The Evaluation of Perioperative Safety of Local Anesthesia with Lidocaine Containing Epinephrine in Patients with Ischemic Heart Disease

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Received: 3 Dec. 2012; Received in revised form: 4 Jan. 2013; Accepted: 15 Feb. 2013

Abstract- The use of local anesthesia with lidocaine containing epinephrine in patients with cardiac disease is controversial in the literature. The aim of our study was determining the safety of use the local anesthesia contain epinephrine in patients with ischemic heart disease that undergoing reconstructive surgery. Thirty two patients that had known ischemic heart disease and candidate to undergo reconstructive surgery for skin tumor enrolled in this study. All patients continued their medication for cardiac disease till morning of the operation. 10 ml lidocaine 2% containing 1:100,000 epinephrine was injected in patients for local anesthesia. The hemodynamic changes and electrocardiographic variables before injection were compared with them after injection, during surgery and till 6 hours postoperation period. A 12 lead electrocardiogram was recorded in all our cases for detection of myocardial ischemic changes. The mean age, weight and height were 58.2±10.4, 74.8.±14.4 kg and 164.5± 8 cm respectively. Twelve patients (37.5%) were diagnosed with systemic hypertension and 10 patients with diabetes (31.2%). The comparison of change of systolic, diastolic and mean blood pressure between baseline, during procedure and after operation defined that our subjects did not have any significant disturbance in blood pressure in perioperative period. The comparison of baseline heart rate with heart rate after injection, during procedure and in postoperation period indicated a significant changes in this variable (P=0.044). The heart rhythm during the perioperative period also failed to exhibit alterations. The ischemic change was not recorded in our patients before injection compared to after injection. None of our patients have any early complications because of infiltration of local anesthetic containing epinephrine in our patients. The use of 10 ml 2% lidocaine with epinephrine 1:100,000 in patients with cardiac disease represent a safe anesthetic procedure. These patients experienced a more profound anesthesia with hemodynamic stability and without myocardial ischemic changes.

Acta Medica Iranica, 2013; 51(8): 537-542.

Keywords: Anesthesia; Epinephrine; Ischemic heart disease; Lidocaine

Introduction

Epinephrine intensifies the effect of local anesthetic by increasing depth and duration of analgesia (1) and routinely incorporated in most commercial preparations for infiltration because of help to better hemostasis (2,3). Furthermore, vasoconstrictor reduces the systemic toxicity of local anesthetic by concentrating and decrease the release of local anesthetic to circulation after infiltration (4). It was shown that the events of infiltration of local anesthetic solutions containing epinephrine during operation were changes in blood pressure and heart rate (5), arrhythmia (6), myocardial ischemia (7,8), increase of endogenous catecholamines (8) and hypokalemia (9). Also it was shown that when the dose of epinephrine exceeds the normal range, the morbidity and mortality was increased (4). This characteristic was important for patients with cardiovascular disease. Recent studies showed that epinephrine associated with local anesthetic have a safety range (10), but its safety in patients with cardiovascular disease is not clear (11). The aim of our

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study was to evaluate possibility of hemodynamic change, arrhythmia and myocardial ischemia following infiltration of lidocaine combined with epinephrine for reconstructive surgery in patients with ischemic heart disease (IHD).

Materials and Methods

Thirty two patients that had known IHD and candidate to undergo reconstructive surgery for skin tumor such as basal cell carcinoma, squamous cell carcinoma and melanoma enrolled in this study between august 2011 till august 2012. Our trial approved by the local ethics committee and all of subjects informed of procedure and then written consent was obtained. Inclusion criteria were IHD including stable angina pectoris, 3 months after previous coronary bypass graft surgery (CABG) or percutaneous coronary intervention (PCI), 6 months after myocardial infarction, and also patients with compensated congestive heart failure (CHF) with New York Heart Association (NYHA) class I-II. Patients with unstable angina pectoris, recent myocardial infarction (less than 6 months), malignant arrhythmias, uncontrolled hypertension, uncompensated CHF, severe mitral or aorta stenosis, uncontrolled diabetes or hyperthyroidism, severe asthma, pheochromocytoma and chronic use of antidepressant were excluded from our study. All patients continued their medication for cardiac disease till morning of the operation. All subjects received 1 mg midazolam as premedication before operation. After injection of 50 µg fentanyl and 20 mg propofol, 10 ml lidocaine 2% containing 1:100,000 epinephrine was injected in patients for local anesthesia. A minimum of 5 minutes was allowed to attain local anesthesia (LA) effectiveness. The hemodynamic changes and electrocardiographic variables before injection were compared with them after injection, during surgery and till 6 hours postoperation period. A noninvasive blood pressure monitor (Saadat S1800, Novin, Iran) was used to record systolic, diastolic and mean of blood pressure before injection as baseline and then at 2 minute interval. Also, saturation of peripheral oxygen (SPO_2) and heart rate (HR) were recorded continuously. A 12 lead electrocardiogram was recorded in all our cases for detection of myocardial ischemic changes. Ischemic pattern was considered as ST segment change elevation ≥1 mm or horizontal or downsloping depression ≥1 mm from baseline. The recording of more than ten ventricular or supraventricular extrasystoles per hour during the study period were defined as cardiac arrhythmia. A general linear model test was used to compare the blood pressure, heart rate and ST segment changes before and after the procedure. Results were considered statistically significant at $P<0.05$.

Results

The mean age, weight and height were 58.2±10.4, 74.8±14.4 kg and 164.5±8.0 cm respectively. Twelve patients (37.5%) were diagnosed with systemic hypertension and 10 patients with diabetes (31.2%). Coronary angiography revealed single-vessel disease in three (9.3%) patients, two-vessel disease in eight (25%) patients, and three-vessel disease in twenty one (65.6%) patients. 14 patients had ejection fraction (EF) less than 40% before operation and were under treatment for CHF. The comparison of change of systolic, diastolic and mean blood pressure between baseline, during procedure and after operation is shown in table 1.

Table 1. The comparison of systolic, diastolic and mean blood pressure before and after injection.

Variables		Measurements (mmHg)	*P*
Systolic Blood Pressure	Before injection	139.6±15.4	0.182
	2 minutes after injection	133.1±27.1	
	4 minutes after injection	128.2±19.9	
	6 minutes after injection	133.3±18.1	
	8 minutes after injection	134.3±19.7	
	10 minutes after injection	135.1±14.5	
	15 minutes after injection	134.1±13.4	
	30 minutes after injection	132.3±13.1	
	60 minutes after injection	133.2±12.6	
	6 hours after operation	135.1±16.1	
Diastolic Blood Pressure	Before injection	77.1±15.7	0.565
	2 minutes after injection	77.5±14.5	
	4 minutes after injection	76.0±12.6	
	6 minutes after injection	75.0±14.0	
	8 minutes after injection	73.6±12.0	
	10 minutes after injection	77.5±10.7	
	15 minutes after injection	75.3±9.9	
	30 minutes after injection	75.1±10.0	
	60 minutes after injection	76.2±12.0	
	6 hours after operation	76.8±14.0	
Mean Blood Pressure	Before injection	97.8±13.9	0.470
	2 minutes after injection	96.0±17.1	
	4 minutes after injection	93.3±13.4	
	6 minutes after injection	94.5±14.2	
	8 minutes after injection	93.8±13.3	
	10 minutes after injection	96.7±8.4	
	15 minutes after injection	94.8±9.2	
	30 minutes after injection	94.1±9.3	
	60 minutes after injection	96.0±10.8	
	6 hours after operation	97.2±12.0	

Table 2. The comparison of heart rate, respiratory rate and oxygen saturation before and after injection.

Variables		Measurements	*P*
Heart rate	Before injection	72.9±16.4	0.044
	2 minutes after injection	76.0±16.1	
	4 minutes after injection	81.1±13.0	
	6 minutes after injection	76.1±14.5	
	8 minutes after injection	71.8±21.5	
	10 minutes after injection	78.4±15.4	
	15 minutes after injection	78.5±16.1	
	30 minutes after injection	75.5±13.4	
	60 minutes after injection	74.4±12.0	
	6 hours after operation	74.0±14.5	
Respiratory rate	Before injection	15.8±3.1	0.090
	2 minutes after injection	15.6±2.9	
	4 minutes after injection	16.3±2.0	
	6 minutes after injection	17.2±1.1	
	8 minutes after injection	15.5±2.3	
	10 minutes after injection	16.3±1.5	
	15 minutes after injection	17.0±1.7	
	30 minutes after injection	15.3±1.0	
	60 minutes after injection	14.2±2.0	
	6 hours after operation	14.8±1.8	
Oxygen saturation (SPO_2, %)	Before injection	97.0±2.5	0.954
	2 minutes after injection	96.9±3.1	
	4 minutes after injection	96.8±2.6	
	6 minutes after injection	96.8±2.7	
	8 minutes after injection	97.0±1.6	
	10 minutes after injection	96.8±2.5	
	15 minutes after injection	97.2±1.4	
	30 minutes after injection	97.1±1.8	
	60 minutes after injection	96.0±2.8	
	6 hours after operation	97.2±2.4	

Table 3. The comparison of arrhythmia episode and ST segment changes before and after injection.

Variables		Measurements	*P*
Arrhythmia (more than ten ventricular or supraventricular extrasystoles per hour)	Before injection	Zero	0.960
	2 minutes after injection	Zero	
	4 minutes after injection	Zero	
	6 minutes after injection	Zero	
	8 minutes after injection	Zero	
	10 minutes after injection	Zero	
	15 minutes after injection	Zero	
	30 minutes after injection	Zero	
	60 minutes after injection	Zero	
	6 hours after operation	Zero	
ST segment changes (mm)	Before injection	-0.23±0.07	0.117
	2 minutes after injection	-0.06±0.04	
	4 minutes after injection	-0.13±0.04	
	6 minutes after injection	-0.13±0.04	
	8 minutes after injection	-0.09±0.04	
	10 minutes after injection	-0.20±0.12	
	15 minutes after injection	-0.13±0.04	
	30 minutes after injection	-0.20±0.04	
	60 minutes after injection	-0.14±0.04	
	6 hours after operation	-0.22±0.08	

The comparison of baseline HR with HR after injection, during procedure and in postoperation period indicated a significant changes in this variable (P=0.044) (Table 2). The unaffected respiratory rate and pulse oximetry values defined that our subjects did not have any respiratory disturbance in perioperative period (Table 2). The heart rhythm during the perioperative period also failed to exhibit alterations (Table 3).
The ischemic changes was defied as ST segment elevation or depression greater than 1 mm from baseline was not recorded in our patients before injection compared to after injection.

The ST segments variations in perioperative period were shown in table 3. None of our patients have any early complications because of infiltration of LA containing epinephrine in our patients.

Discussion

We found that local anesthesia with 10 ml of 2% lidocaine and epinephrine 1:100,000 did not change significantly in blood pressure, ischemic episode and arrhythmic conditions among patients with cardiac disease, suggesting its safety of this solution in these patients. This issue that under what circumstances and with which dose of epinephrine combined with local anesthesia can be use safely within procedure has been debate and at present there are insufficient data to answer many of questions. The aim of our study was determining the safety of use the local anesthesia contain epinephrine in cardiac patient that undergoing reconstructive surgery. Some of the beneficial of use of epinephrine with local anesthetic in superficial surgery are related to decrease blood loss, increase of duration and depth of anesthesia and reduce the local anesthesia toxicity. Patients who underwent procedures with insufficient vasoconstriction within the local anesthetic solution may observe inadequate pain control and lead to increase serum catecholamines especially norepinephrine that this condition may dangerous in patients with cardiac disease (12,5). Also epinephrine is an arrhythmogenic substance; however, there is a debate about the use in patients with cardiac disease to maintain a margin of safety. Previous studies confirmed that use of local anesthetic contained epinephrine even though changed systolic blood pressure and HR significantly, but the mean arterial blood pressure (MAP) is unchanged (14,15). Also in another study the epinephrine increase blood pressure, HR, cardiac automaticity and myocardial oxygen consumption, but the mean arterial pressure is relatively unchanged (8). There was shown that local anesthetic with epinephrine increase HR but less arrhythmia or ST depression when compared to other studies that used local anesthetic alone (15,16). Previous studies showed that use of solution lidocaine 2% contained 1:100,000 epinephrine for local anesthesia would have produced greater cardiac events than the 1:200,000 solution (17,18). Niwa *et al*. (19) showed that use of lidocaine 2% with a higher adrenalin concentration of 1:80,000 can lead to significant hemodynamic and electrocardiographic changes in perioperative period. One study showed ischemic pattern (ST segment depression) in patients with cardiac disease who underwent dental procedure with local anesthesia with epinephrine; however it was not confirmed by another study (20). In previous study showed that serum level of norepinephrine significantly increases in patients that received 4% articaine with 1:100,000 epinephrine as compared to 4% articaine with 1:200,000 epinephrine. Moreover, this study concluded that use of combination of local anesthetic and epinephrine in an appropriate concentration guarantee the depth and duration of surgical anesthesia and avoids pain stress and cardiac toxicity (21). Abraham-Inpijn *et al.* showed that injection of 2% lidocaine with 1:80,000 epinephrine lead to greater increase in blood pressure and significant arrhythmias in hypertensive patients compared to normotensive case (22). Blinder observed ST depression, cardiac rhythm and the number of premature heart beats did not alter significantly in patients with cardiac disease that underwent dental extractions with lidocaine containing a vasopressor (23-25). Cintron *et al.* (26) studied patients with recent myocardial infarction and followed them with Holter ECG monitoring in perioperative period and concluded that the use of lidocaine 2% and 1:100,000 epinephrine for dental surgery did not cause any significant hemodynamic and electrocardiographic changes or other early postoperation events. Similarly, Vanderheyden *et al.* (27) observed that the use of lidocaine and epinephrine for local anesthesia did not provoke myocardial ischemia by ST analyzer. Multiple studies determined that patients who received local anesthetic formulations with epinephrine in dental procedure did not show any hypertension episode and cardiovascular complications (19,26,28). Meyer (29) found that normotensive and hypertensive patients who underwent local anesthesia with 2% lidocaine with and without 1:100,000 epinephrine had similar change of blood pressure and HR. Another study showed that patients undergoing injection of 2% lidocaine with 1:80,000 epinephrine had no change in blood pressure in

hypertensive patients (30). NYHA recommended that a maximum 11 cartridges of 1:100,000 epinephrine can be use at session of dental treatment (31). Also American Heart Association (AHA) guideline defined that concentration of epinephrine used combined with lidocaine in dental procedure are safe in patients with cardiac disease if administered carefully and with preliminary aspiration (32). Niwa *et al.* confirmed that injection of lidocaine combined with 1:80,000 epinephrine was safe and without any complication in patients with an exercise capacity of more than 4 metabolic equivalents (19). Although we used a higher volume of solution of lidocaine with 1:100,000 epinephrine which contain higher dose of epinephrine in cardiac patients for reconstructive surgery, but similar to previous studies we did not found any hemodynamic and electrocardiographic parameters change significantly (33,34). Because epinephrine active both beta 1 and beta 2 receptor, we think that the blood pressure dose not dynamically increase because of beta 2 vasodilatation effect (5,7). Moreover, epinephrine breakdown by catechol-O-methyltransferase (COMT) in the blood, liver, lungs, and other tissues (8), and eliminate from blood in less than 10 minutes. The hemodynamic alteration beyond use of epinephrine are very short in duration because of very short plasma half-life, which is approximately less than 1 minute (8). We propose that a study with more subjects perform to evaluate the comparison of safety of 2% lidocaine contain epinephrine 1:100,000 with 1:200,000 in patients with cardiac disease. We concluded that the use of 10 ml 2% lidocaine with epinephrine 1:100,000 in patients with cardiac disease represents a safe anesthetic procedure. These patients experienced a more profound anesthesia with hemodynamic stability and without myocardial ischemic changes.

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