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Research article

Effect of dexmedetomidine infusion on desflurane consumption and hemodynamics during BIS guided laparoscopic cholecystectomy: A randomized controlled pilot study

Hanan F. Khafagy [a,*], Reeham S. Ebied [a], Ahmed H. Mohamed [a], Mohamed H. El-said [b], Ahmed M. El-haddad [b], Abla S. El-Hadidi [a], Yasser M. Samhan [a]

[a] Department of Anesthesiology, Surgical Intensive Care and Pain Management, Theodor Bilharz Research Institute, Ministry of Higher Education and Scientific Research, El Nile St., Warrak El Hadar, P.O. Box 30, Imbaba, Giza 12411, Egypt
[b] Faculty of Medicine, Cairo University, Ministry of Higher Education and Scientific Research, Kasr Al Ainy St., Al Manial, Cairo 11562, Egypt

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ABSTRACT

Background: Dexmedetomidine is an α-2 adrenoceptor agonist with sedative and analgesic properties. Desflurane is the most rapidly washed volatile anesthetic agent allowing rapid recovery with minimal metabolism. Having a MAC of 6 vol % made it important to look for an adjuvant that would minimize its consumption. This study was undertaken to analyze desflurane consumption when combined with dexmedetomidine infusion guided by bispectral index as well as calculating intraoperative fentanyl requirements and recording hemodynamic changes associated with this technique.

Methods: Forty adult patients ASA class I and II of either sex scheduled for elective laparoscopic cholecystectomy were included in this study. Patients were randomized to one of two groups: Group 'D' (Dexmedetomidine group) receiving 1g/kg over 10 minutes followed by an infusion at 0.5 μg/kg/hr and Group 'P' (Placebo group) who received same volumes of normal saline. Desflurane was started at a concentration of 6% then adjusted to keep BIS level within the range of 40-50. Desflurane consumption, fentanyl requirements as well as hemodynamics were either calculated or recorded.

Results: Desflurane consumption and total fentanyl usage were significantly lower in group D versus group P with P value < 0.001. As regards hemodynamics, group D showed statistically significant lower readings versus the preoperative levels (P<0.05) as well as versus group P at the same timings (P<0.05) for most of the readings.

Conclusions: Continuous intravenous administration of dexmedetomidine resulted in significant reduction of desflurane consumption and intraoperative fentanyl requirements with attenuation of hemodynamic response to intubation, pneumoperitoneum and extubation.

1. Introduction

Dexmedetomidine is an active pharmacological d-isomer of medetomidine. It is a potent selective agonist of α_2 adrenoceptor compared to clonidine and having sedative, amnestic, sympatholytic and pain-relieving properties [1,2]. Thus it can be used in relatively high doses for sedation and analgesia without hemodynamic derangements [3].

Desflurane exhibits very low solubility in water with a corresponding low blood/gas partition coefficient. It is the most rapidly washed volatile anesthetic agent allowing rapid recovery with more flexibility in controlling the anesthetic depth. It undergoes minimal metabolism (0.02%) and is eliminated via the lungs [4]. Having a MAC of 6 vol.%, adding an adjuvant is beneficial to minimize its consumption and reduce adverse effects.

Laparoscopic cholecystectomy is considered as the "gold standard" treatment of cholelithiasis. Carbon dioxide (CO_2) is the gas of choice to produce pneumoperitoneum (PP) during laparoscopic surgical procedures [5]. Hypercapnia and PP lead to stimulation of the sympathetic nervous system, with release of catecholamine and vasopressin [6], leading to alteration in acid-base balance as well as cardiovascular and pulmonary physiology. These cardiovascular changes lead to decrease in cardiac output which is further aggravated by the reverse Trendelenburg position during laparoscopic surgery. The hemodynamic derangement compromises tissue perfusion, increases mean arterial pressure and predisposes

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* Corresponding author.
E-mail address: hanan_khafagy@yahoo.com (H.F. Khafagy).

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to myocardial ischemia in susceptible patients [7]. Hence, α_2 adrenergic receptor agonist can be a good choice for prevention of hemodynamic responses associated with laparoscopic surgery [8].

Previous studies reported the usage of dexmedetomidine with sevoflurane, isoflurane and total propofol intravenous anesthesia [9–13] but no researches were performed to calculate desflurane consumption on using dexmedetomidine adjuvant in laparoscopic cholecystectomy.

Thus we hypothesized that the use of dexmedetomidine infusion can decrease desflurane consumption and preserve hemodynamic stability during laparoscopic cholecystectomy. The primary outcome of the present study was to calculate desflurane consumption when combined with dexmedetomidine infusion guided by bispectral index (BIS). Secondary objectives were calculating intraoperative fentanyl requirements and monitoring intraoperative hemodynamic changes.

2. Patients and methods

This randomized prospective double blind controlled study was performed at Theodor Bilharz Research Institute (TBRI) in the period from 07/2016 till 11/2016, after obtaining the institutional board ethics committee approval and patient informed written consent. The study was registered in a public trial register (www.clinicaltrials.gov) under the identification number: NCT02652312. Forty patients aged from 15 to 60 years American Society of Anesthesiologists status I and II of either sex enlisted for elective laparoscopic cholecystectomy were recruited in the study. Patients with cardiovascular, neurological, psychiatric disorder and hypertension were excluded.

Randomization was performed using computer generated random numbers that patients were alienated to one of two groups: Group 'D' (Dexmedetomidine group) and Group 'P' (Placebo group). Intravenous 0.15 mg/kg ondansetron was administered as a premedication. Fluid regimen consisted of Ringer's acetate solution was given at a rate of 6–8 ml/kg/h infusion throughout the procedure.

Monitoring was achieved by continuous electrokardiogram (EKG), pulse oximetry (SpO_2), non-invasive blood pressure (NIBP), end tidal CO_2 ($ETCO_2$), desflurane inspired fraction (FI_{des}), and desflurane expired fraction (ET_{des}) (Infinity Kappa, Dräger, Lübeck, Germany) as well as BIS for detection of consciousness level (Infinity® BISx™ Smart Pod®, VF5).

All patients received 3 L/min oxygen using a nasal cannula as preoxygenation. Group D, patients received IV dexmedetomidine in a dose of 1 μg/kg over 10 min using a syringe pump prior to anesthetic induction (2 ml; 200 μg dexmedetomidine diluted with saline in 20 ml syringe) so the patient was given 0.1 ml/kg while group P, patients received similar volume of normal saline over 10 min. Both study drug and placebo infusions were set by an anesthetist not involved in the study.

Anesthetic induction was obtained via I.V. fentanyl 1.5 μg/kg followed by propofol titration (10 mg every five seconds) until BIS value decreased to 60 and confirmed with loss of verbal response. Then, atracurium 0.5 mg/kg IV was injected slowly followed by tracheal intubation. Fresh gas flow was started at a rate of 3 L/min mixture of 30–40% O_2/air for 10 min then decreased to 1 L/min through closed system while ventilation was controlled to keep $ETCO_2$ at 30–35 mmHg.

Patients in both groups received desflurane at a concentration of 6% which was then adjusted to keep BIS level within the range of 40–50. A maintenance dose of dexmedetomidine 0.5 μg/kg/h (0.05 ml/kg/h) was infused to group D while Group P received a similar volume of normal saline. Fifteen to twenty minutes before the end of the procedure, the infusion was stopped. A top up dose of atracurium 0.1 mg/kg was repeated every thirty minutes to maintain the neuromuscular block. Any rise in heart rate (HR) and mean arterial blood pressure (MABP) exceeding 20% of the preoperative level in spite of adequate anesthetic level guided by BIS was treated with fentanyl 0.5 μg/kg while any decrease of MABP or HR exceeding 20% was treated by IV ephedrine 5 mg or atropine 0.5 mg respectively. At the end of the procedure, desflurane was discontinued and diclofenac sodium 1 mg/kg was given IM. Neostigmine 0.05 mg/kg and atropine 0.02 mg/kg were given to reverse residual neuromuscular blockade which was followed by extubation and transfer to the recovery room.

The following parameters were studied: demographic data as age, height, weight, body mass index, gender and ASA classification a well as duration of surgery and anesthesia. HR and MABP values were documented before and after induction, after intubation, before pneumoperitoneum (before pp), 5 min (after pp 5), 10 min (after pp 10), 15 min (after pp 15), 30 min (after PP 30), 45 min (after pp 45), 60 min after pneumoperitoneum (after pp 60), after release of CO_2 and after extubation. Total intraoperative fentanyl requirement was also recorded. The calculation of desflurane consumption was done as follows [14]:

Duration of volatile anesthesia was detected from starting time of ET control (t = 0) till the end of procedure as the vaporizer was switched off (t = end).

$$\textit{Desflurane fluid volume}\ (\mathrm{ml}) = \frac{\textit{Fresh gas flow}\ (\mathrm{l/min}) \times \textit{vaporizer}\ (\%) \times 1000}{\textit{Conversion factor}} \times \textit{period of each instance}$$

A conversion factor is the resultant of the amount of vapor derived from every ml volatile anesthetic fluid: 209 for desflurane, obtained as follows [15]:

$$\textit{Conversion factor} = [\textit{density of volatile fluid}\ (\mathrm{g/ml}) \times \textit{volume at ambient pressure and temperature}\ (24{,}000\ \mathrm{ml})] / \textit{molecular weight}\ (\mathrm{g}).$$

A total volatile anesthetic fluid used was calculated by adding the multiplying product of usage rate by the period of each instance.

$$\textit{Average volatile anesthetic}\ (\mathrm{ml/h}) = \frac{\textit{total volatile anestetic fluid used}\ (\mathrm{ml})}{\textit{time of volatile anesthesia}\ (\mathrm{h})}$$

3. Statistical analysis

As no previous study up the time of registering this work was available to evaluate the anesthetic consumption of desflurane co-administered with dexmedetomidine to calculate sample size, we considered this research as a pilot study and 20 patients in each group was suitable.

Data were analyzed via the statistical enclose SPSS version 22. Data were presented using mean and standard deviation in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Unpaired *t*-test was used to compare between groups [16]. For comparison of serial measurements within each group, ANOVA repeated measures were done with simple contrast used to assess significant difference between preoperative value and each other value measured at different times [17]. Chi square (χ^2) test was done to compare categorical data. When expected frequency is <5, exact test was performed instead [18]. Result was considered statistically significant when *P*-value was less than 0.05.