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Effect of Different Epinephrine Concentrations on Local Bleeding and Hemodynamics during Dermatologic Surgery

Mehrdad Shoroghi[1], Seyed Hossein Sadrolsadat[1], Mahmood Razzaghi[1], Farshid Farahbakhsh[2], Mehrdad Sheikhvatan[3], Mahmood Sheikhfathollahi[3], Ali Abbasi[3]

[1]Department of Anesthesia, Razi Hospital, Tehran University of Medical Sciences, Tehran; [2]Department of Anesthesia, Ali-Ebn Abitaleb Hospital, Rafsanjan University, Rafsanjan; [3]Department of Research, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran

Correspondence to:
Ali Abbasi, MD
Tehran Heart Center
North Kargar Street
Post Box: 1411713138
Tehran
Iran
m.shorooghi@yahoo.com;
aliiabbasi@yahoo.com

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SUMMARY In local anesthesia, various epinephrine concentrations are applied for its vasoconstrictive effect. This study was conducted to observe the effect of epinephrine on intraoperative bleeding and also to evaluate hemodynamic changes during skin surgery. Ninety-six patients scheduled for skin surgery under local anesthesia were divided into three groups administered three different concentrations of epinephrine (1:50,000, 1:100,000 and 1:200,000) with 1% lidocaine (an average of 5.7 mL). The rate of bleeding and hemodynamic changes were assessed during surgical procedure. The surgeon's rating of intraoperative bleeding was significantly lower in the group administered epinephrine concentration of 1:50,000 as compared with the group on epinephrine concentration of 1:200,000. However, there was no significant difference between the groups administered epinephrine concentrations of 1:200,000 and 1:100,000. Except for diastolic blood pressure at 1 min after injection of local anesthetics, transient changes of hemodynamic parameters were observed, with no statistically significant difference among the three anesthetic solutions used. It is concluded that, for local anesthesia, the rate of intraoperative bleeding is influenced by epinephrine concentration, and that 1:50,000 epinephrine provides optimal clinical efficacy for the local bleeding control during dermatologic surgery.

KEY WORDS: epinephrine, bleeding, dermatologic surgery, concentration, hemodynamics

INTRODUCTION

The effects of epinephrine in local anesthetics have been well established. Epinephrine is the most commonly used constrictor of blood vessels and blood coagulation accelerator, especially on the skin or mucous membranes for bleeding control at the procedure site (1,2). It can reduce the absorption of local anesthetics into the bloodstream, resulting in decreased systemic toxic side effects, prolonged clinical duration of action and decreased surgical blood loss (3,4). The role of epinephrine, with its nonselective adrenergic properties on the skin and subcutaneous tissues, in a local anesthetic solution is exerted by the constriction of local vasculature and diminished local blood flow (5-7).

However, epinephrine has significant side effects and there are some limitations due to the potential dose-related cardiac effects (8). Further-

more, it seems that change in its concentration has different effects on the severity of bleeding in surgical wound. Therefore, the optimal concentration of epinephrine for the prevention of bleeding has not been clearly determined and is controversial in dermatologic surgeries. This study was conducted to observe the effect of dose dependent epinephrine supplement in local anesthesia on the intraoperative bleeding control and also to determine its impact on hemodynamic properties during dermatologic surgery. We also tried to find out whether the time interval between local anesthetic injection and operation had any effect on these properties.

METHODS

This prospective clinical study included 96 voluntary patients aged 12-88 years with different superficial cutaneous lesions of the head and neck, scheduled for skin surgery under local anesthesia at the Outpatient Clinic of Dermatology, Razi Hospital. The study was approved by the Educational Hospital Ethics Committee, governing the participation of human subjects in research at the Tehran University of Medical Sciences, according to the principles outlined in the Declaration of Helsinki. After taking history and physical examination, otherwise healthy patients were chosen. The procedure and type of anesthetics were explained to all patients and a written informed consent was obtained from them before injection of local anesthetic. All study patients were non-smokers, with no history of cardiovascular disease, asthma or hypersensitivity to amide local anesthetics. Those with coagulopathy or recurrent use of anticoagulant and β-blocker agents were excluded.

Because of the small size of the lesions (less than 10 cm^2) in all study patients, the cutaneous defects were repaired with a local skin flap, with no need to use grafts. Three injection groups were evaluated: group 1 injected at an independent site using 1% lidocaine (mean±SD, 5.6±2.5 mL) with epinephrine 1:50,000 (20 µg/mL concentration to anesthetic solution), pH 3.3-5.0; group 2 administered local anesthesia with 1% lidocaine (mean±SD, 5.46±3.6 mL) and 1:100,000 epinephrine (10 µg/mL concentration to anesthetic solution), pH 3.3-5.0; and group 3 injected with 1% lidocaine (mean±SD, 6.2±2.65 mL) and 1:200,000 epinephrine (5 µg/mL concentration to anesthetic solution), pH 3.3-5.0. In the morning of the operation day, the solutions that had been stored at 4 ^{0}C were put on the table in the operation room to standardize at 25 ^{0}C temperature and new vials were used for each experiment. All injections were administered with a 24G needle and 1 mL syringe. The skin was prepared by cleaning with alcohol swab.

Patient characteristics including demographics, type of cutaneous lesion, duration of surgery, time interval between injection of local anesthetics and onset of surgery (i.e. 5-min *vs*. 10-min surgery delay) and volume of injected anesthetic solution were recorded. Hemodynamic parameters (systolic and diastolic blood pressure and heart rate) were recorded at the time of patient entry to the operation room and at 1, 2, 3, 5, 10, 15, and 30 minutes of the beginning of local anesthesia. The severity of intraoperative bleeding as the main measurement was rated by the surgeon's observation, according to a 3-point category rating scale as mild, moderate or and severe (9,10). Neither the surgeon nor the anesthesiologist who recorded the hemodynamic values was aware of the anesthetic solution used. The same surgeon and anesthesiologists performed all surgeries, anesthesia and postoperative controls.

Results were reported as mean ± standard deviation (SD) or median with 1st and 3rd quartiles (whenever the data did not appear to have normal distribution) for quantitative variables, and categorized variables were summarized as frequencies and percentages. Continuous variables were compared using one-way ANOVA or Kruskal-Wallis test, while categorized variables were compared among the three groups using χ^2-test. Power analysis showed that there was about 69% chance of detecting a significant difference using a two-sided test with a significance level equaling 0.05. Patients were not randomly assigned in the trial because of the possible risks of higher epinephrine level in the elderly. Therefore, for adjustment of the possible confounding variables, Cumulative Logit Models for Ordinal Responses and Proportional Odds Model (the most commonly used model) (11) were applied on multivariate analysis to evaluate the severity of bleeding among the three groups. The group with 1:200,000 concentration of epinephrine was considered as a reference group. Bleeding severity for the other two groups relative to the reference group were presented as odds ratio (OR), 95% confidence interval (CI), and *P* value. On statistical analysis, we used the Statistical Package for Social Sciences version 13.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) for Windows. All *P* values were two-tailed, with a statistical significance set at $P \leq 0.05$.

RESULTS

Patient demographic and clinical data are summarized in Table 1. There were significant differences in the sex ratio and mean age among the three groups. The median of operation time was lower in the group with 1:50,000 concentration of epinephrine as compared with the other two groups.

In terms of hemodynamic parameters, there were no significant differences in the mean values of systolic blood pressure and heart rate either at the time of patient entry in the operation room or at 1, 2, 3, 5, 10, 15 and 30 minutes after the injection of local anesthetics. In addition, the type of anesthetic solution did not affect diastolic blood pressure during the procedure, except for the first minute measurement after local anesthesia (Figs. 1-3).

Univariate analysis showed the concentration of epinephrine in lidocaine anesthetic to correlate significantly with the severity of bleeding (*P*=0.003). After adjustment for confounding variables (including, age, gender, dermatologic diagnosis, duration of surgery delay, duration of surgery and anesthesia volume) in multivariate analysis, the rate of bleeding was significantly lower in group with 1:50,000 concentration of epinephrine than in the group with 1:200,000 concentration of epinephrine (OR: 3.974; 95% CI: 1.175-14.017; *P*=0.028). However, no significant difference in the severity of bleeding was found between the groups with 1:100,000 and 1:200,000 epinephrine concentrations (OR: 2.348; 95% CI: 0.807-7.058; *P*=0.121).

No adverse reactions due to the use of either anesthetic solution were observed by the surgeons and anesthesiologists, or reported by the patients during the surgery or at the first postoperative hour. However, one patient was identified to have left bundle branch block and another patient from the 1:200,000 epinephrine group showed benign arrhythmia.

DISCUSSION

Visualization during dermatologic surgery is enhanced with adequate hemostasis. Several controlled trials were warranted in order to provide conclusive evidence concerning the effect of epinephrine on hemorrhage during different types of operations (1,12-14). Epinephrine is a sympathomimetic amine with both α-and β-adrenergic receptor agonist effects. Different arterioles, especially in the skin and mucosa, display vasoconstriction due to α-receptor predominant stimulation. The minimum epinephrine dose to produce adequate hemostasis with minimal toxicity has yet to be clearly determined in dermatologic surgery. Few studies exist in the literature determining an optimal epinephrine concentration for human subjects. However, local anesthetics

Table 1. Patient characteristics according to groups injected different epinephrine concentrations

Characteristic	*1:50,000 (n=28)*	*1:100,000 (n=43)*	*1:200,000 (n=25)*	P *value*
Gender				
Male	15 (53.6%)	17 (39.5%)	19 (76%)	
Female	13 (46.4%)	2 (60.5%)	6 (24%)	0.015
Age (yrs)	33.5±15.7	48.8±18.1	57.6±20.0	<0.001
Dermatologic diagnosis				
Basal cell carcinoma	7(25.0%)	27 (62.8%)	19 (76.0%)	
Nevus	6 (21.4%)	7 (16.3%)	1 (4.0%)	
Scar	5 (17.9%)	1 (2.3%)	1 (4.0%)	
Squamous cell carcinoma	3 (10.7%)	1 (2.3%)	1 (4.0%)	
Other	7 (25.0%)	7 (16.3%)	3 (12.0%)	0.011
Duration of surgery delay				
5 min	15 (53.6%)	23 (53.5%)	13 (52%)	
10 min	13 (46.4%)	20 (46.5%)	12 (48%)	0.991
Duration of surgery (min)	25.0 (20.0,30.0)	30.0 (15.0,30.0)	30.0 (30.0,30.0)	0.003
Anesthetic material volume (mL)	5.6±2.5	5.4±3.6	6.2±2.6	0.586
Rate of bleeding				
Mild	32.1	23.3	4.0	
Moderate	60.7	55.8	56.0	
Severe	7.1	20.9	40.0	0.003

Data are presented as percentage, mean ± SD, or median (1st quartile, 3rd quartile)

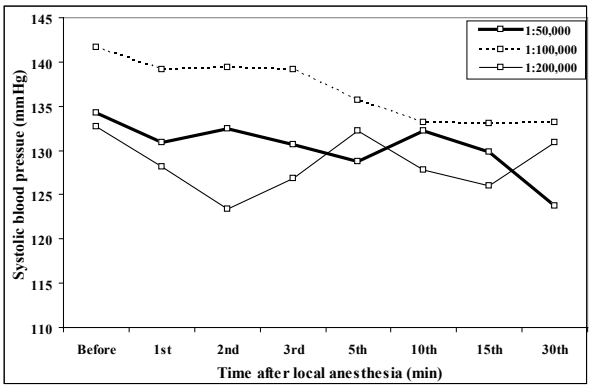

Figure 1. Systolic blood pressure at patient entry to operation room and at 1, 2, 3, 5, 10, 15 and 30 minutes after injection of local anesthetics.

with 1:100,000 epinephrine have been suggested to be associated with adequate vasoconstriction (2). The regulation of epinephrine concentration as a vasoconstrictor not only reduces the extent of unwanted effects, but can also minimize intraoperative bleeding (15).

In the present study, the increase in epinephrine concentration had no side effects on the heart rate and systolic blood pressure immediately before and after the beginning of surgery. Except for the first minute after the injection of local anesthetic, diastolic blood pressure did not change with the increase of epinephrine concentration, while the severity of bleeding was influenced favorably by the increase of epinephrine concentration. The rate of bleeding was lower in the group with 1:50,000 epinephrine concentration than in the other two groups. However, the bleeding rate was similar in the groups on 1:100,000 and 1:200,000 epinephrine. This finding indicated 1:50,000 epinephrine to be the optimal concentration of epinephrine for the prevention of bleeding during dermatologic surgeries. In a study by Dunlevy *et al*., an appropriate initial hemostasis and minimal potential side effects were dependent on epinephrine concentration. Although they recommended an epinephrine concentration of 1:200,000 or 1:400,000 to provide optimal results, changes in epinephrine concentration did not influence skin blood flow (4). O'Malley *et al*. examined the effects of various concentrations of epinephrine which were infiltrated in the neck skin of the patients undergoing head and neck surgery under general anesthesia. No significant difference was found in the onset or magnitude of vasoconstriction between the concentrations of 1:50,000 to 1:400,000 epinephrine. Also, no adverse cardiac effects were observed (8). Similar to our study, the effect of higher epinephrine dosages on the minimization of intraoperative bleeding was demonstrated in other studies (16,17). Lin *et al*. report that injection of a large volume of 1:10000 solution of epinephrine can reduce the rate of bleeding in patients and is superior to the injection of lower dosages of epinephrine (16).

In a number of surgical settings, epinephrine-containing local anesthetic solution has been shown to reduce perioperative bleeding from surgical wound sites (18). It has been indicated that the 1:50,000 concentration of epinephrine will provide best hemostasis when used as an infiltration injection (19). However, due to its rebound effect and systemic cardiovascular side effects such as tachycardia it should be used sparingly (8,20). In our study, hemodynamic changes such as heart rate and systolic blood pressure were not found during the first 15 minutes of skin operation. Only diastolic pressure at the first minute after local

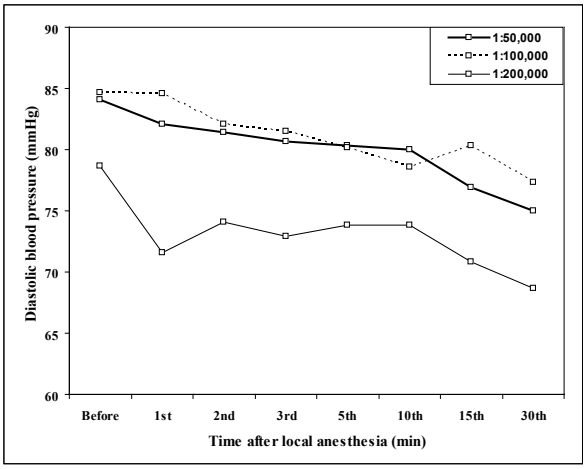

Figure 2. Diastolic blood pressure at patient entry to operation room and at 1, 2, 3, 5, 10, 15 and 30 minutes after injection of local anesthetics.

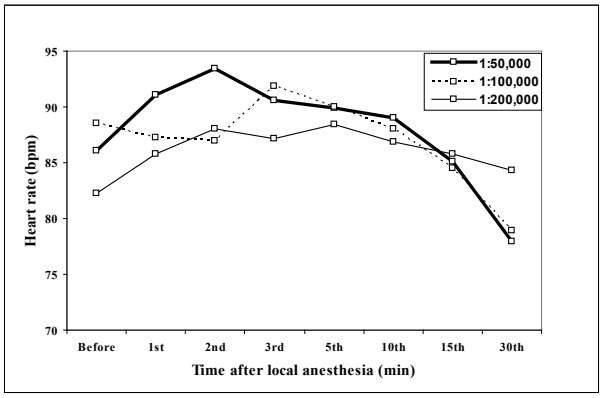

Figure 3. Heart rate at patient entry to operation room and at 1, 2, 3, 5, 10, 15 and 30 minutes after injection of local anesthetics.

anesthesia was different between the three study groups. In a study by Yang *et al*., significant hemodynamic changes, particularly hypotension, were observed in a group receiving lidocaine with 1:200,000 epinephrine compared to controls administered saline without epinephrine. However, they found these changes to have lasted no longer than 4 minutes (21). Also, in another study by Dogru *et al*., heart rate from the 3rd to 6th minute, systolic arterial pressure from the 3rd to 5th minute, and diastolic arterial pressure from 2nd to 6th minute after local injection were higher in patients that received a higher concentration of epinephrine (22).

Our study had some limitations, foremost being that none of the epinephrine toxicities described occurred, presumably because of their already low probability and because of the low study doses. The main study measurement was subjectively evaluated by a single surgeon. However, the surgeon's assessment was blinded to the anesthetic solutions. It seems that obtaining non-significant changes in hemodynamic criteria in our study may have been related to the small sample size in each study group and thus more investigations of the impact of different concentrations of epinephrine on hemodynamic changes in operated patients are needed. Patients with peripheral vascular disease, diabetes mellitus and cardiac problems were not evaluated. Although the study population was not randomly assigned and double-blinded, the Cumulative Logit Model was used for adjustment of the possible confounding variables (11).

Our study findings suggest a conclusion that higher concentration of epinephrine has a favorable effect on the prevention of bleeding. However, its duration of action, the maximum suggested dosage and contraindications must be considered prior to its use. As the effects of different epinephrine concentrations on vital criteria such as heart rate and blood pressure during surgery were not observed, additional investigations are needed in a larger sample size and taking different types of surgeries in consideration.

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By rain, wind and snow – Nivea cream; year 1936.
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