, 41, 43, 45). The tendency to use high adrenaline infusion doses might be explained by the presence of confounding literature regarding adrenaline infusions. Some literature suggests doses up to 1.5 mcg/kg/min, while others have not recommended a ceiling dose. There is simply no general consensus regarding how much adrenaline is too much when used as an infusion.

The titration of drug doses is common practice with many drugs in anaesthesia, allowing for safer administration of drugs with particular side effects. Many junior anaesthetists are taught to titrate adrenaline infusions. The precaution for maximal doses is also of particular concern in anaesthesia, avoiding overdosing patients and causing unwanted side effects. It is evidenced by the questionnaire's results that adrenaline infusions are generally run at higher doses than what is safely recommended. This observation is possibly explained by the concern in life threatening situations where higher adrenaline doses are a last resort.

A defensive stance on this point is that since the teaching and general practice is to titrate adrenaline to its effect in critically ill patients, where adrenaline infusions are common, the recommended ceiling dose may not be effective. In other words, critically ill patients may require higher dosing of adrenaline in a scenario where a risk/benefit decision has been made and higher adrenaline infusion doses might be the most plausible treatment option. Again, this does not excuse the lack of knowledge regarding what dose is recommended, only that it is the result of a confusing body of evidence regarding what is a "safe" maximal adrenaline infusion. The American Heart Association guidelines on advanced cardiac life support clearly recommend that a dose range of 0.1-0.5 mcg/kg/min be used for post cardiac arrest hypotension (4). However, it is still not understood why anaesthetists are not complying with recommended guidelines.

General

With regard to this study's questionnaire results, it is argued that anaesthetists' knowledge is lacking, regarding adrenaline. Again, it should not be forgotten that knowledge is subject to fade, and thus a function of repeated knowledge update. Since there is no formal continued learning requirement it is not surprising that the anaesthetists are subject to knowledge fade. Only 69% of the sample of anaesthetists had completed an ACLS course, of which 26% were completed in the last two years, the recommendation being to update this knowledge every two years (21, 85). Therefore, only 18% of the sample had updated ACLS knowledge (Figure 4.2).

Exposure to the knowledge of pharmacology in anaesthesia practice is common in academic institutions and may constitute being regularly updated, especially regarding emergency drugs. Why then, is knowledge regarding adrenaline doses so poor?

Cabana et al. (17) discussed the attitude of the physician and how this influences the engagement of the learner with knowledge. This was discussed in the literature review and has an important impact on knowledge and learning. Studies investigating clinical guidelines have consistently shown that clinical practice guidelines alone have a limited effect on the behavioural change of the practicing physician (18-20), tying in to the fact that despite the ACLS guideline, anaesthetists at Wits are still making dosing decisions that do not comply with these guidelines. Possibly, the reasons for non-compliance are because anaesthetists are making clinical decisions based on their knowledge and experience, and are therefore justifying veering from clinical guidelines (17).

The knowledge of anaesthetist regarding adrenaline doses in three clinical scenarios was found to be poor, with an overall average score of 50% for the questionnaire. Only 14% of anaesthetists passed the questionnaire. Interestingly, of the anaesthetists who had ever acquired an ACLS certification 19% passed the questionnaire. This is compared to those anaesthetists who had never acquired an ACLS certification, of whom only 3% passed.

This was statistically significant (p=0.0339). Therefore, ACLS training improves the knowledge of anaesthetists regarding adrenaline doses in emergencies, although the pass rate is still not adequate.

To further investigate whether the more recent acquisition of knowledge was contributing to a better pass rate, only those anaesthetists with ACLS were compared. Those participants who were recently certified were compared with those who were certified more than two years prior. No difference was found, implying that recently updating knowledge made no difference to the anaesthetists' pass rate of the questionnaire. There were however, a larger proportion of anaesthetists passing if they had acquired the ACLS course recently, and since the groups were different in sample size, perhaps the sample was underpowered.

Analysing the pass rates one scenario at a time shows repeatedly that those anaesthetists who were ACLS certified had more knowledge. Scenarios one and two show significant differences between the ACLS and no ACLS groups' pass rates. However, in scenario three no difference was found. As explained before, this is probably due to there being no formal consensus about how much adrenaline is too much as an infusion, and thus anaesthetists are drawing conclusion based on clinical experience with the drug.

In determining whether a correlation exists between the knowledge of adrenaline and the years of anaesthetic experience, a positive correlation was shown (r=0.2460, p=0.0118) indicating that anaesthetic experience improved knowledge of adrenaline in emergencies. Similarly, in a study carried out on Canadian anaesthesiologists, Porayko and Butler (87) found that anaesthesiologists with more experience scored better at knowledge questionnaires aimed at testing knowledge of perioperative emergencies. Although the correlation found in our study was weakly positive, it was limited by a short questionnaire that did not allow for a wider range of questionnaire results. A wider series of results might have improved the correlation coefficient. Furthermore, there were fewer anaesthetists in the categories with high numbers of anaesthetic year experience; this may also have limited the correlation.

Convincingly, when anaesthetists' knowledge was compared across professional designations, a statistically significant difference between interns and consultants was found ($p<0.01$), reiterating that more experience equated to more knowledge regarding emergency adrenaline (87). No differences were found between the intern and registrar groups despite their questionnaire score medians being 33% and 50%, respectively. This was also the case for the registrar and consultant groups where the median scores were 50% and 67%, respectively. This lead us to believe that the observation may have been underpowered as the questionnaire score medians certainly appear to be different. Furthermore, the groups were not matched in sample size as there was no control over who participated in the study.

These result were not surprising, since gaining more knowledge with experience is logical, but as described by Cabana et al (17), may be restricted or hindered by adherence barriers as discussed in the literature, chapter 2.

4.4 Conclusion

The knowledge of Wits anaesthetist's regarding the use of adrenaline in cardiac arrest, anaphylaxis and as an infusion is generally very poor. There is a general trend for knowledge to improve with more experience gained in anaesthesia, but even so, large knowledge deficits are still prominent.

Generally, having previously completed an ACLS course significantly improved knowledge about adrenaline in emergencies.

Interns training in anaesthesia were shown to have the least knowledge and should be educated regarding adrenaline use. Furthermore, the advent of ACLS is shown to be of significance in acquiring the necessary knowledge doctors need to treat cardiac emergencies and should therefore be considered as a compulsory method of education for junior doctors and as a refresher for doctors with more experience.

4.5 Summary

The results of this study have been presented in this chapter and discussed as per the research objectives. The data presented include demographic data of the study population and responses to a questionnaire regarding professional designation, years of experience, ACLS accreditation, updated ACLS, and the knowledge of adrenaline in three clinical scenarios; cardiac arrest, anaphylaxis and as an infusion. The findings have been described and analysed using descriptive and inferential statistics.

In the final chapter a summary, the limitations, recommendations and conclusions of the study are presented.

CHAPTER 5: Study summary, limitations, recommendations and conclusion

5.1 Introduction

In this chapter, a summary of the aim and objectives, research methods and results of the study will be presented. The limitations of the study will also be discussed and recommendations made regarding future clinical practice and research on adrenaline use. A conclusion will also be presented.

5.2 Study summary

5.2.1 Aim

The aim of this study was to determine the knowledge of anaesthetists working in the Department of Anaesthesiology at Wits regarding the appropriate administration of adrenaline for anaphylaxis, cardiac arrest and inotropic infusions.

5.2.2 Objectives

The primary objectives of this study were to:

- describe the knowledge of anaesthetists regarding adrenaline doses in three different clinical scenarios
- compare whether the overall knowledge of anaesthetists, with and without ACLS certification, regarding adrenaline was adequate
- compare whether the knowledge of anaesthetists, with and without ACLS certification, regarding each scenario was adequate
- correlate knowledge of adrenaline with years of anaesthetic experience

The secondary objective was to:

- compare the knowledge of anaesthetists between different professional designations.

5.2.3 Summary of methodology

This study was a prospective, contextual, descriptive study on a sample that consisted of anaesthetists working in the Wits Department of Anaesthesiology.

In consultation with a bio-statistician a sample of 85 Wits anaesthetists was estimated. This was based on the assumption that 67% of anaesthetists in the Wits Department of Anaesthesiology would have adequate knowledge of adrenaline to an accuracy of within 10%, and with 95% confidence.

This study used a convenience sampling method, as is appropriate for a descriptive study (78). Importantly, for the purpose of this study, a sample of anaesthetists who were in the same place at the same time was required in order to distribute a "surprise" questionnaire, thus eliminating the possibility of pre-empting answers to questions. Therefore, anaesthetists who attended the weekly academic meeting and who were willing to participate in the study were included. Incomplete questionnaires returned were included and a score of zero was allocated to unanswered questions. Blank questionnaires returned were excluded.

No questionnaires pertaining to the appropriate administration of adrenaline were identified in the literature. To ensure content validity the draft questionnaire was based on a review of the literature. To further achieve face and content validity, three anaesthesiologists were consulted. Following consultation minor corrections were made. Finally, a questionnaire was drafted to include three clinically relevant emergency situations whereby adrenaline would need to be used.

Before distribution of the questionnaires, all sheets were numbered so as to keep track of questionnaires completed. Numbering the questionnaires also helped prevent reproduction of results. Furthermore, a response rate could then be calculated.

Data was collected during February 2014 and June 2014 at departmental academic meetings. The researcher and two assistants were present during completion of the questionnaires to assist with queries and prevent data contamination. To further prevent data contamination, the researcher collected data at non-consecutive departmental meetings.

At the start of the meeting the researcher addressed anaesthetists, giving them a brief introduction to the study and inviting them to participate. Information letters and questionnaires were distributed allowing 10-15 minutes to complete the questionnaire.

All the questionnaires, complete and incomplete, were placed in an unmarked envelope, sealed and dropped into a collection box. This helped to ensure anonymity and confidentiality of the anaesthetists partaking in the study.

Based on the results of the study, an update on the appropriate use of adrenaline will be presented at a departmental academic meeting.

Using Microsoft Excel 2010, data was captured onto spreadsheets. The statistical program, GraphPad InStat, was used to analyse data. A p-value of less than 0.05 was considered significant in this study.

5.2.4 Summary of results

104 anaesthetists responded to the self-administered questionnaire. It was found that large knowledge gaps exist in clinical scenarios where adrenaline is necessary. This was evidenced by the pass rate of the questionnaire, where only 15 (14%) anaesthetists managed to pass. Interestingly it was shown that anaesthetists who were ACLS certified had a higher pass rate than those anaesthetists who were not ACLS certified, highlighting the importance of attaining an ACLS certification. Updating the ACLS course however, did not seem to make a difference to the overall pass rate.

With regard to the adrenaline questionnaire (Appendix 4), it was shown that questions 1-6 were answered correctly by 86%, 48%, 60%, 20%, 79%, and 9%, respectively. This highlights the largest problem areas in adrenaline knowledge being with the anaphylaxis scenario, and with regard to maximal infusion doses of adrenaline.

A weak positive correlation ($r=0.2460$) was also found between knowledge that anaesthetists have and the number of years spent in anaesthetic practice. This correlation was supported by showing that a difference exists when comparing the knowledge of anaesthetic interns and consultants ($p<0.001$).

5.3 Limitations

Due to the study being contextual, it limits the generalisation of the findings to anaesthetic doctors, but knowledge of adrenaline in emergencies is crucial to all who practice medicine.

The sample size of the study, while adequate, was not equally represented by anaesthetists from different professional categories. This was due to the study sample being a random convenience sample from the anaesthetic department meetings, thus no control over who was participating could be achieved.

The sample size necessary to power the study was predicted based on the assumption that two thirds (67%) of anaesthetists would pass the questionnaire. Since the actual findings show that only 15% of anaesthetists passed, then perhaps the study was underpowered.

While the questionnaire was reviewed by three anaesthesiologists before being distributed to the anaesthetist sample group, it is not a standard questionnaire and may be open to misinterpretation of the questions. If this were the case then perhaps the data set has a higher pass rate than what was represented by the questionnaire results.

Many knowledge studies often have post-test lectures on the subject matter being investigated and then a follow up questionnaire is done two to three months later to determine if there was knowledge retention on the subject. This proved a difficult task in this study as, ethically, total anonymity was required. It would therefore not have been possible to pair the data set's post-test questionnaire results, to determine whether there was knowledge retention.

Considering the poor pass rate of the study questionnaire, a post-test lecture on adrenaline should have been given to the participants. This is an ethical dilemma that will still be addressed in the future.

5.4 Recommendations

5.4.1 Clinical practice

Anaesthetists at Wits should be reminded of the adrenaline guidelines in emergencies by means of an informative lecture.

Wits Anaesthetist's should ensure that they are all currently certified with an ACLS course.

All ACLS certified anaesthetists could ensure that their certification is still current.

Knowledge studies show that knowledge retention on average spans three months and therefore continuous updating of information is necessary.

The American Heart Association and ACLS provide a concise and informative pocket card with all the relevant emergency management details on them. Drug doses and routes of administration can quickly and easily be accessed in the case of an emergency. Anaesthetists at Wits should all acquire these cards, so as to assist in the memory retention process, and in the state of an emergency.

Protocol posters based on the ACLS guideline information could be put up in all theatres so as to make for quick referencing during emergencies.

5.4.2 Further research

Should the abovementioned recommendations be put into practice at Wits, further research should be considered in order to examine the effectiveness of such interventions on knowledge.

Given that the knowledge of adrenaline among Wits anaesthetists is lacking, it is important to consider investigating the knowledge of other emergency scenarios that are pertinent to the practice of anaesthesia.

5.5 Conclusion

The knowledge of anaesthetists, at Wits, regarding adrenaline use in emergencies is inadequate. Anaesthetists are trained to deal with life threatening cardiac emergencies by means of protocols that guide the proper treatment of such emergencies. Incorrectly dosing patients with adrenaline can lead to death by overdose or by undertreating the emergent condition, and may also mean untoward litigation for the anaesthetists responsible.

To improve the quality of care and decrease the variation in practice, standard practice guidelines are endorsed by medical councils the world over. The attitudes of doctors towards such guidelines however, are a major contributor to decision making during emergencies.

By making the anaesthetist aware of knowledge deficits and that their attitudes toward management protocols deters them from the recommended guidelines' practice, then perhaps it is possible to improve adherence of doctors to emergency protocols. In conjunction with regular knowledge updates, an improvement in Wits anaesthetists' management of emergencies concerning adrenaline is possible.

References

1. Audet AM, Greenfield S, Field M. Medical practice guidelines: current activities and future directions. Annals of internal medicine. 1990 Nov 1;113(9):709-14. PubMed PMID: 2221652. Epub 1990/11/01. eng.

2. Africa RCoS. Severe Anaphylactic Reactions 2013 [cited 2013 19 February 2013]. Available from:www.resuscitationcouncil.co.za/Docs/Page%208%20%20Severe%20Anaphylactic%20Reactions1.pdf.

3. Allergy Society of South Africa. Treatment of Severe Anaphylactic Reactions (Adult and Child). 2012 [14 February 2013]. Available from: www.allergysa.org/B_Brochures.asp.

4. American Heart Association. Advanced Cardiac Life Support 2013 [14 February 2013]. Available from: www.heart.org/HEARTORG/CPRAndECC/HealthcareProviders/AdvancedCardiovascularLifeSupportACLS/Advanced-Cardiovascular-Life-Support-ACLS_UCM_001280_SubHomePage.jsp.

5. Neumar RW, Otto CW, Link MS, Kronick SL, Shuster M, Callaway CW, et al. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010 Nov 2;122(18 Suppl 3):S729-67. PubMed PMID: 20956224. Epub 2010/10/22. eng.

6. Kanwar M, Irvin CB, Frank JJ, Weber K, Rosman H. Confusion about epinephrine dosing leading to iatrogenic overdose: a life-threatening problem with a potential solution. Annals of emergency medicine. 2010 Apr;55(4):341-4. PubMed PMID: 20031267. Epub 2009/12/25. eng.

7. Budhwani N, Bonaparte KL, Cuyjet AB, Saric M. Severe reversible left ventricular systolic and diastolic dysfunction due to accidental iatrogenic epinephrine overdose. Reviews in cardiovascular medicine. 2004 Spring;5(2):130-3. PubMed PMID: 15188772. Epub 2004/06/11. eng.

8. Campbell RL. Cardiovascular effects of epinephrine overdose: case report. Anesthesia progress. 1977 Nov-Dec;24(6):190-3. PubMed PMID: 276280. Pubmed Central PMCID: PMC2516151. Epub 1977/11/01. eng.

9. Carter BT, Westfall VK, Heironimus TW, Atuk NO. Severe reaction to accidental subcutaneous administration of large doses of epinephrine. Anesthesia and analgesia. 1971 Mar-Apr;50(2):175-8. PubMed PMID: 5102629. Epub 1971/03/01. eng.

10. Fyfe AI, Daly PA, Dorian P, Tough J. Reversible "cardiomyopathy" after accidental adrenaline overdose. The American journal of cardiology. 1991 Feb 1;67(4):318-9. PubMed PMID: 1990800. Epub 1991/02/01. eng.

11. Litvinov IV, Kotowycz MA, Wassmann S. Iatrogenic epinephrine-induced reverse Takotsubo cardiomyopathy: direct evidence supporting the role of catecholamines in the pathophysiology of the "broken heart syndrome". Clinical research in cardiology : official journal of the German Cardiac Society. 2009 Jul;98(7):457-62. PubMed PMID: 19513776. Epub 2009/06/11. eng.

12. Meaudre E, Barbou F, Sallaberry M, Cantais E, Petit D, Palmier B. Rapid reversal of global left ventricular dysfunction after accidental injection of 0.75 mg epinephrine in a 20-year-old patient. Acta anaesthesiologica Scandinavica. 2004 Aug;48(7):914-6. PubMed PMID: 15242440. Epub 2004/07/10. eng.

13. Rolfe S, Harper NJ. Ability of hospital doctors to calculate drug doses. BMJ (Clinical research ed). 1995 May 6;310(6988):1173-4. PubMed PMID: 7767153. Pubmed Central PMCID: PMC2549558. Epub 1995/05/06. eng.

14. Sood JD, Empson M, Fitzharris P, Stewart J. Too much of a good thing, is it bad? Adrenaline on trial. The New Zealand medical journal. 2007;120(1252):U2494. PubMed PMID: 17460744. Epub 2007/04/27. eng.

15. Zeller B, Bangstad HJ. [Accidental administration of racemic adrenaline. Three life-threatening cases after intravenous injection in children]. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke. 1998 Mar 10;118(7):1080-1. PubMed PMID: 9531834. Epub 1998/04/09. Feiladministrering av racemisk adrenalin. Tre livstruende tilfeller etter intravenos injeksjon hos barn. nor.

16. Adapa RM, Mani V, Murray LJ, Degnan BA, Ercole A, Cadman B, et al. Errors during the preparation of drug infusions: a randomized controlled trial. British journal of anaesthesia. 2012 Nov;109(5):729-34. PubMed PMID: 22850220. Epub 2012/08/02. eng.

17. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. JAMA : the journal of the American Medical Association. 1999 Oct 20;282(15):1458-65. PubMed PMID: 10535437. Epub 1999/10/27. eng.

18. Hayward RS. Clinical practice guidelines on trial. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 1997 Jun 15;156(12):1725-7. PubMed PMID: 9220924. Pubmed Central PMCID: PMC1227587. Epub 1997/06/15. eng.

19. Lomas J, Anderson GM, Domnick-Pierre K, Vayda E, Enkin MW, Hannah WJ. Do practice guidelines guide practice? The effect of a consensus statement on the practice of physicians. The New England journal of medicine. 1989 Nov 9;321(19):1306-11. PubMed PMID: 2677732. Epub 1989/11/09. eng.

20. Woolf SH. Practice guidelines: a new reality in medicine. III. Impact on patient care. Archives of internal medicine. 1993 Dec 13;153(23):2646-55. PubMed PMID: 8250661. Epub 1993/12/13. eng.

21. Ragavan S, Schneider H, Kloeck WG. Basic resuscitation--knowledge and skills of full-time medical practitioners at public hospitals in northern province. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 2000 May;90(5):504-8. PubMed PMID: 10901824. Epub 2000/07/21. eng.

22. World Medical Association. WMA Declaration of Helsinki-Ethical principles for medical research involving human subjects. Seoul: World Medical Association, 2013.

23. Department of Health. Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa. Pretoria, South Africa: 2006.

24. Clinical Practice Guidelines:Directions for a New Program. Field MJ, Lohr KN, editors: The National Academies Press; 1990.

25. Droste J, Narayan N. Hospital doctors' knowledge of adrenaline (epinephrine) administration in anaphylaxis in adults is deficient. Resuscitation. 2010 Aug;81(8):1057-8. PubMed PMID: 20627522. Epub 2010/07/16. eng.

26. Wheeler DW, Remoundos DD, Whittlestone KD, Palmer MI, Wheeler SJ, Ringrose TR, et al. Doctors' confusion over ratios and percentages in drug solutions: the case for standard labelling. Journal of the Royal Society of Medicine. 2004 Aug;97(8):380-3. PubMed PMID: 15286190. Pubmed Central PMCID: PMC1079557. Epub 2004/08/03. eng.

27. Breakwell G, S. H, Fife-Shaw C. Research Methods in Psychology. 2nd ed. London: Sage; 2000.

28. Callaway CW. Epinephrine for cardiac arrest. Current opinion in cardiology. 2013 Jan;28(1):36-42. PubMed PMID: 23196774. Epub 2012/12/01. eng.

29. Chassin MR. Practice guidelines: best hope for quality improvement in the 1990s. Journal of occupational medicine : official publication of the Industrial Medical Association. 1990 Dec;32(12):1199-206. PubMed PMID: 2292739. Epub 1990/12/01. eng.

30. Peterson O. Endocrine System. In: Peterson O, editor. Lecture Notes: Human Physiology. Malden, Ma: Blackwell; 2007. p. 260-1.

31. Milner A, Welch E. Autonomic Nervous System. In: A. M, Welch E, editors. Applied Pharmacology in Anaesthesiology and Critical Care. Pietermaritzburg: Intrepid Printers; 2012. p. 145-89.

32. Guyton AC, Hall JE. The Autonomic Nervous System and the Adrenal Medulla. In: Guyton AC, Hall JE, editors. Textbook of Medical Physiology. Philadelphia, Pennsylvania: Elselvier Saunders; 2006. p. 751-5.

33. Africa ASoS. Anaphylaxis. 2013 [19 February 2013]. Available from: www.allergysa.org.

34. Association WA. Anaphylaxis: Global Overview 2013 [19 February 2013]. Available from: www.worldallergy.org/professional/allergic_diseases_center/anaphylaxis/anaphylaxisglobal.php.

35. Lieberman P. Epidemiology of anaphylaxis. Current opinion in allergy and clinical immunology. 2008 Aug;8(4):316-20. PubMed PMID: 18596588. Epub 2008/07/04. eng.

36. Lieberman P, Camargo CA, Jr., Bohlke K, Jick H, Miller RL, Sheikh A, et al. Epidemiology of anaphylaxis: findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working Group. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology. 2006 Nov;97(5):596-602. PubMed PMID: 17165265. Epub 2006/12/15. eng.

37. Kirkbright SJ, Brown SG. Anaphylaxis--recognition and management. Australian family physician. 2012 Jun;41(6):366-70. PubMed PMID: 22675674. Epub 2012/06/08. eng.

38. Rutkowski K, Dua S, Nasser S. Anaphylaxis: current state of knowledge for the modern physician. Postgraduate medical journal. 2012 Aug;88(1042):458-64. PubMed PMID: 22467837. Epub 2012/04/03. eng.

39. Sheikh A, Shehata YA, Brown SG, Simons FE. Adrenaline for the treatment of anaphylaxis: cochrane systematic review. Allergy. 2009 Feb;64(2):204-12. PubMed PMID: 19178399. Epub 2009/01/31. eng.

40. Rivers EP, Wortsman J, Rady MY, Blake HC, McGeorge FT, Buderer NM. The effect of the total cumulative epinephrine dose administered during human CPR on hemodynamic, oxygen transport, and utilization variables in the postresuscitation period. Chest. 1994 Nov;106(5):1499-507. PubMed PMID: 7956410. Epub 1994/11/01. eng.

41. Ewy GA, Kern KB. Recent advances in cardiopulmonary resuscitation: cardiocerebral resuscitation. Journal of the American College of Cardiology. 2009 Jan 13;53(2):149-57. PubMed PMID: 19130982. Epub 2009/01/10. eng.

42. Larsson PT, Hjemdahl P, Olsson G, Egberg N, Hornstra G. Altered platelet function during mental stress and adrenaline infusion in humans: evidence for an increased aggregability in vivo as measured by filtragometry. Clinical science (London, England : 1979). 1989 Apr;76(4):369-76. PubMed PMID: 2523769. Epub 1989/04/01. eng.

43. Ditchey RV, Lindenfeld J. Failure of epinephrine to improve the balance between myocardial oxygen supply and demand during closed-chest resuscitation in dogs. Circulation. 1988 Aug;78(2):382-9. PubMed PMID: 3396175. Epub 1988/08/01. eng.

44. Burnett AM, Segal N, Salzman JG, McKnite MS, Frascone RJ. Potential negative effects of epinephrine on carotid blood flow and ETCO2 during active compression-decompression CPR utilizing an impedance threshold device. Resuscitation. 2012 Aug;83(8):1021-4. PubMed PMID: 22445865. Epub 2012/03/27. eng.

45. McQueen C, Gates S, Perkins GD. Adrenaline for the pharmacological treatment of cardiac arrest... going, going, gone? Resuscitation. 2012 Aug;83(8):921-2. PubMed PMID: 22794111. Epub 2012/07/17. eng.

46. Levy B, Perez P, Perny J, Thivilier C, Gerard A. Comparison of norepinephrine-dobutamine to epinephrine for hemodynamics, lactate metabolism, and organ function variables in cardiogenic shock. A prospective, randomized pilot study. Critical care medicine. 2011 Mar;39(3):450-5. PubMed PMID: 21037469. Epub 2010/11/03. eng.

47. Africa RCoS. Algorithms 2013 [cited 2013 19 February]. Available from: www.resuscitationcouncil.co.za/councilInfo_Algorithms.cfm.

48. Droste J, Narayan N. Anaphylaxis: lack of hospital doctors' knowledge of adrenaline (epinephrine) administration in adults could endanger patients' safety. European annals of allergy and clinical immunology. 2012 Jun;44(3):122-7. PubMed PMID: 22905594. Epub 2012/08/22. eng.

49. Pumphrey R. Anaphylaxis: can we tell who is at risk of a fatal reaction? Current opinion in allergy and clinical immunology. 2004 Aug;4(4):285-90. PubMed PMID: 15238794. Epub 2004/07/09. eng.

50. Herout PM, Erstad BL. Medication errors involving continuously infused medications in a surgical intensive care unit. Critical care medicine. 2004 Feb;32(2):428-32. PubMed PMID: 14758159. Epub 2004/02/06. eng.

51. Valentin A, Capuzzo M, Guidet B, Moreno RP, Dolanski L, Bauer P, et al. Patient safety in intensive care: results from the multinational Sentinel Events Evaluation (SEE) study. Intensive care medicine. 2006 Oct;32(10):1591-8. PubMed PMID: 16874492. Epub 2006/07/29. eng.

52. Donaldson TM, Mani V, Wheeler DW. Factors affecting the concentration of electrolyte infusions prepared from stock solutions. Postgraduate medical journal. 2011 Feb;87(1024):83-8. PubMed PMID: 20870647. Epub 2010/09/28. eng.

53. McDowell SE, Ferner HS, Ferner RE. The pathophysiology of medication errors: how and where they arise. British journal of clinical pharmacology. 2009 Jun;67(6):605-13. PubMed PMID: 19594527. Pubmed Central PMCID: PMC2723197. Epub 2009/07/15. eng.

54. Parshuram CS, To T, Seto W, Trope A, Koren G, Laupacis A. Systematic evaluation of errors occurring during the preparation of intravenous medication. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2008 Jan 1;178(1):42-8. PubMed PMID: 18166730. Pubmed Central PMCID: PMC2151118. Epub 2008/01/02. eng.

55. Lesar TS, Briceland L, Stein DS. Factors related to errors in medication prescribing. JAMA : the journal of the American Medical Association. 1997 Jan 22-29;277(4):312-7. PubMed PMID: 9002494. Epub 1997/01/22. eng.

56. Wheeler DW, Carter JJ, Murray LJ, Degnan BA, Dunling CP, Salvador R, et al. The effect of drug concentration expression on epinephrine dosing errors: a randomized trial. Annals of internal medicine. 2008 Jan 1;148(1):11-4. PubMed PMID: 18166759. Epub 2008/01/02. eng.

57. Tissot E, Cornette C, Limat S, Mourand JL, Becker M, Etievent JP, et al. Observational study of potential risk factors of medication administration errors. Pharmacy world & science : PWS. 2003 Dec;25(6):264-8. PubMed PMID: 14689814. Epub 2003/12/24. eng.

58. Stucki C, Sautter AM, Wolff A, Fleury-Souverain S, Bonnabry P. Accuracy of preparation of i.v. medication syringes for anesthesiology. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 2013 Jan 15;70(2):137-42. PubMed PMID: 23292267. Epub 2013/01/08. eng.

59. Heard AM, Green RJ, Eakins P. The formulation and introduction of a 'can't intubate, can't ventilate' algorithm into clinical practice. Anaesthesia. 2009 Jun;64(6):601-8. PubMed PMID: 19453312. Epub 2009/05/21. eng.

60. Balk SJ, Landesman LY, Spellmann M. Centers for disease control and prevention lead guidelines: do pediatricians know them? The Journal of pediatrics. 1997 Aug;131(2):325-7. PubMed PMID: 9290627. Epub 1997/08/01. eng.

61. Christakis DA, Rivara FP. Pediatricians' awareness of and attitudes about four clinical practice guidelines. Pediatrics. 1998 May;101(5):825-30. PubMed PMID: 9565409. Epub 1998/05/23. eng.

62. Feldman EL, Jaffe A, Galambos N, Robbins A, Kelly RB, Froom J. Clinical practice guidelines on depression: awareness, attitudes, and content knowledge among family physicians in New York. Archives of family medicine. 1998 Jan-Feb;7(1):58-62. PubMed PMID: 9443701. Epub 1998/01/27. eng.

63. Grilli R, Apolone G, Marsoni S, Nicolucci A, Zola P, Liberati A. The impact of patient management guidelines on the care of breast, colorectal, and ovarian cancer patients in Italy. Medical care. 1991 Jan;29(1):50-63. PubMed PMID: 1986177. Epub 1991/01/01. eng.

64. Mansfield CD. Attitudes and behaviors towards clinical guidelines: the clinicians' perspective. Quality in health care : QHC. 1995 Dec;4(4):250-5. PubMed PMID: 10156394. Pubmed Central PMCID: PMC1055335. Epub 1995/11/04. eng.

65. Olesen F, Lauritzen T. Do general practitioners want guidelines? Attitudes toward a county-based and a national college-based approach. Scandinavian journal of primary health care. 1997 Sep;15(3):141-5. PubMed PMID: 9323781. Epub 1997/11/05. eng.

66. Pierre KD, Vayda E, Lomas J, Enkin MW, Hannah WJ, Anderson GM. Obstetrical attitudes and practices before and after the Canadian Consensus Conference Statement on Cesarean Birth. Social science & medicine (1982). 1991;32(11):1283-9. PubMed PMID: 2068611. Epub 1991/01/01. eng.

67. Wigder HN, Arai DA, Narasimhan K, Cohan S. ACEP chest pain policy: emergency physician awareness. Annals of emergency medicine. 1996 May;27(5):606-9. PubMed PMID: 8629782. Epub 1996/05/01. eng.

68. Hudak BB, O'Donnell J, Mazyrka N. Infant sleep position: pediatricians' advice to parents. Pediatrics. 1995 Jan;95(1):55-8. PubMed PMID: 7770310. Epub 1995/01/01. eng.

69. Phipps DL, Beatty PC, Parker D, Nsoedo C, Meakin GH. Motivational influences on anaesthetists' use of practice guidelines. British journal of anaesthesia. 2009 Jun;102(6):768-74. PubMed PMID: 19398453. Epub 2009/04/29. eng.

70. Phipps DL, Parker D, Meakin GH, Beatty PC. Determinants of intention to deviate from clinical practice guidelines. Ergonomics. 2010 Mar;53(3):393-403. PubMed PMID: 20191414. Epub 2010/03/02. eng.

71. Ward JE, Boyages J, Gupta L. Local impact of the NHMRC early breast cancer guidelines: where to from here? The Medical journal of Australia. 1997 Oct 6;167(7):362-5. PubMed PMID: 9379976. Epub 1997/11/05. eng.

72. Bandura A. Social foundations of thought and action: A social cognitive theory. Inc. P-H, editor. Engelwood Cliffs, New Jersey: Prentice-Hall; 1986.

73. Winkler JD, Lohr KN, Brook RH. Persuasive communication and medical technology assessment. Archives of internal medicine. 1985 Feb;145(2):314-7. PubMed PMID: 3977492. Epub 1985/02/01. eng.

74. Woo B, Woo B, Cook EF, Weisberg M, Goldman L. Screening procedures in the asymptomatic adult. Comparison of physicians' recommendations, patients' desires, published guidelines, and actual practice. JAMA : the journal of the American Medical Association. 1985 Sep 20;254(11):1480-4. PubMed PMID: 4032651. Epub 1985/09/20. eng.

75. Resnicow KA, Schorow M, Bloom HG, Massad R. Obstacles to family practitioners' use of screening tests: determinants of practice? Preventive medicine. 1989 Jan;18(1):101-12. PubMed PMID: 2496405. Epub 1989/01/01. eng.

76. Phipps DL, Parker D, Pals EJ, Meakin GH, Nsoedo C, Beatty PC. Identifying violation-provoking conditions in a healthcare setting. Ergonomics. 2008 Nov;51(11):1625-42. PubMed PMID: 18941971. Epub 2008/10/23. eng.

77. Ajzen I. The Theory of Planned Behaviour. Organizational Behaviour and Human Decision Processes. 1991;50:179-211.

78. Burns N, Grove S. The Practice of Nursing Research. Henderson L, Robertson R, editors. Missouri: Saunders Elselvier; 2009.

79. Brink H, van der Walt C, van Rensburg G. Fundamentals of Research Methodology for Healthcare Professionals. Ristić D, editor. Cape town: Juta & Company Ltd; 2012.

80. De Vos A, Strydom H, Fouche C, Poggenpoel M, Schurink E, Schurink W. Research at Grass Roots. De Vos A, editor. Pretoria: Van Schaik; 1998. 281 p.

81. Botma Y, Greeff M, Mulaudzi M, Wright S. Research in Health Sciences. First ed. Cape Town: Pearson Educational South Africa (PTY) Ltd; 2010.

82. Jose R, Clesham GJ. Survey of the use of epinephrine (adrenaline) for anaphylaxis by junior hospital doctors. Postgraduate medical journal. 2007 Sep;83(983):610-1. PubMed PMID: 17823230. Pubmed Central PMCID: PMC2600009. Epub 2007/09/08. eng.

83. Jose RJ. Anaphylaxis-Junior doctors' knowledge of guidelines. Resuscitation. 2009 Sep;80(9):1091. PubMed PMID: 19604617. Epub 2009/07/17. eng.

84. Schunk JE, Corneli HM. What dose of epinephrine is being used in pediatric resuscitation? Results of a survey. Pediatric emergency care. 1993 Feb;9(1):4-7. PubMed PMID: 8488144. Epub 1993/02/01. eng.

85. Secher N, Mikkelsen MM, Adelborg K, Mikkelsen R, Grove EL, Rubak JM, et al. Direct mail improves knowledge of basic life support guidelines in general practice: a randomised study. Scandinavian journal of trauma, resuscitation and emergency medicine. 2012;20:72. PubMed PMID: 23062629. Pubmed Central PMCID: PMC3493296. Epub 2012/10/16. eng.

86. Gompels LL, Bethune C, Johnston SL, Gompels MM. Proposed use of adrenaline (epinephrine) in anaphylaxis and related conditions: a study of senior house officers starting accident and emergency posts. Postgraduate medical journal. 2002 Jul;78(921):416-8. PubMed PMID: 12151658. Pubmed Central PMCID: PMC1742422. Epub 2002/08/02. eng.

87. Porayko LD, Butler R. Perioperative resuscitation knowledge base. Canadian journal of anaesthesia = Journal canadien d'anesthesie. 1999 Jun;46(6):529-35. PubMed PMID: 10391599. Epub 1999/07/03. eng.

APPENDICES

APPENDIX 1: Approval of research topic

Faculty of Health Sciences
Private Bag 3 Wits, 2050
Fax:
Tel: 027117172040

Reference: Ms Mpumi Mnqapu
E-mail: mpumi.mnqapu@wits.ac.za

14 June 2013
Person No: 9802512H
PAG

Dr PC Anamourlis
310 Interlaken
38 8tj Street
Killarney
2193
South Africa

Dear Dr Anamourlis

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Anaesthetists' knowledge of appropriate adrenaline administration in three clinical scenarios* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX 2: Approval from ethics

M130306

R14/49 Dr Prodromos C Anamourlis

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130306

NAME: (Principal Investigator)	Dr Prodromos C Anamourlis
DEPARTMENT:	Department of Anaesthesiology Department of Anaesthesiology
PROJECT TITLE:	Anaesthetists' Knowlesge of Appropriate Adrenaline Administration in Three Clincal Scenarios
DATE CONSIDERED:	05/04/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Juan Scribante
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 05/06/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX 3: Participants' information sheet

Dear Colleague,

Hello, my name is Christopher, and I am an anaesthesiology registrar in the Wits Department of Anaesthesiology.

I would like to invite you to participate in a research study titled, "Anaesthetists' Knowledge of Appropriate Adrenaline Administration in Three Clinical Scenarios". This study will be handed in to the Faculty Health Sciences at the University of the Witwatersrand in fulfilment of my MMed degree.

This study aims to determine the current knowledge of anaesthetists at the University of the Witwatersrand regarding adrenaline doses and its route of administration. Doctors specialising in anaesthesia are expected to know the appropriate resuscitation guidelines regarding the use of adrenaline. In different scenario, specific doses and routes of administration are recommended. It is not known if anaesthetists working in the Wits Department of Anaesthesiology know how to appropriately administer adrenaline in an emergency. This will be determined by means of a self-administered questionnaire.

Participation is voluntary and consent will be implied on completion of a questionnaire. All information will be confidential and anonymity maintained as no personal information will be required to complete a questionnaire. No penalty will be incurred for not participating in this study.

All questionnaires whether complete or not, should be placed into the box supplied. Numbering of questionnaires is simply for practical purposes as it prevents reproduction of information when data capturing occurs. No numbers will identify the participant involved. All survey contents will only be viewed by me and my supervisors.

The questionnaire should not take longer than 10 minutes to complete and participants are encouraged not to share the information provided on the questionnaire, as this gives an inaccurate representation of the study aims.

No incentives will be provided for the completion of the questionnaire. Identifying the current knowledge of adrenaline within the department will assist in our continued professional development and reduce variation in practice regarding such emergencies.

Before completion of this survey, please ensure that you understand the above information.

Your time is greatly appreciated. Any questions regarding this study can be directed to the following people:

- Professor Cleaton-Jones (chairperson of the HREC): (011) 717-1234
- Christopher Anamourlis (researcher): 073 908 5947

Sincerely,

Christopher Anamourlis

APPENDIX 4: Questionnaire

SECTION 1:

Please provide the following information by use of the tick box:

Professional designation:

Intern	☐
Medical Officer	☐
Registrar	☐
Career Medical Officer	☐
Consultant	☐

Years of experience in anaesthesia:	< 1 Year	☐
	1- 5 Years	☐
	6-10 Years	☐
	11-15 Years	☐
	16-20 Years	☐
	> 20 Years	☐

Advanced Cardiac Life Support (ACLS):

YES	☐
NO	☐

ACLS certified/updated in the last 2 years:

YES	☐
NO	☐

Scenario 1

A healthy ASA 1 patient presents for a routine caesarean section under spinal anaesthesia. Ten minutes post spinal induction, cardiac arrest ensues secondary to a hypotensive episode. Resuscitation is initiated as per cardiac arrest algorithm using the Resuscitation Council of Southern Africa and American Heart Association guidelines.

1. What is the dose of adrenaline administered under these guidelines and what is the recommended route of administration?

____

____

____

2. What is the cardiac arrest dose of adrenaline in micrograms/kilogram?

____

Scenario 2

A healthy patient presents for a minor elective procedure requiring a general anaesthetic and intubation. Five minutes after the elective sequence induction, which utilised rocuronium as the non-depolarising muscle relaxant, the patient becomes tachycardic, hypotensive and you notice erythema on all limbs. She is having an acute anaphylactic reaction and is in anaphylactic shock. You opt to give adrenaline intravenously, as there is an established peripheral line.

3. What is the recommended intravenous dose, in micrograms/kilogram?

____

4. What other doses and modes of administration do you know of, for adrenaline, as per recommendation by ACLS (please specify injection site)?

____

____

____

Scenario 3

The above patient responds to adrenaline boluses and the elective procedure is abandoned. Appropriate steroid and antihistamines are given intravenously, but despite this hypotension is refractory and an infusion of adrenaline through a central line is required.

5. Give the minimum starting infusion dose of adrenaline, from which you will titrate, to treat the peripheral dilation and give inotropic support.

____

6. What is the maximum recommended infusion dose?

____