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Research article

Effect of perioperative dexmedetomidine infusion on blood glucose levels in non-diabetic morbid obese patients undergoing laparoscopic bariatric surgery☆

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ABSTRACT

Background: This study was designed to assess the clinical efficacy of dexmedetomidine premedication on neuroendocrine stress response by analysis of perioperative fluctuation of blood sugar level during laparoscopic bariatric surgery. Dexmedetomidine when used as an additive to general anesthesia blocks stress response to various noxious stimuli, maintains perioperative hemodynamic stability.

Settings and design: Sixty patients undergoing laparoscopic sleeve gastrectomy were divided randomly into two groups. The dexmedetomidine group (Group D), received dexmedetomidine infusion, while the control group (Group C) received normal saline 0.9% in the same amount and rate as placebo. In group D, dexmedetomidine was given intravenously (IV) as loading dose of 1 μg/kg over 10 min prior to induction. After induction, it was given as infusion at a dose of 0.5 μg/kg/h for maintenance.

Perioperative blood sugar levels were analyzed preoperatively, at 30 min after beginning of surgery then hourly till surgery ends, and six h after surgery. Anesthetic and surgical procedures were standardized. All patients were also assessed for intraoperative hemodynamic changes at specific timings, intraoperative narcotic consumption and recovery profile.

Results: Perioperative administration of dexmedetomidine infusion had essentially weakened the stress response. In the C group there was significantly higher blood sugar values compared to group D one hour after start of surgery up to 6 h later. Also, regarding hemodynamics there was significant reduction in heart rate (HR) and mean arterial blood pressure (MAP) in D group.

Conclusions: During the laparoscopic sleeve gastrectomy, dexmedetomidine premedication has effectively regulated the neuroendocrine stress response of general anesthesia as analyzed by perioperative blood sugar variation. Also, it maintained the hemodynamic stability.

1. Introduction

The surgical procedure's stress response is a major cytokine and neuroendocrine sequel to surgical injury which lead to rapid increase in catecholamine and steroid hormones levels [1]. This has been contemplated as a physiological defense mechanism that is an important risk factor for the body's adaptation to the noxious insults [2].

Hypothalamus stimulation during stress results in adrenocorticotrophic hormone release that in turn starts sudden increase in cortisol level. The cortisol mobilizes protein and fat from the body stores, and renders them available for synthesis of glucose leading to hyperglycemia [3].

The resulting hyperglycemia can adversely affect patient outcomes by producing hazardous effects on immunity thus increasing the % of postoperative complications. Increase in mean intraoperative blood sugar readings as minimal as 20 mg/dL; have been attached to increased adverse outcomes by 30% [4].

The laparoscopic surgery has the privilege of being a low stress level surgery with fewer pulmonary complications, but still causing increased hemodynamic stress responses [5,6].

Various pharmacological agents were used to attenuate surgical stress of laparoscopic procedures to improve outcome such as nitroglycerine, beta blocker, and opioids. α-2 agonists have been also used [7].

☆ This study was done in the surgical department of Ain Shams university educational hospital, Cairo, Egypt.

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The α-2 receptor activation reduces norepinephrine surge, which can be utilized as an effective agent to induce sympatholysis [8]. Because of its sympatholytic properties, Dexmedetomidine was gradually developed as a premedication, aiming for decreasing the sympathetic response to perioperative stressful conditions as laryngoscopy and endo-tracheal intubation [9]. Therefore, monitoring blood sugar level can reflect the metabolic stress response to surgery and Dexmedetomidine role in blunting this stress response.

Dexmedetomidine additionally has an analgesic effect. Because dexmedetomidine has no depressant effects on ventilation, its analgesic effect may offer a significant advantage for morbid obese (MO) patients who might be at risk for respiratory complications [10].

The 1^{ry} goal of the current study was to record the influence of perioperative dexmedetomidine adminstration on modulation of neuroendocrine stress response during laparoscopic bariatric surgery by analyzing the variation of perioperative serial blood sugar levels. The 2^{ry} outcome measures were intraoperative hemodynamics changes and narcotic consumption in addition to postoperative adverse effects and recovery profile.

The originality of this study lies in the context that it is the 1st time to explore a newly added advantage of dexmedetomidine medication in lowering blood sugar level in this specific patients' group: "morbidly obese patients" (who might be diabetic) and who would really get benefit from perioperative blood sugar level control.

2. Subjects and methods

2.1. Selection of patients and randomization

The protocol of this double-blind prospective randomized study was endorsed by the Institutional Ethical Committee, and written informed consent was gotten from all patients. Sixty morbid obese non diabetic adult patients of American society of anesthesiologists (ASA) physical status II and III of either sex, aged 20–50 years, scheduled for elective laparoscopic gastric sleeve under GA with body mass index (BMI) ranging from 35 to 55 kg/m^2 from February 2017 to April 2017 in Ain Shams University – Assembled operating theater. No patient suffered from cardiac, pulmonary, liver, kidney, or metabolic disorders, or was receiving medications that might affect sympathetic response or hormonal secretions. Also, none have other endocrinal disorders that affect blood sugar levels such as; Cushing syndrome and hyperthyroidism or were receiving drug therapy significantly affecting blood sugar level such as corticosteroid therapy. Patients allergic to Dexmedetomidine or positive pregnancy test were disbarred from the study. Also, patients with allergy to eggs or soy were disbarred. Complicated surgeries with prolonged duration > 2 h were also excluded.

All patients have undergone a detailed pre-anesthetic evaluation. All basic investigations (e.g. fasting blood sugar, serum hemoglobin, kidney function tests, liver function tests, coagulation profile, Glycated hemoglobin (HbA1c), chest x-rays and electrocardiogram (ECG) were checked. Patients with HbA1c levels ≥6.5% (indicating undiagnosed Diabetes Mellitus) were excluded.

The patients were arbitrarily distributed into two study groups of 30 patients each as per a computer-generated code.

Both groups' patients were operated by standard surgical technique during morning hours to minimize variability in the secretion of hormones.

2.2. Anesthetic technique

Once arriving to operation room; basic monitors were applied to the patient. Ringer intravenous infusion was started, followed by administration of an antiemetic. Group D patients (n = 30) were given intravenous dexmedetomidine 1 μg/kg diluted in fixed volume of normal saline (100 ml) and Group C patients (n = 30) were given normal saline with same volume as Group D, over a 10 min duration before starting anesthesia. Drug doses utilized throughout the anesthetic procedure were ascertained in view of the 100 kg weight. Lean body weight is the ideal dosing scalar for most medications used in anesthesia. So dosages were given according of a 100 kg patient and then top up doses could be given if needed [11]. After proper assessment of the airway and anticipation of difficult airway, pre-oxygenation with 100% O_2 on 8 L/min. for 3 min. via face mask is started. Induction of anesthesia was achieved with propofol 2 mg/kg IV and fentanyl 2 μg/kg IV and atracurium besylate 50 mg IV, and anesthesia maintenance was done by 2–3% sevoflurane. After oro-tracheal intubation, controlled mechanical ventilation (CMV) was started. For both groups, CMV was achieved by tidal volumes of 8–10 ml/Kg to avoid barotraumas and respiratory rates of up to 12–14 breaths/min to maintain normocapnia and Positive End Expiratory Pressure (PEEP) of 5–10 cm H_2O. Patients were then placed in the semi-lithotomy position. Operation was performed through five abdominal trocars. Intra-abdominal pressure was kept at the range of 12–15 mmHg. Supplemental boluses of Atracurium besylate 0.1 mg/kg IV were administered every 20 min to maintain muscle relaxation during surgery.

Maintenance of anesthesia was done by sevoflurane 2–3% to keep the HR and MAP within 20% of preinduction values and/or HR < 85 beats/min during surgical stimulation.

Each Group D patient received a loading dose of dexmedetomidine 1 μg/kg lean body weight (LBW) over 10 min. prior to induction, followed by an infusion rate of 0.5 μg/kg/hr using a syringe pump. The infusion was discontinued when the laparoscopy ports were removed. The chosen loading and maintenance dexmedetomidine doses can be safely administered in MO patients as documented by previous studies [12,13].

Group C patients received the same volume of 0.9% saline, followed by a saline infusion.

Upon finishing the surgery, patients were extubated after fulfilling the extubation criteria. All subjects were transferred to the post-anesthesia care unit (PACU), where they were monitored for an additional 2 h and got nasal O_2 supplementation.

Hemodynamic parameters as HR and MAP were documented preceding premedication, before induction and after intubation, followed by/5 min for 30 min, thereafter every 15 min till surgery finishes and after extubation in all patients.

Any increase or decrease of HR or blood pressure intraoperatively, was managed as required. For example, MAP rise of > 20% above baseline was treated by administering a 0.5 μg/kg iv bolus of fentanyl and raising the end-tidal sevoflurane concentration to 3.5%. MAP drop of > 20% below baseline was dealt with at first with reduction of the end-tidal sevoflurane concentration to 1% and rapid intravenous fluid bolus (250 ml crystalloids). If still hypotensive, 6 mg ephedrine was given intravenously.

Additionally, total intraoperative narcotic consumption was recorded.

Recovery profile was evaluated by measuring several specific durations: tracheal extubation time, time to eye opening and time to follow verbal commands. All measured in minutes.

After transferal to PACU, patients were observed for any respiratory depression (respiratory rate < 8 breaths/min), or emesis and managed accordingly. Blood samples were analyzed by glucometer (Abbott Optium Xceed) for blood sugar level preoperatively, at 30 min after beginning of surgery then every hour till end of surgery, and 6 h after surgery.

Assessment of postoperative pain was done with the aid of visual analogue scale (VAS) in which patients were requested to estimate their pain on vertical VAS 0–10 cm where (0) is marked as no pain and (10) is marked as the worst pain ever felt. [14]. This was recorded at specific timings: 10, 30, and 60 min and at 2, 3, 6, 12 and 24 h postoperatively. Total dose of rescue analgesics given for each patient in the first postoperative day was recorded. 30 mg ketorolac was given intravenously if VAS score was > or equal to 4 at any of the mentioned times (with a