A COMPARISON OF THE HEMODYNAMIC AND METABOLIC CHANGES PRODUCED BY PROPOFOL - FENTANYL AND ISOFLURANE - FENTANYL ANESTHESIA FOR PATIENTS HAVING CORONARY ARTERY BYPASS GRAFT SURGERY

A Thesis
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Anesthesia

by

Gihan Abd El - Halim Gomaa
M.B. B.ch., M.Sc.

supervised by

PROF. DR. SALAH EL - HALABY
Prof. of Anesthesia and Intensive Care
Faculty of Medicine - Ain Shams University

PROF. DR. AHMED GAMAL EISSA
Prof. of Anesthesia and Intensive Care
Faculty of Medicine - Ain Shams University

PROF. DR. SEIF EL ESSLAM ABD EL AZIZ
Prof. of Anesthesia and Intensive Care
Faculty of Medicine - Ain Shams University

Faculty Of Medicine
Ain Shams University
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To My Husband

To My Mother

To My Children

بسم الله الرحمن الرحيم

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Introduction

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Anesthesia for cardiac surgery requires a technique associated with minimal hemodynamic changes, maintenance of myocardial oxygen balance and suppression of reflex responses to surgical stimuli. High dose fentanyl anesthesia provides good analgesia with minimal myocardial depression. ***(Lunn JK, et al 1979)***

Without supplementation, however, breakthrough hypertension is a frequent occurrence ***(Edd RR, et al 1981)*** and the observation of myocardial lactate production in some patients is evidence that high - dose opioids alone do not adequately protect the myocardium from ischemia. ***(Moffitt EA et al, 1986)***

Opioids have been combined with volatile anesthetics and benzodiazipines to provide controlled myocardial depression and better myocardial oxygenation. ***(Moffit EA et al, 1985)***

The hemodynamic effects of propofol have been described in patients with ischemic and valvular heart disease following intravenous bolus doses but reports of the effects of continuous infusion in combination with fentanyl have mainly been used in patients undergoing coronary artery bypass grafting. ***(Vermeyan KM, et al, 1987)***

In our study we have compared the hemodynamic effects of propofol -supplemented fentanyl anesthesia versus Isoflurane - supplemented fentanyl anesthesia in patients undergoing coronary artery bypass graft surgery. The systemic metabolic changes (e.g. renal and liver functions) have been also measured and compared between the two groups.

Our study was conducted at the department of cardiothoracic **surgery "Ain Shams University hospitals"**. Our hemodynamic data for each patient was obtained by introduction of pulmonary artery catheter connected to cardiac output computer.

Aim of the work

AIM OF THE WORK

This study was done to compare between two groups of patients suffering from coronary artery disease and were scheduled for coronary artery bypass graft surgery. In both groups anesthesia was induced by moderate dose fentanyl and maintained by either propofol intravenous infusion or isoflurane inhalation and accordingly we had two groups of patients:

* Propofol - fentanyl group: Twenty patients received propofol - fentanyl anesthesia.
* Isoflurane - fentanyl group: Twenty patients received Isoflurane - fentanyl anethesis.

The comparison was done between the two groups as regards

* Hemodynamic variables obtained from cardiac output computer connected to pulmonary artery catheter namely :
  - heart rate
  - Mean arterial blood pressure
  - Cardiac output
  - Cardiac index
  - Mean pulmonary arterial pressure
  - Pulmonary capillary wedge pressure
  - Coronary perfusion pressure
  - Left ventricular stroke work index
  - Central venous pressure

* Systemic metabolic variables in the form of :
  - **Liver function tests :**
    * Total serum bilirubin
    * Serum glutamic oxaloacetic transaminase (SGOT) or (AST)
    * Serum glutamic pyruvate transaminase (SGPT) or (ALT)
  - **Renal functions tests :**
    * Blood urea
    * Creatinine
  - **Serum electrolytes :**
    * K^+
    * Na^+
    * HCO_3

All the above mentioned hemodynamic as well as metabolic variables were compared between the two groups aiming to estimate the advantages and disadvantages of each of the two drugs compared to the other:
Propofol as an intravenous agent and **Isoflurane** as an inhalation agent when used to supplement fentanyl anesthesia in coronary artery bypass graft surgery.

The aim of systemic metabolic variables measurements in our study is to assess the effects of the drugs used on body parynchematous organs (namely liver and kidney) which may result from major cardiovascular events (e.g. sever hypotension) and can affect their blood flow and / or from pharmacokinetics of the drugs and if they are hepatotoxic or nephrotoxic.

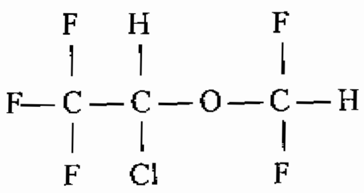
Review of Literature

ISOFLURANE

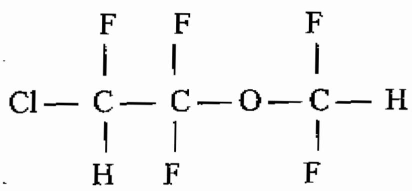
Although currently popular inhaled anesthetics include nitrous oxide, halothane and isoflurane, a greater variety of inhaled agents can produce anesthesia.

Chemical structure and physical properties :

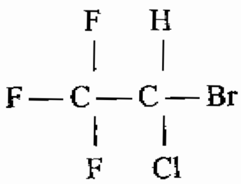
Isoflurane is like its isomer enflurane a methyl ethyl ether, it was discovered in 1965 by ***R.C. Terrell*** at **Ohio Medical Products** and was introduced into clinical practice ***by W.C. Stevens and colleagues*** at the university of **California** in 1971.
The chemical structure of Isoflurane as well as that of enflurane and halothane are shown in **figure 1** ***(Stevens W.C. , et al 1971)***



Isoflurane (Forane)



Enflurane (Ethrane)



Halothane (Fluthane)

[Fig. (1)]

Physical Properties :

-Isoflurane is a clear colourless, non- inflammable liquid with a specific gravity 1.52 at 25 ^{0}C. It boils at 48.5 ^{0}C and has a vapour pressure of 250 mm Hg (33.3 K Pa) at 20 ^{0}C.

-Isoflurane contains no chemical stabilizer, is non corrosive, does not attack materials used for construction of anesthetic apparatus and may be stored in clear glass. It is stable in warm soda lime .

-Isoflurane has slightly pungent ethereal smell which limits the rate at which the inspired concentration may be increased and thus the induction of anesthesia .

-Isoflurane as suggested, by its physiochemical properties, behaves like halothane and enflurane in clinical practice.

-The relatively low blood / gas solubility coefficient of 1.4 at 37 ^{0}C suggests the possibility of rapid induction and emergence from anesthesia with isoflurane.

-The greater chemical stability of isoflurane is reflected in lesser metabolism in body tissues which in turn reduce the likelihood of toxicity due to metabolites. ***(Kissin I., et al 1983)***

Pharmacology of Isoflurane

Anesthetic Potency :

The best estimate of anesthetic potencies is MAC

*The minimum alveolar concentration (at one at m) of an agent that produces immobility in 50 percent of those subjects exposed to noxious stimulus. The potency of isoflurane lies midway between that of halothane and enflurane. Using 100 % oxygen, the minimum alveolar concentration of halothane in middle age patients is 0.75 %, the value of isoflurane is 1.15 % and that of enflurane is 1.68 %. ***(Eger EI II , et al 1965)***

Pharmacological action of Isoflurane

[I] - On the cardiovascular system

A- Effects on myocardial contractility :

Studies on isolated cardiac tissues suggest that Isoflurane is a direct myocardial depressant, using equipotent doses, Isoflurane is less depressant than halothane and enflurane . In human the cardiac out put is not affected by 1- 1.8 MAC isoflurane. In contrast, within this range of anesthetic concentration, halothane and enflurane produces a dose related myocardial depression. ***(Freedman et al 1983)***, the less depressant effect of isoflurane anesthesia on myocardial contractility could be attributed to the fact that beta sympathetic stimulation opposes the direct myocardial depressant effect of isoflurane. ***(Balasaraswathi et al , 1983)***

B- Effect on Heart Rate :

Isoflurane tends to increase heart rate in both unstimulated volunteers and in patients undergoing surgery at a given MAC value, the heart rate is higher with isoflurane than with halothane the difference is usually 5 - 7 beats per minute, tachycardia is more common in younger age group. Two main mechanisms underlying isoflurane - induced tachycardia are :

- Beta sympathetic stimulation
- Activation of baroreceptor reflex which is a consequence of the hypotensive effect of Isoflurane anesthesia. ***(Eger , 1984)***

C- Effect on heart rhythm :

Isoflurane does not affect the heart rhythm. It does not predispose the human heart to premature ventricular contractions.

(Eger EL, 1981)

Animal and human studies have shown that the dose of adrenaline or other sympathomimetics required to produce premature ventricular contractions is approximately three to four times greater than that with halothane. ***(Jhonston , et al 1976)***

D- Effect on systemic vascular resistance :

Total systemic vascular resistance is reduced in a dose - related manner by isoflurane and reaches 50 % of awake control values at 2 MAC . Halothane and enflurane, had a moderate effect on systemic vascular resistance compared to isoflurane, the capacity of isoflurane to decrease vascular tone applies to all vascular beds, the tissues most affected are the skin and muscles. The vascular effect of isoflurane is attributed to a possible direct effect on the vessel wall or to the beta sympathetic stimulation, this would explain the marked dilatation of muscle blood vessels, blood flow to the muscle is particularly enhanced 2 or 3 folds, despite drop of perfusion pressure by general vasodilatation. ***(Eger, 1984)***

E- Effect on arterial blood pressure :

Halothane, Isoflurane and Enflurane all decrease systemic arterial blood pressure in a dose related fashion. At a comparative depth of anesthesia, isoflurane reduces arterial blood pressure more than halothane. ***(Eger, 1984)***

With halothane and enflurane the drop of arterial blood pressure is mainly a consequence of myocardial depression and reduced cardiac output. The hypotensive effect of isoflurane results most entirely from a decrease in systemic vascular resistance ***(Jones, 1985),*** as well as myocardial depression. Isoflurane can be used in induced hypotensive techniques, unlike sodium nitroprusside, there is no evidence of tachyphylaxis with prolonged isoflurane - induced hypotension . ***(Bishay, et al, 1984)***

F- Effect on coronary circulation :

Halothane anesthesia causes slight increase in myocardial vascular resistance with no impairment of myocardial oxygenation . Current evidences suggest that isoflurane is a significant coronary vasodilator and it might alter their ability to autoregulation. The increased coronary blood flow coupled with the minimal myocardial depressant effect and lack of myocardial sensitization to catecholamines, suggest that isoflurane is a suitable agent for patients with ischemic heart disease, and it has the potential to produce coronary artery steal and associated myocardial ischemia. ***(Becker L, 1987)***