Department of Anesthesia,
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The Effect of Dexmedetomidine and Labetalol in Controlled Hypotensive Anesthesia for middle Ear Surgery: A Comparative Study with Nitroglycrin

THESIS

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بسم الله الرحمن الرحيم

قَالُوا سُبْحانَكَ لاَ عِلْمَ لنا إِلاَّ مَا عَلَّمْتَنا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

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Mohamed Salah

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List of Abbreviations

ATP	Adenosine tri phosphate
Bp	Blood pessue
CBF	Cerebral blood flow
cGMP	Cyclic guanosine monophosphate
CGRP	Calcitonin gene- related peptide
CN	Cyanide
CNS	Central nervous system
CO	Cardiac output
CO2	Carbon dioxide
CPP	Cerebral perfusión pressure
CVP	Central venous pressure
Dex	Dexmedetomidine
ECG	Electrocardiography
EEG	Electroencephalography
ETCO2	End tidal Carbon dioxide
GABA	Gamma amino butyric acid
HR	Heart rate
IM	Intramuscular
IPPV	Intermittent positive pressure ventilation
IQR	Interquartile range
IV	Intravenous
Kg	Kilogram
L	Litre
MAC	Minimal alveolar concentration
MAP	Mean arterial blood pressure
MAP	Mean arterial pressure
Mcg	Microgram

List of Abbreviations (Cont.)

mg .... Milligram
Min................ Minute
ml .... Milliliter
NE................. Nor epinephrine
PaCO2 .... Carbon dioxide arterial pressure
PEEP .... Positive end expiratory pressure
PGE1............. Prostaglandine E1
PKa…………..Acid dissociation constant
RSS…………..Ramsay sedation score
SNP............... Sodium nitroprusside
SVR............... Systemic vascular resistance
T½ .... Half life
TMN.............. Tuber mamillary nucleus
Vd.................. Volume of distribution
VLPO .... Ventrolateral preoptic nucleus

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Introduction

The need for intentionally reducing blood pressure to hypotensive level in a variety of surgical procedures is gaining popularity today.

Controlled hypotension involves reducing the systolic arterial blood pressure 40-50% below its normal range or reducing mean arterial pressure to 60 mmHg intentionally and recoverably and maintaining it at this level throughout the operation process ***(Savarese, 2002).***

Middle ear surgery has undergone a revolution with the introduction of hypotensive anesthesia to provide a relatively bloodless field while using an operating microscope ***(Nasreen et al., 2009).***

Various agents (e.g., magnesium sulphate, sodium nitroprusside, nicardipine, nitroglycrin, esmolol, α2-agonist, labetalol, and high doses of potent inhaled anesthetics) have been used to achieve controlled hypotension. Some of the disadvantages associated with these drugs include resistance to vasodilators, tachyphlaxis (with nitroglycrin), cyanide toxicity (with sodium nitroprusside), the possibility of myocardial depression (with esmolol and magnesium sulfate), and a long post-anesthetic recovery period (with isoflurane) ***(Kol et al., 2009).***

Nitroglycrin is a short acting non-specific direct vasodilator on the venous and arterial vessels, its predominant action is on the venules causing an increase in the venous capacitance and decrease in the cardiac preload ***(Yosry and Othman, 2008).***

Dexmedetomidine, an imidazol compound, a pharmacologically active dextroisomer of medetomidine that displays specific and selective α2-adrenoceptor agonism which cause decrease in heart rate and arterial blood pressure. These hemodynamic changes are associated with a reduction in norepinephrine and epinephrine plasma levels ***(Bhana et al., 2000).***

Labetalol is a non-selective β-adrenergic receptor antagonist, and a post synaptic α-adrenergic receptor agonist. The β/α ratio of antagonism is 7:1 after intra venous administration, labetalol decreases the blood pressure with limited effect on cardiac output and heart rate at recommended dosages ***(Maccarthy and Bloomfield, 1983).***

Ideally, hypotensive agents should be easy to administer, have a short time to onset, have effects that disappear quickly when administration is discontinued, have rapid elimination without toxic metabolites, have negligible effects on vital organs, and have predictable and dose-dependant effects ***(Degoute, 2007).***

Aim of the Work

The aim of this study is to compare the potential of dexmedetomidine and labetalol as an ideal hypotensive intravenous agent in middle ear surgery.

Hypotensive Anesthesia & Techniques

1) Definition of deliberate hypotension :

It is the elective lowering of arterial blood pressure. The primary advantages of this technique are minimization of surgical blood loss and better wound visualization***(Thinker and Michenfelder, 2000)***.

Many terms have been used such as, controlled hypotension, induced hypotension, hypotensive anesthesia, elective hypotension and deliberate hypotension ***(Morgan et al., 2002).***

2) Level of hypotension required:

There is a debate upon the level of hypotension required to produce a desirable effect locally at the surgical site. Aken and Miller stated a decrease of MAP of 50 to 65 mmHg or a 30% reduction of baseline mean arterial blood pressure at the surgical site was believed to decrease blood loss significantly***(Aken and Miller, 2002)*** . Nevertheless, one should avoid the temptation to select any particular blood pressure as the end point of hypotensive anesthesia. The minimum acceptable blood pressure must be individualized to each particular patient's intercurrent illness ***(Ornstein, 2003).***

3) Techniques For Deliberate Hypotention:

A) Physiological factors which reduce blood loss:

The appropriate use of physiological maneuvers helps decreasing the dose of potentially toxic drugs needed to produce hypotension.

1-Posture:-

For each 2.5 cm of vertical height or approximately 3° tilt of a standard table, there is a 2mmHg difference in systolic pressure above and below the heart ***(Rosenblum and Zandsberg, 2003).***

2-Intermittent positive pressure ventilation (IPPV):-

During IPPV, inspiration is associated with positive intrathoracic pressure, resulting in a reduction in venous return and therefore the cardiac output may be reduced. In general, if IPPV is augmented by head up posture, the resultant reduction in venous return and therefore cardiac output (CO) might be expected to be considerable ***(Robert et al., 2002).***

3-Positive End Expiratory Pressure (PEEP):-

In the past, PEEP has been proposed, however, adverse effects may occur, e.g., an increase in cerebral venous pressure which tend to decrease cerebral perfusion pressure aggrevating cerebral ischemia ***(Gronert et al., 2000).***

4-Effects of Carbon Dioxide (CO_2) and Oxygen control:-

CO_2 is a vasodilator and hypercarbia is thought to increase blood loss and venous oozing within the surgical field. Hypocapnia inducing vasoconstriction can be achieved by moderate hyperventilation. Cerebral blood flow (CBF) is directly proportionate to $PaCO_2$ between tension of 20 and 80mmHg, so care must be taken during hyperventilation with patients in the head up position as vasoconstriction may reduce CBF to critical values ***(Ornstein, 2003).***

5-Smooth adequate level of anesthesia:-

Induced hypotension must not become a substitute for good anesthesia which involves meticulous attention to oxygenation, CO_2 elimination and analgesia ***(Ornstein, 2003).***

B) Mechanical Methods of Blood Flow Reduction:

1-Arteriotomy:-

In 1946, Gardner reduced arterial blood pressure with controlled hemorrhage through arteriotomy. Arteriotomy is only of historical interest ***(Gardner, 1946).***

2-Tourniquets:-

Tourniquets are alternatives rather than adjunctive to induce hypotension. In a normotensive patient, pressure commonly used is 250 mmHg for upper limb and 300 mm Hg for lower limb. Tourniquet time must be limited to 60 minutes in the upper limb and 90 minutes for lower limb (***Simpson, 1992).***

3-Local infiltration with sympathomimetic amines:-

Adrenaline concentrations of 1:200.000 - 1:400.000 are used commonly similar to those used with local anaesthetic; the total dose of adrenaline should be limited to 500 µg (***Simpson, 1992).***

C) Pharmacological methods which reduce blood loss:

Pharmacological methods which are used to reduce BP act either by lowering the systemic vascular resistance (SVR) or by lowering the cardiac output (CO).

* **The ideal agent for controlled hypotension would have:**

- Ease of administration.

- Predictable and dose dependent effect.
- Rapid onset and recovery from effect.
- Quick elimination without production of toxic metabolites.
- Minimal effects on blood flow to vital organs.
- The ideal agent should not increase the brain size or affect cerebral auto regulation.

I-Reduction Of systemic vascular resistance (SVR):-

The sympathetic reflex arc may be blocked at six discrete sites ***(Ornstein, 2003).***

1-Baroreceptors:

A decrease in arterial pressure results normally in an increase in HR. mediated by baroreceptor reflex. The baroreceptors operate over a discrete range of arterial pressure and their sensitivity to changes in pressure may be reduced by the volatile anesthetic agent (halothane in particular), thus, lower levels of arterial pressure may be achieved without reflex tachycardia when halothane is used ***(Ornstein, 2003).***

2-Vasomotor center:

All general anesthetics depress the central nervous system resulting in reduction in sympathetic tone and in arterial pressure ***(Ornstein, 2003).***

3- Preganglionic sympathetic nerve fibers:

Sharrock described a technique in which in which total sympathetic blockade was applied by extensive epidural anesthesia up to T1 level. A vasopressor infusion was used to modify the physiological responses to epidural anesthesia. In this opinion, when epinephrine infusion was used with total