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Research Article

Ivabradine versus propranolol given orally in microlaryngoscopic surgeries in attenuating stress response: A comparative prospective double blind randomized study

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KEYWORDS

Microlaryngoscopic surgeries;
Ivabradine;
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Abstract *Background and objective:* In this study we evaluated oral ivabradine (a relatively new heart rate lowering agent) versus oral propranolol (a classic commonly used beta-blocker) in achieving a hemodynamic stability and controlling possible changes in blood glucose level due to stress response in microlaryngoscopic surgeries.

Methods: A total of 50 American Society of Anesthesiologists (ASA) 1,2 patients scheduled for microlaryngoscopic surgeries were included in this prospective, randomized controlled double blind study. They were given either oral ivabradine (5 mg tablet) group I or oral propranolol (10 mg tablet) group P in the evening before the operation and 1 h before the induction of anesthesia. Hemodynamic variables (systolic, diastolic, mean blood pressure and heart rate) and blood glucose level were recorded perioperatively.

Results: The changes in blood pressure and heart rate in both groups were mild after intubation, laryngoscope fixation for surgery and extubation but these changes in ivabradine group were significantly less than the changes in propranolol group ($P < 0.05$). No significant difference ($P > 0.05$) was found between both groups in blood glucose level perioperatively. No statistically significant complications were observed in both groups.

Conclusion: Premedication with 5 mg of oral ivabradine or 10 mg of oral propranolol before microlaryngoscopic surgeries was effective in achieving a good degree of hemodynamic stability but ivabradine was more effective. Both drugs didn't show an obvious effect on blood glucose level perioperatively. No complications were recorded.

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1. Introduction

There has been an increase in laryngoscopic surgeries which may be due to the marked increase in laryngeal tumours in recent years. Laryngeal tumours may be benign or malignant including vocal nodules, vocal polyps, vocal fold cysts and papilomas. Poor vocal hygiene and smoking are often considered to be risk factors. In some cases, in order to obtain an accurate diagnosis of a vocal fold lesion it is necessary to perform laryngoscopy, which also allows for proper dysphonia treatment through microsurgery [1]. Manipulation of the larynx such as laryngoscopy and tracheal intubation is associated with hemodynamic response consisting of an increase in heart rate, arterial blood pressure, myocardial oxygen demand and induction of dysrhythmias. In microlaryngoscopic surgery, these responses are more intense [2]. In patients with coronary artery disease, hypertension or cerebrovascular disease, these changes may precipitate myocardial ischemia, myocardial infarction and cerebral hemorrhage [3,4]. Laryngoscopy and surgical procedures also induce complex stress responses, manifested by metabolic, neurohumoral, and immunological changes. Hyperglycemia is a feature of this metabolic response [5].

The choices of premedication and anesthetic techniques are able to influence the neurohormonal stress response by modulating the pathophysiological pathways [6–8].

Ivabradine is a very unique drug. It is a highly selective inhibitor of 'I_f' channels (funny current or funny channels or pacemaker current). It is useful in patients with angina pectoris, coronary artery disease and heart failure. Ivabradine is quite different from a beta blocker as it reduces the heart rate without jeopardizing hemodynamics in unhealthy, compromised patients [9]. The drug can be used not only in hypertensive patients but also in normotensive patients, diabetic patients and patients with bronchial asthma where beta blockers are contraindicated [10].

The rationale of the present study is to minimize stress response in microlaryngoscopic surgeries. We evaluated the effect of oral ivabradine on the hemodynamics and blood glucose level in these surgeries under general anesthesia compared with a commonly used beta-blocker propranolol given orally.

2. Patients and methods

This was a prospective, randomized, double blind, comparative clinical study performed in Ain Shams University Hospitals from March 2015 till October 2015. After getting approval from the institutional ethical committee, an informed consent was taken from every patient enrolled in the study.

Fifty patients aged $\geqslant 25$ to $\leqslant 60$ years, planned for elective microlaryngoscopic surgeries were included in this study. The exclusion criteria included the following: ASA physical status >2, taking beta-blockers or sedatives or antihypertensives, inability to communicate with the patient due to any reason, patients with history of respiratory troubles or diabetes mellitus and those with anticipated difficult airway. Exclusion criteria also included patients with history of chest pain, palpitations, syncope or with baseline heart rate <60 beats per minute, baseline systolic blood pressure <100 mm Hg and those with ECG abnormalities. Routine preoperative investigations were done for all patients.

The patients were randomly allocated by simple randomization into two groups (having 25 patients in each group):

GROUP I: who received oral ivabradine, 5 mg one tablet at 8.00 pm in the evening before the day of the surgery and one 5 mg tablet one hour before the induction of anesthesia.

GROUP P: who received oral propranolol, 10 mg one tablet at 8:00 pm in the evening before the day of the surgery and one 10 mg tablet one hour before the induction of anesthesia.

Randomization sequence was concealed in sealed envelopes performed by the help of an independent personnel. An appropriate code number was assigned to each patient, with an allocation ratio of 1:1. The test medications were given to patients by an attending anesthesiologist who was not involved in patient care or data collection. Data collection was carried out by investigators in a double-blind manner. All patients, investigators and anesthesiologists were blinded to the administered test drugs.

No hypnotic medication was given on the evening before surgery. Patients were premedicated with glycopyrrolate 0.02 mg/kg i.v. and ondansetron 4 mg i.v. in the preoperative room. Upon arrival in the operating room, monitors were attached to the patients and heart rate, NIBP, oxygen saturation, temperature, end tidal CO_2, and ECG were recorded.

After pre-oxygenation with O_2 100% for 3 min, anesthesia was induced with a standard anesthetic protocol using midazolam 0.03 mg/kg, fentanyl 1 μg/kg, thiopentone sodium 3–5 mg/kg, and tracheal intubation was facilitated by atracurium 0.5 mg/kg intravenously. Lungs were mechanically ventilated with O_2 50% and anesthesia was maintained with isoflurane 0.8% and atracurium 0.1 mg/kg every 25 min. Ventilation was adjusted to maintain normocapnia (end-tidal carbon dioxide [$EtCO_2$] 40 ± 5 mmHg). After tracheal intubation with a cuffed endotracheal tube (size 5.0–5.5), the surgeon fixed the laryngoscope and the procedure started. During surgery, Ringer's lactate solution was administered in maintenance dose as per Holliday-Segar formula. The anesthesiologists were ready to manage any hypotension (MAP < 20% preoperative) with a fluid bolus of normal saline 250–300 ml and ephedrine 15 mg i.v if needed. Any incidence of bradycardia (HR < 50/min) was ready to be treated with atropine 0.7 mg i.v.

At the end of the surgery, residual neuromuscular block was reversed by the injection of neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/kg i.v. and the patients were extubated when respiration was sufficient, and they were able to obey commands.

Patients were transferred to the postanesthesia care unit (PACU) where they were monitored for at least 3 h for any evidence of complications or adverse events. Systolic (SBP), diastolic (DBP), mean (MBP) arterial blood pressures and heart rate (HR) were recorded at the following points of time:

(1) Baseline in the evening before the day of operation immediately before taking the test drugs.
(2) Immediately before induction of anesthesia.
(3) One minute after intubation.
(4) Three minutes after intubation.
(5) Five minutes after laryngoscope fixation.
(6) Fifteen minutes after laryngoscope fixation.
(7) One minute after extubation.
(8) Three minutes after extubation.

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