

**EFFECT OF DEXMEDETOMIDINE ON POSTOPERATIVE GLUCOSE AND
INSULIN SECRETION PATTERNS IN OBESE PATIENTS WITH IMPAIRED
GLUCOSE TOLERANCE**

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Objectives: The primary objective of this prospective study is to compare the effect of dexmedetomidine vs placebo in the plasmatic glucose levels and insulin secretion pattern in obese patients with impaired glucose tolerance undergoing sleeve gastrectomy. The secondary objectives consist of intraoperative fentanyl administration, postoperative morphine consumption, the presence of postoperative nausea and vomiting, postoperative pain score and the level of postoperative sedation.

Design: Prospective, double blind, interventional, randomized, single center, placebo-controlled trial.

Methods

Study population: Patients candidates to be recruited are adults, men and women, between 18 to 60 years old, ASA II, with the clinical diagnosis of insulin resistance (made by specialist and laboratory test), scheduled for laparoscopic sleeve gastrectomy, under general anesthesia. The study requires the approval of the Ethics Committee of the Faculty of Medicine of the Pontifical Catholic University of Chile and the patients have to authorize and sign the respective informed consent previous recruitment.

Exclusion Criteria: Patients are excluded in case of baseline glycemic level ≥ 200 mg•dl⁻¹, previous diagnosis of Diabetes Mellitus (made by specialist and laboratory test), use of corticosteroids, oral hypoglycemic agents and/or clonidine in the last 7 days prior to surgery, use of insulin during the previous 24 hours to surgery and history of allergy to any drug used while the study period.

Randomization: Forty patients are randomized and assign to one of two groups, in a 1:1 ratio using blocks of 2 and 4 permuted at random. Interventions: Dexmedetomidine group (D group): Bolus of Dexmedetomidine of $1\mu\text{g}\cdot\text{kg}^{-1}$ in 10 minutes, followed by a continuous infusion of $0.5\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ until the surgical

procedure is completed. Placebo Group (P group): Saline solution is administered at the same infusion rate and duration as D group.

Preparation of study drug: The study drug (dexmedetomidine or placebo) is prepared in 50 ml syringes, by an independent researcher, who was not involved in the anesthetic management or study analysis. Dexmedetomidine is diluted in saline solution to obtain a concentration of $4\mu\text{g}\cdot\text{ml}^{-1}$.

Anesthetic management: During the pre-anesthetic visit of a potential patient, the protocol is explained and written informed consent is obtained. Subsequently, patients selected to participate are randomly assigned to one of the two study groups. Patients in both groups receive standard surgical and anesthetic management. During anesthesia all patients are monitored with continuous electrocardiogram, non-invasive blood pressure and peripheral oxygen saturation and an intravenous line is inserted into the left arm. The anesthetic technique for this type of surgery consisted of: anesthetic induction with propofol $2\text{mg}\cdot\text{kg}^{-1}$, fentanyl $3\mu\text{g}\cdot\text{kg}^{-1}$ and vecuronium $0.1\text{mg}\cdot\text{kg}^{-1}$ followed by orotracheal intubation and connected to mechanical ventilation with oxygen 50%, tidal volume of $6\text{-}8\text{ml}\cdot\text{kg}^{-1}$ to achieve an end-tidal carbon dioxide between 35-40mmHg during surgery. After the airway is secured a second intravenous line is inserted into the right arm to take blood samples. The maintenance is carried out with 1 MAC of sevoflurane or isoflurane in 50% oxygen, and fentanyl boluses $1\mu\text{g}\cdot\text{kg}^{-1}$ are administered in case of an increase in heart rate or blood pressure $> 25\%$ compared to baseline. The bolus and subsequent continuous infusion of the drug/placebo are begun after the airway is secured and maintained until the end of surgery. During the intraoperative period, a dose of intravenous parecoxib 40 mg is given to all patients.

Plasmatic measurements: Once the intravenous line is placed for anesthesia induction and prior to the administration of the study drug, baseline HbA1c, glucose and insulin levels are immediately sampled. The following glucose and insulin

measurements are done every 2 hours during the first 12 hours from the onset of the study drug.

Clinical measurements: The following measurements are performed: intraoperative fentanyl (μg), postoperative morphine consumption (mg), pain intensity (on numeric rating scale, NRS 0-10) and the occurrence of emesis are all read every 2 hours during the first 12h and at 24h from the onset of the study drug. The postoperative sedation levels, however, are recorded every 2 hours during the first 12h from the onset of the study drug (Sedation Agitation Scale, SAS 1-7, score of 1= Unarousable; 2= Very sedated; 3= Sedated; 4= Calm and cooperative; 5= Agitated; 6= Very agitated; 7= Dangerous agitation).

Postoperative management:

Postoperative monitoring and medical management do not have any restriction and are at the discretion of the attending physician (regarding the concomitant comorbidities and the proposed surgery). Nonetheless, the following aspects are handled in the same way in all patients: a) the management of postoperative pain is with NSAIDs and morphine patient-controlled analgesia (PCA) and b) the treatment of emetic events (nausea and vomiting are managed with antiemetics and no patient receive prophylaxis with dexamethasone).