Hanaa Mohammed

بسم اللّه الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني

Safaa Mahmoud

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

Dexmedetomidine versus Fentanyl on Stress Response and Pain Control in Adult Patients Undergoing Laparoscopic Surgery

Thesis

Submitted for the partial fulfillment of MD degree
in Anesthesiology, Intensive Care & Pain Medicine

Presented by

Marian Greiss Sobhy

M.B.B.Ch., M.Sc. in Anesthesiology

Under Supervision of

Prof. Dr. Bassem Boulos Ghobrial

Professor of Anesthesia, Intensive Care & Pain Medicine
Faculty of Medicine - Ain Shams University

Prof. Dr. Waleed Mohamed Abd Elmageed

Professor of Anesthesia, Intensive Care & Pain Medicine
Faculty of Medicine - Ain Shams University

Assist. Prof. Dr. Dalia Mahmoud Elfawy

Assistant Professor of Anesthesia, Intensive Care & Pain Medicine
Faculty of Medicine - Ain Shams University

Assist. Prof. Dr. Raham Hasan Mostafa

Assistant Professor of Anesthesia, Intensive Care & Pain Medicine
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2022

Acknowledgement

The completion of this work could not have been possible without the expertise of my supervisor, ***Prof. Dr. Bassem Boulos Ghobrial.*** *I would like to express my sincerest gratitude to him for giving me the opportunity to conduct this research, and for his guidance, as well as sharing his vast knowledge.*

I would also like to acknowledge and give my sincere thanks to ***Prof. Dr. Waleed Mohamed Abd Elmageed,*** *for his encouragement and enlightening critique.*

I would like to express my appreciation to ***Assist. Prof. Dr. Dalia Mahmoud Elfawy,*** *for her contribution in this project. I am grateful to her kind help and necessary suggestions.*

Last but not least, my warmest thanks to ***Assist. Prof. Dr. Raham Hasan Mostafa,*** *for her continuous support, extended help, invaluable advice, and keenness throughout all the stages of this work.*

I am extending my heartfelt thanks to my family and friends for their patience, love, and support to complete this thesis successfully.

List of Contents

List of Abbreviations

Abbr.	Full-term
ACTH	**:** Adrenocorticosteroid hormone
ANOVA	**:** Analysis of variance
ASA	**:** American Society of Anesthesiology
BMI	**:** Body mass index
CNS	**:** Central nervous system
CO_2	**:** Carbon dioxide
ECG	**:** Electrocardiogram
$EtCO_2$	**:** End tidal carbon dioxide
HR	**:** Hear rate
IAP	**:** Intra-abdominal pressure
ICP	**:** Intra-cranial pressure
ICU	**:** Intensive care unit
IV	**:** Intravenous
MAP	**:** Mean arterial pressure
NRS	**:** Numeric rating scale
$PaCO_2$	**:** Partial pressure of arterial carbon dioxide
PACU	**:** Post-anesthesia care unit
PONV	**:** Postoperative nausea and vomiting
SD	**:** Standard deviation
SpO_2	**:** Arterial oxygen saturation
SPSS	**:** Statistical package for social science
VAS	**:** Visual analogue score
Vd	**:** Volume of distribution

List of Tables

List of Figures

Abstract

Laparoscopic procedures are widely indicated; however, the ideal approach for pain control remains debatable. This trial compared between the effects of dexmedetomidine and fentanyl infusion on stress response and pain control in patients undergoing elective laparoscopic surgeries. A prospective randomized double-blinded comparative study included 82 adult participants randomly allocated into two equal-sized groups. Group D received 1 ^g/kg of intravenous (IV) dexmedetomidine over 10 min as a loading dose just before induction of anesthesia, then 0.2-0.7 ^g/kg/h till 10 min before the surgery ends. Group F received 1 ^g/kg of IV fentanyl as a loading dose, then 0.2-0.7 ^g/kg/h. Primary objective was postoperative analgesic consumption in 24 h. Collected data were heart rate (HR), mean arterial blood pressure (MAP), blood glucose and serum cortisol levels, visual analogue score (VAS), and the perioperative analgesic consumption. Group D consumed significantly less postoperative morphine doses in 24 h ($p = 0.003$), and 41.5% of Group D patients did not need any postoperative morphine. Group D had better-controlled hemodynamic changes 5 min post-extubation (HR and MAP$p = 0.021$ and $p = 0.022$ respectively), showed significantly less postoperative stress response as manifested in the blood glucose and serum cortisol levels 4 h postoperatively ($p = 0.006$ and $p = 0.001$ respectively), and less VAS pain scores at early and late postoperative periods. Intraoperative IV dexmedetomidine administration as a sole analgesic agent for patients undergoing elective laparoscopic surgeries serves as a convenient anesthetic approach, since it provided a good postoperative pain control, and reduced the surgical stress response and the perioperative analgesic consumption.

Keywords: Dexmedetomidine; Laparoscopic surgery; Postoperative pain; Stress response; VAS score; Opioid-free anesthesia

Introduction

Laparoscopic surgeries have several advantages, such as shorter hospital stays, lesser postoperative pain, and cosmetically satisfying surgical incisions. Contrarily, hemodynamic changes such as hypertension, tachycardia, and other surgery-related complications represent some of the disadvantages of laparoscopic surgeries ***(Panchgar et al., 2017)***.

Surgical procedures trigger complex stress responses, manifested by neurohumoral, metabolic and immunological derangements ***(Marana et al., 2003)***. High blood glucose level is one feature of the metabolic response to surgery, and it depends on patient's age, anesthesia technique, magnitude of tissue trauma, type and severity of surgery, total operative time, amount of blood loss, and postoperative pain ***(Gupta et al., 2013)***.

These metabolic and endocrine changes also lead to adverse effects, such as increased oxygen consumption, catabolism, and impaired immunity. These derangements are usually associated with poor postoperative clinical course ***(Marrocco-Trischitta et al., 2004)***.

Laparoscopic surgeries pose the added stress of pneumoperitoneum during surgery, which is well known for elevating the heart rate (HR) as well as the mean arterial pressure

(MAP) and lowering the cardiac index. This consequently may lead to mismatch in the cardiac demand supply and has the potential to cause myocardial ischemia especially in the elderly and cardiac patients ***(Bhagat et al., 2016)***.

Pain developing after laparoscopic surgery involves various factors. This pain is quite complex, and it is generally regarded as visceral. Factors include irritation of phrenic nerve resulting from carbon dioxide (CO_2) insufflation into the peritoneal cavity, abdominal distension, port-site incisions, trauma associated with the surgery itself, sociocultural status, and individual factors ***(Ahiskalioglu et al., 2017)***.

Stress-induced deterioration in postoperative organ functions may be implicated in postoperative complications development. Modulation of stress responses to surgeries can reduce postoperative morbidity and mortality ***(Watanabe et al., 2014)***.

High-dose opioid anesthetic techniques offer hemodynamic stability and decrease intraoperative stress episodes ***(Beleña et al., 2016)***. However, opioids like fentanyl can cause adverse reactions upon emergence from anesthesia such as nausea, vomiting, dizziness, drowsiness, and respiratory depression ***(Zheng et al., 2016)***. Research into opioid use reduction explored acetaminophen, non-steroidal anti-inflammatories, magnesium, lidocaine, ketamine, and α_2-adrenoceptor agonists ***(Gabriel et al., 2019)***.

Alpha-2 (α_2) adrenoceptor agonists act on central and presynaptic receptors to inhibit central sympathetic outflow and reduce release of peripheral norepinephrine ***(Wijeysundera et al., 2003)***, attenuating the stress response, and therefore potentially reducing cardiovascular complications ***(Laha et al., 2013)***. Dexmedetomidine is a highly selective α_2-adrenoceptor agonist that produces dose-dependent anxiolysis and sedation ***(Jadhav et al., 2017)***. Dexmedetomidine has shown analgesic effects without significant respiratory depression, whilst exhibiting good perioperative hemodynamic stability, and decreased intraoperative opioid requirements ***(Bielka et al., 2018)***.

Aim of the Work

The aim of this study is to evaluate the influence of intraoperative dexmedetomidine infusion as a sole analgesic compared to fentanyl infusion on stress response and postoperative pain control in patients undergoing elective laparoscopic surgeries. The study compares the resultant effect of both drugs as regards the following:

1. Perioperative hemodynamic changes.
2. Blood glucose and serum cortisol levels.
3. Perioperative analgesic consumption.
4. Postoperative pain intensity.
5. Incidence of perioperative complications.

Pathophysiology of Laparoscopic Procedures

Laparoscopic surgery provides an alternative to conventional open surgery for various types of surgery due to many advantages, such as minimal invasiveness, reduced bleeding risk, less postoperative pain, and consequently an earlier discharge ***(Robba et al., 2016)***. Laparoscopy has existed since the development of diagnostic laparoscopy in the 1960s. Semm K and Mühe E are the pioneers of laparoscopy, and they turned it from a diagnostic into a surgical procedure at the beginning of the 1980s ***(Reynolds et al., 2001)***.

Indications and Examples

Laparoscopy has a wide field of indications such as cholecystectomy, appendectomy, hernia repair, splenectomy, colorectal surgeries, esophageal cancer surgery, liver resection, bariatric procedures, and it is the gold standard surgery for gastroesophageal reflux disease ***(Buia et al., 2015)***.

Laparoscopic gynecological surgeries include treatment of many benign and malignant diseases. Indications are ovarian and tubal surgeries, myomectomy, and hysterectomy ***(Kundu et al., 2017)***. Diagnostic laparoscopy indications are infertility, pelvic inflammatory disease, chronic pelvic pain, ectopic pregnancy ***(Togni et al., 2016)***, as well as cancer diagnosis and staging as it facilitates exploration and biopsy of visceral

tumors, peritoneal metastases or lymph nodes, and hepatic focal lesions ***(Rau et al., 2005)***.

Pathophysiology

Laparoscopic surgery begins with intraabdominal placement of the insufflation needle or trocar, followed by CO_2 insufflation of the abdominal cavity to an intraabdominal pressure (IAP) of 12–15 mmHg ***(Atkinson et al., 2017)***. Pneumo-peritoneum and CO_2 absorption across the peritoneal surface can have different systemic physiological effects ***(Robba et al., 2016)***. Laparoscopic surgery consists of four phases: induction of anesthesia, abdominal insufflation, abdominal desufflation, and recovery from anesthesia. Each phase has its unique hemodynamic changes (**Figure 1**) ***(Atkinson et al., 2017)***.

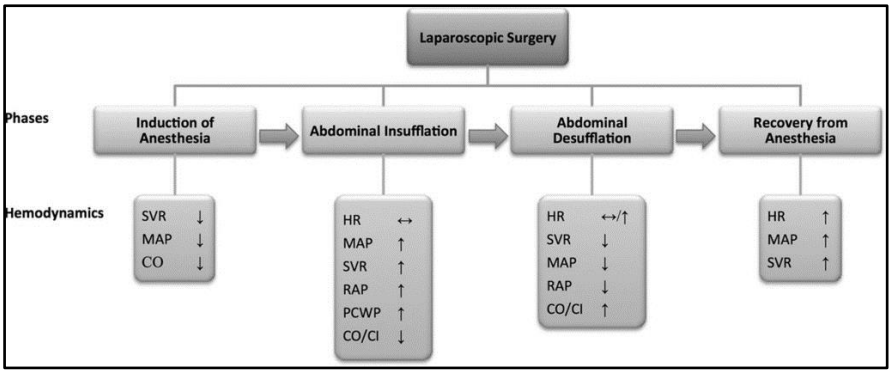

Figure (1): Phases of laparoscopic surgery. CI, cardiac index; CO, cardiac output; HR, heart rate; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; and SVR, systemic vascular resistance ***(Atkinson et al., 2017).***

The following are the main factors contributing to the different pathophysiologic changes caused by laparoscopic procedures: