بسم الله الرحمن الرحيم

قَالُوا سُبْحَانكَ لاَ علِمَ لَنَا إلاّ مَا

عَلّمْتَنَا إنَّكَ أنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة آية (٣٢)

Sedation following Coronary Artery Bypass Graft Surgery, A Comparative Study between Dexmedetomidine and Propofol

Thesis

Submitted for partial fulfillment of MD Degree
in **Anesthesia**

Presented By

Rania Mahrous Aly Hussein Saad
(M.B.B.Ch., M.Sc.)

Under Supervision of

Prof. Dr. Gamal Fouad Saleh Zaki
Professor of Anesthesia and Intensive Care
Faculty of Medicine – Ain Shams University

Prof. Dr. Nevine Ahmed Hassan Kashef
Assistant Professor of Anesthesia and Intensive Care
Faculty of Medicine – Ain Shams University

Dr. Walid Ahmed Abd El Rahman Mansour
Lecturer of Anesthesia and Intensive Care
Faculty of Medicine – Ain-Shams University

Faculty of Medicine
Ain-Shams University
2012

التهدئة عقب عمليات توصيل الشرايين التاجية فى القلب دراسة مقارنة بين عقار الدكسمدتومدين وعقار البروبوفول

رسالة

توطئة للحصول على درجة الدكتوراه

في التخدير

مقدمة من

الطبيبة/ رانيا محروس على حسين سعد

بكالوريوس الطب والجراحة - جامعة عين شمس

ماجستير التخدير - جامعة عين شمس

تحت إشراف

الأستاذ الدكتور/ جمـــال فـــؤاد صالـــح زكـــى

أستاذ التخدير والرعاية المركزة

كلية الطب – جامعة عين شمس

الأستاذ الدكتور/ نيفين أحمد حسن كاشف

أستاذ مساعدالتخدير والرعاية المركزة

كلية الطب- جامعة عين شمس

الدكتور/ وليد أحمد عبد الرحمن منصور

مدرس التخدير والرعاية المركزة

كلية الطب- جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٢

Sedation Following Coronary Artery Bypass Graft Surgery A Comparative Study Between Dexmedetomidine and Propofol

Prof. Dr. Gamal Fouad Saleh Zaki ,Prof. Dr. Nevine Ahmed Hassan Kachef,Dr. Walid Ahmed Abd El Rahman Mansour, Rania Mahrous Aly Hussein Saad

Abstract

Introduction

The intensive care unit (ICU) is an uncomfortable and stressful environment for patients. The use of adequate sedation and analgesia is important to modulate physiologic responses to stress and pain, especially after coronary artery bypass graft surgery(CABG). Stress is considered to be a major risk factor in myocardial ischemia after surgery. The stress response to CABG surgery is characterized by activation of the sympathetic nervous system increasing myocardial oxygen demand, so worsening coronary stenosis and failure of coronary autoregulation(Ebert, 2002).The ideal sedative after CABG surgery should have rapid onset, immediate resolution of both pain and anxiety, promotes cardiac and respiratory stability, maintains arousability during sedation, allows rapid recovery after discontinuation, and attenuates the cardiovascular, neuroendocrine, and inflammatory response. All these properties may improve outcome in cardiac patients after CABG ***(Schweickert and Kress, 2008).***

Current sedative agents used in intensive care unit includes benzodiazepines, opioids, and propofol. Benzodiazepines and opioids have cumulative effects and can cause respiratory and cardiovascular depression. Propofol is commonly used for sedation in the ICU. It has a very short duration of action, but without analgesic activity so opioids must be given to control pain , also propofol causes respiratory depression and hyperlipidaemia, so can exert deteriorating effects in patients with limited myocardial reserve(***Treggiari et al,2009).***

The alpha 2 agonist dexmedetomidine is a new class of sedatives now used in the ICU. Dexmedetomidine is a highly selective alpha2 agonist It is a potent sedative, anxiolytic, analgesic and sympatholytic agent. It acts both centrally and peripherally. At the central nervous system ,it acts on the post alpha-2 inhibitory receptor, resulting in sympatholytic and sedative effects. Its action on the spinal cord results in analgesic effect, whereas its action at the presynaptic membrane of the peripheral nerves

and autonomic ganglia, reduces the release of catecholamines, resulting in a decrease in heart rate and blood pressure. This reduction in heart rate reduces myocardial oxygen demand, increases coronary blood supply thus endocardial perfusion is preserved ,reducing incidence of postoperative myocardial ischemia and infarcation. **(*Wijeysundera et al 2003*)**.

Dexmedetomidine has several unique properties including sedation and analgesic effects ,while maintaining patient arousability, patients is easily awakened to take neurologic tests. Propofol does not maintain arousability so it must be stopped before assessing patient for neurologic functions. ***(Donnelly et al., 2005).***

Propofol may cause respiratory depression that can be amplified in presence of opioids. So it must be discontinued before weaning, this eliminates the calming effect at time of high stress, but continous sedation with dexmedetomidine does not interfere with the normal course of ventilator weaning and extubation because it does not depress respiratory drive or decrease oxygen saturation., so can be continued after extubation. ***(Corbett et al,2008).***

Circulating Interleukin 6 (IL-6) reflects the inflammatory response to surgical trauma. Both dexmedetomidine and propofol have an effect on the release of Il-6**.** ***(Desborough ,2000).***

Increased protein turn over is a characteristics feature of patients in ICU which may prolong ventilation as a result of respiratory muscle weakness ,this may be attributable to resistance to growth hormone (GH).

Dexmedetomidine affects GH secretion, however dexmedetomidine had only minor effects on the other endocrine changes, as on adrenal steroidogenesis. ***(Kennedy, 1999).***

In comparison to Propofol, Dexmedetomidine is more effective to be used in the ICU after coronary artery bypass graft surgery. **(*Azrina Ralib et al, 2007).***

Objective

To compare dexmedetomidine-based to propofol-based sedation after coronary artery bypass graft (CABG) surgery in the intensive care unit (ICU).

Design
Randomized, open label study.

Setting
Ain Shams university hospital.

Participants
50 patients undergoing coronary artery bypass graft surgey.

Interventions
At sternal closure, patients randomized to group D received 1.0 μg/kg of dexmedetomidine over 10 minutes as the loading dose, followed by a maintenance infusion of 0.4μg/kg/h .Patients randomized to group P will receive 1mg/kg of propofol over 10 minutes as the loading dose followed by a maintenance infusion of 1- 3 mg/kg/h to maintain a Ramsay sedation score ≥3 during assisted ventilation and ≥2 after extubation, and hemodynamics .Supplemental morphine is provided to both groups as needed for pain, therapy with both drugs will be continued for 24 hours in the ICU.

Results
A total of 50 patients were included in the study. There were no significant differences in the demographic and sedative characteristics between the two groups . Heart rate in dexmedetomidine group was significantly lower than in the propofol group ($p < 0.001$) . There were no significant differences in mean arterial blood pressure,central venous pressure, $PaCO_2$,pH and serum cortisol between the two groups. Mean sedation levels were within target ranges in both groups. Mean times to weaning and extubation were lower in dexmedetomidine group. Spo_2 values of the dexmedetomidine group during sedation were significantly higher than those of the propofol group ($P< 0.05$) . Opioid requirements were significantly lower in the dexmedetomidine group than for propofol group .Patients receiving dexmedetomidine showed a decrease in IL-6 concentrations but no statistically significant difference between both groups.Serum concentrations of growth hormone increased in patients receiving dexmedetomidine than in the propofol group.

Conculsion

This study showed that by comparing dexmedetomidine to propofol in the provision of sedation in post open-heart surgical patients.

Dexmedetomidine proved to be an attractive option during cardiothoracic surgery.

List of Contents

List of Abbreviations

ABG	: Arterial blood gas
ASA	: American Society of Anesthesiologists
BE	: Base excess
BIS	: The Bispectral index
CABG	: Coronary artery bypass graft surgery
CAMP	: Cyclic adenosine monophosphate
CICU	: Cardiothoracic intensive care unit
CNS	: Central nervous system
CPB	: Cardiopulmonary bypass
CVP	: Central venous pressure
ECG	: Electrocardiography
EEG	: Electroencephalogram
ELISA	: Enzyme-linked immunoassay
GABA	: Gammaaminobutyric acid
GH	: Growth hormone
ICU	: The intensive care unit
IL-6	: Interleukin 6
MAP	: Mean arterial blood pressures
NSAID	: Nonsteroidal Anti-inflammatory Agents
PRIS	: Propofol infusion syndrome
PSI	: Patient state index
RASS	: Richmond Agitation–Sedation Scale
RSS	: Ramsay Sedation Scale
SAS	: Sedation-Agitation Scale
SD	: Standard deviation
TSH	: Thyroid stimulating hormone
TMN	: Tubermamillary nucleus
UOP	: urine output
VLPO	: ventrolateral preoptic nucleus
α	: Alpha
ß	: Beta

List of Tables

List of Figures