Prevention of Bradycardia by Atropine Sulfate During Urological Laparoscopic Surgery
A Randomized Controlled Trial

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Introduction: Cardiac arrhythmias are a well-recognized complication of anesthesia for laparoscopy. The aim of this study was to evaluate the efficacy of atropine sulfate for prevention of bradyarrhythmia during laparoscopic surgery.

Materials and Methods: Sixty-four candidates for urological laparoscopic surgery were randomly assigned into 2 groups to receive either atropine sulfate or hypertonic saline solution (as placebo), intravenously 3 minutes before induction of anesthesia for the laparoscopic procedure. Then, all of the patients underwent anesthesia intravenous sodium thiopental and atracurium, followed by isoflurane or halothane inhalation. Heart rate and blood pressure were recorded preoperatively in the recovery room, preoperatively in the operation room, after induction of anesthesia, after induction of pneumoperitoneum, and postoperatively.

Results: A significant decreasing trend was seen in the heart rates during the operation in patients without atropine sulfate. Nine of 32 patients (28.1%) in this group developed bradycardia, while none of the patients with atropine sulfate prophylaxis had bradycardia perioperatively ($P < .001$). The mean decreases in systolic blood pressure between induction of anesthesia and pneumoperitoneum were 15.7 ± 10.2 mm Hg in group 1 and 23.5 ± 9.8 mm Hg in group 2 ($P < .001$). The mean decreases in diastolic blood pressure between these two measurements were 8.7 ± 5.2 mm Hg in group 1 compared to 12.1 ± 6.2 mm Hg in group 2 ($P = .001$).

Conclusion: This study suggests that routine prophylaxis with an anticholinergic agent might be helpful in prevention of sinus bradycardia during urological laparoscopic surgery.

Keywords: urologic diseases, laparoscopy, bradycardia, atropine, cholinergic antagonists

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INTRODUCTION

Laparoscopic surgery is growing in popularity, and laparoscopic procedures are being done in a broad population of patients. As a result, we can anticipate more cases of cardiac arrhythmias, which are a well-recognized complication of anesthesia for laparoscopy.[1] Conditions leading to development of arrhythmias are CO_2 insufflations, hypercapnea, increased vagal tone owing to traction on the pelvic or peritoneal structures, Trendelenburg position, anesthetic drugs (especially, halothane in combination with spontaneous ventilation), preoperative patient's anxiety, endobronchial intubation, and gas embolism.[1,2]

Anesthesiologist should be aware of the risk of cardiac arrhythmias and of the problems inherent to the pneumoperitoneum during laparoscopy. Excessive vagal activity which causes severe bradycardia and hypotension can be life threatening.[2] Prompt treatment is needed with the use of anticholinergic and sympathomimetic drugs.[3,4] There are studies addressing administration of anticholinergic agents, especially glycopyrrolate and atropine, for prevention of bradycardia during open surgeries in children and adults.[3-6] Such studies have also been done for gynecologic laparoscopic surgeries[7]; however, there are limited data on the efficacy of these drugs during urological laparoscopic surgeries. The aim of this study is to evaluate the efficacy of atropine sulfate for prevention of bradyarrhythmia during urological laparoscopic operations.

MATERIALS AND METHODS

In a randomized double-blinded placebo-controlled trial, we enrolled patients who were candidates for elective urological laparoscopic surgical operation. After obtaining informed consent and approval of the study by ethics committee of our university, we selected patients aged between 15 and 50 years old who were candidates for elective urological laparoscopic surgery. All of the patients were in the American Society of Anesthesiologists' categories I and II and did not have any history of cardiac disease. The exclusion criteria were history of cardiac arrhythmias (such as sick sinus syndrome), drug-induced bradycardia, and cardiac disease, as well as contraindication of general anesthesia or laparoscopic surgery. A total of 64 eligible patients were selected and were randomly assigned into 2 groups by simple randomization method.

In group 1, atropine sulfate, 0.6 mg, and fentanyl, 100 μg, were administered intravenously immediately before induction of anesthesia for the laparoscopic procedure. In group 2 (control), hypertonic saline solution, dispensed in similar bottles to atropine sulfate bottles, was administered intravenously along with fentanyl, before induction of anesthesia.

Then, all of the patients underwent a balanced anesthesia, including induction of anesthesia with intravenous sodium thiopental, 5 mg/kg to 6 mg/kg, followed by atracurium, 0.5 mg/kg. After endotracheal intubation, maintenance of anesthesia was continued by inhalational anesthetic drugs (isoflurane or halothane) and positive pressure ventilation.

The patients were secured slightly head down in the supine or semilateral position, and their intra-abdominal pressure was maintained below 15 mm Hg during the operation. They were monitored with a noninvasive arterial pressure measurement device, electrocardiography, pulse oximetry, and capnography. Controlled ventilation was used throughout to maintain eucapnia. Heart rate and blood pressure were recorded as following in all of the patients: (1) preoperatively in the recovery room, (2) preoperatively in the operation room, (3) after induction of anesthesia, (4) after induction of pneumoperitoneum, and (5) postoperatively. If arrhythmia or bradycardia developed, it would be controlled by atropine sulfate or other anti-arrhythmic drugs.

The collected data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 11.5, SPSS Inc, Chicago, Illinois, USA). The *t* test was used to compare the age, heart rate, and blood pressure variables, and the chi-square test, to compare the frequency of bradycardia between the two groups.

RESULTS

All of the patients completed the study. The mean age of them were 24.4 $\pm$ 7.8 years and 20.8 $\pm$ 8.5 years in groups 1 and 2, respectively ($P = .06$). There were no significant differences in sex distribution between the participants in groups 1 and 2 ($P = .27$). The mean heart rates were not significantly different between the two groups preoperatively; however, a significant decreasing trend was seen in the heart rates during the operation in group 2, but not in group 1 with atropine sulfate (Table). Nine of 32 patients (28.1%) in group 2 developed bradycardia (heart rate < 60/min), while none of the patients in group 1 had bradycardia perioperatively ($P < .001$).

Heart Rate at Different Times in Relation to Laparoscopic Surgical Operation in Patients With Atropine Sulfate (Group 1) and Without It (Group 2)

Time	Mean Heart Rate, /min		*P*
	Group 1	Group 2	
In recovery	88.4 ± 10.6	90.7 ± 13.7	.45
Preoperation	94.1 ± 9.4	98.1 ± 12.9	.05
Induction of anesthesia	101.6 ± 12.2	89.1 ± 6.4	.001
Induction of pneumoperitoneum	107.6 ± 6.1	69.4 ± 15.7	< .001
Postoperation	104.6 ± 10.8	105.8 ± 5.8	.56

There were significant differences in the mean systolic and diastolic blood pressures after induction of pneumoperitoneum between groups 1 and 2 ($P = .01$ and $P < .001$, respectively). The mean decreases in systolic blood pressure between induction of anesthesia and pneumoperitoneum were 15.7 ± 10.2 mm Hg in group 1 and 23.5 ± 9.8 mm Hg in group 2 ($P < .001$). The mean decreases in diastolic blood pressure between these two measurements were 8.7 ± 5.2 mm Hg in group 1 compared to 12.1 ± 6.2 mm Hg in group 2 ($P = .001$).

DISCUSSION

During anesthesia, changes in heart rate may suggest alterations in the depth of anesthesia, vagal activity, CO_2 pressure, and the effects of drugs. Simple vagal reactions, for instance, are usually improved when the stimulus is stopped.[2,3] Cardiac arrhythmias are frequently seen during anesthesia in laparoscopic procedures, the most common of which is sinus tachycardia.[3] Bradyarrhythmias (eg, atroventricular dissociation, nodal rhythm, sinus bradycardia) may develop independently or in combination with tachycardia during the same procedure.[1,3] In rare cases, asystolic cardiac arrest and cardiovascular collapse may develop.[5]

The present study revealed prophylactic effect of intravenous atropine sulfate on cardiac arrhythmias (sinus bradycardia) during anesthesia with halothane for laparoscopic urological surgeries in adults. Anticholinergic agents alter the balance between sympathetic and parasympathetic activity in the autonomic nervous system by blocking the parasympathetic muscarinic receptors.[6,7] In a study by Annila and colleagues that evaluated intravenous atropine sulfate and glycopyrrolate on cardiac arrhythmias for adenoidectomy in children, the use of anticholinergics did not influence the incidence of ventricular arrhythmias during anesthesia with halothane in children. Bradycardia was more common in the placebo group than in the atropine group.[3] Although patients were young and the procedure was not laparoscopic, bradycardia was more common in the placebo group, which is similar to our results.

Adult sympathetic predominance may cause arrhythmias.[5,7] Furthermore, suppressing vagal activity is an important protector against sudden cardiac death.[5] Our results does not support the suggestion that anticholinergics are arrhytmogenic. Bradycardia was more common in adults receiving no medication before the procedure than in those who received atropine sulfate. However, even in those with no atropine, the events were short and resolved after treatment with atropine or spontaneously after desufflation or cessation of painful stimulants.

During laparoscopic surgery, the head-up position and high insufflator pressure reduce venous return and cardiac output with a decrease in the mean arterial pressure and cardiac index. Conversely, the head-down position increases venous return and normalizes blood pressure.[8] In our study, the patient's position was head-down and CO_2 pressure was below 15 mm Hg. Therefore, only during the postinduction period, there was a significant decrease in blood pressure between the two groups that could be due to the protecting effect of atropine againts bradycardia.

Sinus tachycardia occurred in none of our patients. Heart rate tended to be higher during the operation, especially pneumoperitoneum induction; however, there was no significant difference in heart rate between the two

groups postoperatively and in recovery room. Hypercarbia, hypoxia, and type of the surgical operation affect the incidence of cardiac arrhythmias. These parameters were similar in our groups of patients, and there were no case of hypoxia or hypercarbia. Bradycardia events were short and resolved spontaneously in atropine group or were treated with atropine sulfate. In conclusion although the use of new drugs such as propofol and isoflurane decreases the rate of cardiac complications, continuous monitoring of cardiovascular and pulmonary parameters is essential.

CONCLUSION

This study suggests that prophylactic treatment with cholinergic antagonists such as atropine sulfate can be helpful in prevention of sinus bradycardia during laparoscopic surgeries.

CONFLICT OF INTEREST

None declared.

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