

Ephedrine Is More Effective Than Atropine for the Treatment of Symptomatic Bradycardia in Elderly Patients

Ali Shahriari,^{1,*} and Maryam Khooshideh²

¹Departement of Anesthesiology, Razi Hospital, Tehran University of Medical Sciences, Tehran, IR Iran

²Departement of Obstetrics and Gynecology, Arash Hospital, Tehran University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Ali Shahriari, Tehran University of Medical Sciences, Tehran, IR Iran. Tel/Fax: +98-2155412222, E-mail: ashahriari@tums.ac.ir

Received 2017 January 30; Revised 2017 March 01; Accepted 2017 March 14.

Abstract

Background: Bradycardia may result in the exacerbation of myocardial dysfunction in elderly patients.

Objectives: In this retrospective cohort study, ephedrine and atropine were compared for the treatment of symptomatic bradycardia.

Methods: In this study, patients (above 65 years) with symptomatic bradycardia during skin tumor resection were evaluated. Symptomatic bradycardia was defined as heart rate below 49 beats per minute and systolic blood pressure below 85 mmHg. According to the anesthesiologist's decision, 1 group of patients (atropine group) received atropine (0.5 mg) as the first-line drug, while the other group (ephedrine group) received ephedrine (10 mg) as the first-line drug to restore hemodynamic parameters. If the initial treatment had no effects on the management of the symptoms, ephedrine (10 mg) was administered to the patients in both groups. The number of patients, who received treatment with a single drug to normalize their hemodynamic parameters, was compared with those who required a second drug.

Results: Among 194 subjects with symptomatic bradycardia, 86 and 108 patients were allocated to the atropine and ephedrine groups, respectively. Based on the findings, 35 patients in the atropine group required the second drug for bradycardia management; therefore, 51 patients were treated with only atropine (efficacy: 51/86, 59.30%). Moreover, 21 patients in the ephedrine group required the second dose of ephedrine for the management of bradycardia; consequently, 87 patients were treated with only ephedrine (efficacy: 87/108, 80.55%). There was a statistically significant difference between the 2 groups ($P = 0.001$).

Conclusions: Ephedrine is more effective than atropine in the management of symptomatic bradycardia in elderly patients.

Keywords: Atropine, Ephedrine, Bradycardia, Elderly

1. Background

Bradycardia can be a life-threatening condition for elderly patients, as they may experience some degree of myocardial dysfunction. In 70% - 80% of patients with acute coronary syndrome, atropine (1 - 3 mg) can be useful for the treatment of symptomatic bradycardia; in fact, intravenous administration of atropine can lead to increased heart rate. However, some elderly patients with bradycardia are resistant to atropine, and therefore, other drugs such as aminophylline (1), isoproterenol (2), and ephedrine (3) are used for the management of symptomatic bradycardia.

Razi hospital is a referral hospital, specialized in the removal and reconstruction of malignant skin tumors. Three plastic surgeons are responsible for skin tumor resection, flap coverage, or skin grafting. Lidocaine is commonly used as a topical anesthetic in plastic surgeries for the removal of skin tumors. Systemic absorption of this drug is determined by the site of injection, drug dosage, drug volume, and concomitant use of vasoconstrictors.

Sometimes, a higher dose of lidocaine is used to improve patient comfort, especially for those who have multiple skin tumors and are exposed to an increased risk of toxicity. Toxicity can involve the cardiovascular and central nervous systems and occur when the plasma lidocaine level rises above 10 $\mu\text{g}/\text{mL}$; it can in fact lead to severe bradycardia, hypotension, and need for early interventions. High dose of lidocaine in elderly patients can cause hemodynamic instability. Moreover, it is suspected that lidocaine can cause ventricular contractile depression. In cardiomyopathy patients with very poor left ventricular function, the negative inotropic effects may cause significant hemodynamic instability (4).

Management of bradycardia is associated with the severity of symptoms, degree of hypotension, and some reversible factors. Ephedrine and atropine are used as the drugs of choice for the treatment of bradycardia in elderly patients (above 65 years) due to lidocaine overdose in our hospital. The aim of this study was to compare the efficacy of atropine and ephedrine in the management of symptomatic sinus bradycardia in elderly patients.

2. Methods

This retrospective cohort study was conducted during November 2013-November 2015 among patients who met the inclusion criteria and were admitted to Razi hospital. This study was approved by the ethic committee of Razi hospital (registration number, 96-01-30-34288, approved by the Vice Chancellor for Research of Tehran University of Medical Sciences). Informed consents were also obtained from the patients.

Before the operation, a 22-gauge intravenous cannula was placed in the patient's forearm for continuous infusion of Ringer's solution. Oxygen was continuously administered to patients through a nasal probe. Heart rate, electrocardiogram (EKG), and oxygen saturation (using a digital probe) were continuously monitored. Blood pressure was also measured automatically every 3 minutes, using an automatic monitoring device. Mild to moderate sedation was practiced to facilitate these procedures.

The sedation protocol was as follows for patients aged 10 - 65 years (except children undergoing general anesthesia): midazolam (1 - 2 mg), fentanyl (1 - 1.5 μ /kg), propofol (0.5 - 1 mg/kg), and ketamine (0 - 0.5 mg/kg). For patients above 65 years, the sedation protocol was as follows: midazolam (1 mg), fentanyl (0 - 1 μ /kg), and ketamine (0 - 0.5 mg/kg). Lidocaine 1% - 2%, along with adrenaline (1:100,000), was administered topically, besides anesthetizing the tumor resection site. In hypertensive patients, the solution was prepared with adrenaline (1:200,000). Also, hypertensive patients were treated with labetalol, hydralazine, or nitroglycerin infusion.

Symptomatic bradycardia was defined as heart rate below 49 beats per minute and systolic blood pressure below 85 mmHg. Intervention was initiated by inotropic and chronotropic drugs. Two protocols were designed for restoring hemodynamic parameters in patients with symptomatic bradycardia. According to the anesthesiologist's decision, the patients were enrolled in atropine or ephedrine group.

In the atropine group, 0.5 mg of atropine was administered as the first-line drug, and if no clinical responses were observed within 45 seconds, 10 mg of ephedrine was injected to restore hemodynamic parameters. If the response was unacceptable, another dose of ephedrine (10 mg) was administered. On the other hand, in the ephedrine group, ephedrine (10 mg) was injected as the first-line drug for the management of symptomatic bradycardia; if no clinical responses were observed in 45 seconds, another dose of ephedrine was administered.

For intensive symptomatic bradycardia (systolic blood pressure < 70 mmHg and heart rate < 49/min), another management protocol was designed. The efficacy of each

drug (atropine 0.5 mg and ephedrine 10 mg) was determined by dividing the number of patients, who required only 1 dose of the drug for a significant rise in their hemodynamic parameters (heart rate > 55/min, systolic blood pressure > 90 mmHg), by the number of patients in that group.

Statistical tests were performed, using SPSS version 13 for Windows. The results are reported as absolute values and mean \pm SD. Also, nominal variables were analyzed by Chi square test. P value less than 0.05 was considered statistically significant.

3. Results

In this retrospective cohort study, performed during November 2013-November 2015, 5840 patients were admitted to the operating room of Razi hospital for skin tumor resection. Among these patients, 2336 were above 65 years. Overall, the study was conducted on 194 patients who met the inclusion criteria (sudden hypotension and bradycardia).

Demographic and disease characteristics of these patients are illustrated in [Table 1](#). There was no significant difference in terms of age, weight, and hemodynamic characteristics before the operation between the groups ([Table 1](#)). Also, duration of operation was similar in the 2 groups. Among 194 patients with bradycardia and hypotension, 86 were allocated to the atropine group, and 108 patients were allocated to the ephedrine group.

Among 86 patients in the atropine group, 35 received the second drug for the management of bradycardia; consequently, 51 patients were treated only with atropine (efficacy of atropine: 51/86, 59.30%). On the other hand, among 108 patients who were first treated with ephedrine, the need for administration of the second drug was reported in 21 patients; overall, 87 patients were treated with only ephedrine (efficacy of ephedrine: 87/108, 80.55%; $P = 0.001$). There was a statistically significant difference between the 2 groups (51, 59.30% in the atropine group vs. 87, 80.55% in the ephedrine group; $P = 0.001$).

The patients' normal heart rate and blood pressure were quickly restored, and they were transferred from the recovery room within 2 to 3 hours. No signs of myocardial ischemia, ST elevation, chest pain, or neurologic symptoms were detected among the patients. Desirable responses were observed after the second drug injection in all the patients who required the first drug for restoring hemodynamic parameters, and no further intervention was required.

Table 1. Baseline Demographic and Intraoperative Characteristics of the Patients^a

	Atropine Group (n = 86)	Ephedrine Group (n = 108)	P Value
Age, y	69.32 ± 4.21	68.44 ± 3.43	0.12
Weight, kg	63.24 ± 5.75	60.32 ± 8.54	0.27
Heart rate before operation, beat/min	61.68 ± 12.21	64.45 ± 15.68	0.18
Systolic blood pressure, mmHg	146 ± 27	139 ± 37	0.14
Duration of operation, min	37.23 ± 25.41	33.54 ± 19.38	0.25
Dose of lidocaine injected, mg	310.57 ± 41.81	324.76 ± 39.41	0.01
Sex			
Male	81 (94)	99 (91)	0.50
Female	7 (8.13)	9 (8.33)	0.42
Frequency of diabetes	9 (10.47)	13 (12.04)	0.73
Consumption of antihypertensive drugs	21 (24)	28 (25)	0.81
Treated only with one drug ^b	51 (59.30)	87 (80.55)	0.001

^aValues are expressed as mean ± standard deviation or No. (%).

^bTreated only with one drug (atropine in the atropine group and ephedrine in the ephedrine group).

4. Discussion

The present study, which was performed in a large group of patients, showed that lidocaine infiltration besides sedation is a safe method, even in elderly and very old patients. Nevertheless, large doses of lidocaine can lead to some adverse effects, such as bradycardia and hypotension (5).

In symptomatic sinus bradycardia, atrioventricular (AV) node block can be one of the symptoms of acute inferior myocardial infarction or occlusion of the dominant right coronary artery. Occlusion, which might cause damage to the free right ventricle wall, frequently compromises the blood supply to the sinoatrial node, atrium, and AV node, producing effects such as sinus bradycardia, atrial infarction, atrial fibrillation, and AV block (6).

Degenerative fibrosis of the sinoatrial node and nodal tissues is the most common cause of conductive changes, usually in aging hearts, as heart rate changes with age due to alterations in the functional autonomy of the sinus node. Recent evidence suggests quantitative and qualitative differences in cholinergic receptors among individuals (7); due to these conductive disorders, atropine can be ineffective for elderly patients.

The majority of studies on symptomatic bradycardia are conducted among patients with severe coronary artery diseases, while management of these patients with pacemakers and intravenous drug intervention has not been compared in any clinical trial. In this regard, Popescu et al. performed a study on 130 patients undergoing percutaneous carotid angioplasty for symptomatic stenosis. The mean age of the patients was 55 years. In their study, hypotension and/or bradycardia was reported in 26 patients (20%). They analyzed the effects of angiotensin-converting-enzyme (ACE) inhibitors, diuretics, and beta-blockers and found that only use of beta-blockers is associated with an increased risk of hemodynamic instability (8).

Ephedrine is a sympathomimetic amine. The principal mechanism of action in ephedrine depends on the indirect stimulation of the adrenergic receptor system through increasing the activity of noradrenalines in postsynaptic α - and β -receptors. Ephedrine also releases noradrenaline from the storage sites; inotropic effects occur due to these multiple mechanisms. Atropine has a unique mechanism (vagolytic effect) for increasing the heart rate. However, there is no consensus regarding the use of ephedrine in elderly patients due to the fear of tachycardia and hypertension, associated with its use. In multiple studies, ephedrine was used in elderly patients after spinal anesthesia for the treatment of hypotension (3). It should be noted that although metoraminol and phenylephrine could be better options for the management of these patients, they were not accessible in our hospital.

4.1. Conclusions

Based on the present retrospective study, ephedrine is more effective than atropine in the management of symptomatic bradycardia in elderly patients due to lidocaine administration.

Footnote

Conflicts of Interest: The authors declare no conflicts of interest.

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