EFFECTS OF INTRATHECAL BUPIVACAINE-FENTANYL VERSUS BUPIVACAINE-DEXMEDETOMIDINE IN LOWER LIMB SURGERIES IN DIABETIC PATIENTS

Thesis

Submitted for partial fulfillment of M.D. degree in Anesthesia

By

Sawsan Haridi Ahmed Abu El hassan

M.B.B.Ch, M.Sc. of Anesthesia
Faculty of Medicine
Ain Shams University

Supervised by

Prof. Dr. Gihan Seif El Nasr Mohammed

Professor of Anesthesia
Faculty of Medicine, Ain Shams University

Prof. Dr. Hazem Mohammed Abdelrahman Fawzy

Professor of Anesthesia
Faculty of Medicine, Ain Shams University

Dr. Assem Adel Moharram

Lecturer of Anesthesia
Faculty of Medicine, Ain Shams University

Dr. Tamer Nabil Mohamed Toaima

Lecturer of Anesthesia
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2018


بسم الله الرحمن الرحيم
اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ * خَلَقَ الْإِنسَانَ مِنْ عَلَقٍ
* اقْرَأْ وَرَبُّكَ الْأَكْرَمُ * الَّذِي عَلَّمَ بِالْقَلَمِ * عَلَّمَ
الْإِنسَانَ مَا لَمْ يَعْلَمْ *
صدق الله العظيم
القرآن الكريم .. سورة العلق (١-٥)

ACKNOWLEDGMENT

*First of all I would like to thank **ALLAH** for supporting me all over my life and stands beside me in all my difficulties.*

*Secondly, I can't express my deep thanks and gratitude to Professor Dr. **Gihan Seif El Nasr Mohammed** Professor of Anesthesia Ain Shams University for her Keen interest, and excellent guidance and valuable supervision.*

*My deep sincere thanks and appreciations goes to professor Dr. **Hazem Mohammed Abdelrahman Fawzy** Professor of Anesthesia Ain Shams University for his great help and assistance, intensive effort to whom I remain inspired by his grateful thoughts.*

*I am also very grateful to Dr. **Assem Adel Moharram** Lecturer of Anesthesia Ain Shams University for his support that allowed this work to be fulfilled.*

*I highly appreciate the indispensable advice, the keen interest and valuable assistance of Dr. **Tamer Nabil Mohamed Toaima** Lecturer of Anesthesia Ain Shams University to whom no words can be enough to his hard effort during the whole study.*

I cannot also forget to thank all the members of Anesthesia Department, Ain Shams University for their great help and valuable cooperation.

Dedication

I dedicate this work to my lovely husband who is the gift of Allah for my life and without his kind help and continuous support this work can never to be done, to my kind Mother and Father and to all the members of my family for their continuous support and help …

For my lovely tiny and angelic kids.....

Sawsan Abu El Hassan
2018

CONTENTS

- Introduction ……... 10
- Aim of the Work ……... 14
- Review of Literature ……. 15

Chapter 1: Pathophysiology of Diabetes Mellitus …… 15

Chapter 2: Anesthetic Management of Diabetes Mellitus …… 24

Chapter 3: Pharmacology of Local anesthetics and Additives …….. 49

- Patients and Methods ……. 61
- Statistical analysis and Results …….. 67
- Discussion ……. 87
- Conclusion ……...……. 97
- Recommendations……. 98
- Summary…… 99
- References ……... 101
- Arabic summary …….. 1-4

LIST OF ABBREVIATIONS

- *ADA - American Diabetes Association .*
- *ASRA - American Society of Regional Anesthesia.*
- *AR - Adrenergic Receptor.*
- *CNS - Central Nervous System .*
- *CSF – Cerebrospinal Fluid .*
- *CBF - Cerebral Blood Flow.*
- *CMR - Cerebral Metabolic Rate.*
- *CBC - Complete Blood Picture.*
- *DKA - Diabetic Ketoacidosis .*
- *EASD - European Association for the Study of Diabetes.*
- *FPG - Fasting Plasma Glucose .*
- *GDM - Gestational Diabetes Mellitus.*
- *GRA - Great Radicular Artery .*
- *GABA - γ-aminobutyric acid.*
- *HDL - High density lipoproteins.*
- *HGBA1C - Hemoglobin A1C.*
- *HSS - Hyperosmolar Hyperglycemic State.*
- *HR - Heart rate.*
- *HOCM - Hypertrophic Obstructive Cardiomyopathy .*
- *ICU - Intensive Care Unit.*
- *INR - International Normalized Ratio.*
- *IVRA - Intravenous Regional Anesthesia.*
- *MODY - Maturity-Onset Diabetes of the Young.*
- *MOR - Mu Opioid Receptor.*
- *MAP – Mean Arterial blood Pressure.*
- *OGTT - Oral Glucose Tolerance Test .*
- *PT - Prothrompin Time .*
- *PTT - Partial Thromboplastin Time .*
- *PDPH - Post-Dural Puncture Headache .*
- *SGOT - Serum Glutamic Oxaloacetic Transaminase.*
- *SGPT - Serum Pyruvic Glutamic Transaminase.*
- *SPO2 - Arterial Oxygen Saturation.*
- *T1DM - Type 1 Diabetes.*
- *T2DM - Type 2 Diabetes .*
- *TG - Triglycerides .*
- *TNS - Transient Neurologic Symptoms .*
- *VAS - Visual Analogue pain Scale*
- *Vd - Volume of distribution.*

LIST OF FIGURES

FIGURE NO.	TITLES	PAGE NO.
Fig. 1.	*Sagittal view through the lumbar vertebrae and sacrum.*	28
Fig. 2.	*Arterial blood supply to the spinal cord.*	29
Fig. 3.	*Surface landmarks for identifying spinal levels*	31
Fig. 4.	*Sitting position for neuraxial blockade.*	33
Fig. 5.	*Lateral decubitus position for neuraxial blockade.*	34
Fig. 6.	*A Sagittal section through the vertebral column showing layers traversed by spinal needle.*	35
Fig. 7.	*View of spinal needle traversing the ligamentum flavum and dura mater.*	36
Fig. 8.	*Paramedian approach for spinal anesthesia uses an entry point 1 cm lateral and inferior to the superior spinous process and directed at a 15-degree angle medially and cephalad.*	37
Fig. 9.	*Spinal Needles.*	38
Fig. 10.	*Areas of sensory innervation by spinal nerves and the sensory level required for various surgical procedures*	40
Fig. 11.	*Chemical structure of an ester (procaine) and an amide (lidocaine).*	49
Fig. 12.	Visual analogue pain scale	65
Fig. 13.	*Comparison between the three groups according to age (years).*	69
Fig. 14.	*Comparison between the three groups according to sex.*	69
Fig. 15.	*Comparison between groups according to the maximal sensory block level.*	71
Fig. 16.	*Comparison between the three groups according to the degree of motor block.*	73
Fig. 19.	*Comparison between the three groups according to recovery*	77

	of motor block in second hour.	
Fig.20.	*Comparison between the three groups according to postoperative pain in the first hour.*	79
Fig. 21.	*Comparison between the three groups according to postoperative pain in the second hour.*	79
Fig. 22.	*Comparison between the three groups according to the need of rescue analgesia in the first hour*	81
Fig. 23.	*Comparison between the three groups according to the need for rescue analgesia in the second hour.*	81
Fig. 24.	*Comparison between the three groups according to patients who need analgesia.*	83
Fig. 25.	*Comparison between the three groups according to intraoperative findings*	84
Fig. 26.	*Comparison between the three groups according to postoperative complications*	86

LIST OF TABLES

Table no.	*Titles*	*Page no.*
Table 1	*2018 Guidelines for regional anesthesia.*	48
Table 2	*Modified Bromage Scale*	64
Table 3	*Comparison between the three groups according to demographic data.*	68
Table 4	*Comparison between the three groups according to the maximal sensory block level.*	70
Table 5	*Comparison between the three groups according to the degree of motor block.*	73
Table 6	*Comparison between the three groups according to the duration of spinal anesthesia (minutes).*	74
Table 7	*Comparison between the three groups according to the degree of recovery of motor block.*	76
Table 8	*Comparison between the three groups according to the postoperative pain.*	78
Table 9	*Comparison between the three groups according to the need for rescue analgesia*	80
Table 10	*Comparison between the three groups according to patients who need analgesia.*	83
Table 11	*Comparison between the three groups according to the intraoperative findings.*	84
Table 12	*Comparison between the three groups according to postoperative complications.*	85

EFFECTS OF INTRATHECAL BUPIVACAINE-FENTANYL VERSUS BUPIVACAINE-DEXMEDETOMIDINE IN LOWER LIMB SURGERIES IN DIABETIC PATIENTS

Thesis

Submitted for partial fulfillment of M.D. degree in Anesthesia

By

Sawsan Haridi Ahmed Abu El hassan

M.B.B.Ch, M.Sc. of Anesthesia
Faculty of Medicine
Ain Shams University

Supervised by

Prof. Dr. Gihan Seif El Nasr Mohammed

Professor of Anesthesia
Faculty of Medicine, Ain Shams University

Prof. Dr. Hazem Mohammed Abdelrahman Fawzy

Professor of Anesthesia
Faculty of Medicine, Ain Shams University

Dr. Assem Adel Moharram

Lecturer of Anesthesia
Faculty of Medicine, Ain Shams University

Dr. Tamer Nabil Mohamed Toaima

Lecturer of Anesthesia
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2018

INTRODUCTION

Between 1990 and 2010, the number of adults who were diagnosed with diabetes mellitus more than tripled from 6.5 million to 20.7 million. Diabetes mellitus, a disease that complicates most organ systems, is characterized by increased concentrations of blood glucose due to a relative lack of endogenous insulin secretion or insulin insensitivity ***(Pardo and Miller, 2018).***

The age of onset of diabetes is coming down. So, more and more number of diabetic patients will require surgery and hence anesthesia. Diabetic patients who require surgery present special challenges in the perioperative management. Special attention must be paid for prevention and treatment of metabolic disturbances. The surgical outcome and prognosis of those patients is affected by the perioperative glycemic control and end-organ effects of diabetes ***(Patel, 2015)***.

By proper pre-anesthetic evaluation and risk assessment, meticulous glycemic control, good anesthetic techniques, and efficient postoperative management, safe anesthesia can be made for diabetic patients. Diabetic Patients have a higher incidence of morbidity and mortality following surgery and also have an increased length of hospital stay ***(Patel, 2015).***

Perioperative hyperglycemia may result from various causes including stress-induced neuroendocrine changes, patient's underlying metabolic state and exogenous glucose administration ***(Pardo and Miller, 2018).***

Neuraxial anesthesia is indicated as the primary anesthetic for major and minor surgeries or as an adjunctive anesthetic for intraoperative pain control in addition to general anesthesia. It is most useful as the primary

anesthetic in surgeries involving the abdomen, perineum, or lower extremities ***(Farag et al., 2018).***

Regional anesthesia in diabetic patients avoids hormonal and metabolic changes that occur with general anesthesia and allows early mobilization. So, regional anesthesia facilitates minimal interruption of the normal daily routine of diet and treatment for diabetic patients ***(Pani et al., 2010).***

Spinal anesthesia is the most common and popular technique for lower limb surgeries. The most common local anesthetic used for this technique is 0.5% hyperbaric bupivacaine: However the anesthesia provided by bupivacaine alone may be short in duration for prolonged surgeries. The current practice in modern anesthesia is to add small doses of adjuvants to local anesthetics to fasten the onset time, improve quality of intra-operative anesthesia, prolong analgesia and decrease the complications associated with intrathecal administrations of high dose of hyperbaric bupivacaine alone ***(Mishra et al., 2017).***

A variety of medications may exert a direct analgesic effect on the spinal cord and nerve roots, or prolong the duration of sensory and motor blockade. The coadministration of such drugs often allows a reduction in the dose of local anesthetic, with the advantage of motor block sparing and faster recovery while still producing the same degree of analgesia. ***(Pardo and Miller, 2018).***

Various adjuvnts are often added to local anesthetics solutions such as vasoconstrictors (epinephrine 1:200,000), opioids (fentanyl, morphine, and sufentanil), and alpha-2-adrenergic agonists (clonidine and dexmedetomidine), to prolong the duration and intensify the effect of a spinal anesthetic ***(Farag et al., 2018).***

Opioids such as fentanyl and morphine can be added to enhance surgical analgesia and improve postoperative pain without prolonging motor or sympathetic blockade. These opioids work at the μ (mu) opioid receptors located in the dorsal horn of the spinal cord ***(Farag et al., 2018).***

Fentanyl in various doses when added to hyperbaric bupivacaine for subarachnoid block produce prolonged duration of analgesia. But it is associated with respiratoy depression, pruritus and retention of urine ***(Mishra et al., 2017)***.

The functional μ (mu) opioid receptors in the dorsal horn of spinal cord in diabetics are either reduced or impaired in their function. This may be one of the mechanisms underlying the reduced spinal analgesic effect of μ opioid in diabetic neuropathic pain ***(Tarbeeh and Mohamed, 2012).***

Dexmedetomidine is a highly selective alpha 2-adrenoceptor agonist with sedative, anxiolytic, sympatholytic, and analgesic sparing effects, and minimal depression of respiratory function. It is potent and highly selective for alpha 2-receptors with an alpha 2: alpha 1 ratio of 1620:1 ***(Weerink et al., 2017).***

It is approved for short term sedation in an intensive care unit (ICU) setting or in non-intubated patients prior to and/or during surgical and other procedures. Dexmedetomidine is the dextro isomer of medetomidine with eight times greater selectivity for α2-adrenergic receptors than clonidine. This action in the central and peripheral nervous systems results in sedation and analgesia (sedoanalgesia). Dexmedetomidine is devoid of opioid and gabaergic activity and is not

associated with respiratory depression resulting in cooperative and conscious (semi arousable) sedation ***(Chue et al., 2017).***

Dexmedetomidine has numerous benefits when used for neuroaxial block. It acts on both pre and post synaptic sympathetic nerve terminals as well as on central nervous system thereby decreasing the sympathetic outflow and also noradrenaline release causing sedation, anxiolytic, analgesic and sympatholytic effects. It lacks opioid like properties so opioid related side effects are not found ***(Mishra et al., 2017).***

EFFECTS OF INTRATHECAL BUPIVACAINE-FENTANYL VERSUS BUPIVACAINE-DEXMEDETOMIDINE IN LOWER LIMB SURGERIES IN DIABETIC PATIENTS

Thesis

Submitted for partial fulfillment of M.D. degree in Anesthesia

By

Sawsan Haridi Ahmed Abu Elhassan

M.B.B.Ch, M.Sc. of Anesthesia
Faculty of Medicine
Ain Shams University

Supervised by

Prof. Dr. Gihan Seif El Nasr Mohammed

Professor of Anesthesia
Faculty of Medicine, Ain Shams University

Prof. Dr. Hazem Mohammed Abdelrahman Fawzy

Professor of Anesthesia
Faculty of Medicine, Ain Shams University

Dr. Assem Adel Moharram

Lecturer of Anesthesia
Faculty of Medicine, Ain Shams University

Dr. Tamer Nabil Mohamed Toaima

Lecturer of Anesthesia
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2018