

# Epinephrine's Effect in Varying Concentrations on the End Artery Organ in an Animal Model

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## ABSTRACT

**Objective:** To determine the concentration of epinephrine that causes end artery necrosis and ischemia.

**Study Design:** An experimental study.

**Place and Duration of Study:** Animal Laboratory of Khordad Hospital, Tehran, Iran, from September 2007 to June 2008.

**Methodology:** This study was done on 54 ear flaps from 9 rabbits [9 (rabbits) x2 (ears) x3 (splits) =54] divided into three groups of 18 ear flaps each. Nine of the ear flaps were randomized as control and nine of them were randomized as study group. The different concentrations of epinephrine and lidocaine 1% were injected in study groups but only 1% lidocaine was injected in control groups. Study group 1 received 1/200000, group 2 received 1/100000 and group 3 received 1/500000 concentration of epinephrine respectively.

**Results:** There was no evidence of necrosis in the control and study groups 1 and 2. However, 4 out of 9 of the ear flaps showed clear evidence of tissue necrosis in group 3.

**Conclusion:** Injecting epinephrine in 1/200000 and 1/100000 concentrations had no side effect for the end artery of the rabbit ear flaps, but 1/50000 concentration is shown that it can cause tissue necrosis. Further studies need to be done in order to find out the effects of epinephrine with the same concentrations on the human end artery.

**Key words:** Epinephrine. Necrosis. End organ. Rabbit. End artery. Ear flap.

## INTRODUCTION

Diluted epinephrine is mostly used with lidocaine during surgery to achieve anaesthesia and a clean field. Due to the probable theoretical risks of ischemia, several medical textbooks have prohibited the application of this combination in the end artery such as the penis, finger, nose tip and external ear. However, they have not given any practical evidence for their arguments<sup>1-4</sup>. In spite of this fact, most surgeons use a tourniquet to have a clean surgical field despite the fact that this method is only applicable in limbs. In addition, tourniquet may have some problems. It may cause hyperkalemia distal to the place of tourniquet;<sup>3,5</sup> injury to the underlying organs such as the skin, nerves, and vessels;<sup>3,6</sup> limited time for application<sup>2,6,7</sup> and necessity of applying sedation when the patient feels severe pain in the place of tourniquet which can cause the patient to stop breathing.

In authors practice injecting epinephrine with 1/200000 concentration to the nose tip causes no necrosis. Injecting epinephrine with 1/200000 concentration to the human finger tip causes no necrosis.<sup>3,4,7</sup>

The objective of this was, therefore, to determine the safe threshold of epinephrine concentration, which can be used on an end artery without causing necrosis.

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## METHODOLOGY

It was an experimental double blind random research. Nine, white New Zealand rabbits (weighting  $2 \pm 0.5$  kg) were used for this study. These rabbits were chosen from among 20 rabbits by screening under surveillance for 2 weeks for health evaluation. Those which fell sick or died in this period, were excluded from the study. Afterwards, the remaining 9, healthy rabbits were divided into three groups equally. At this stage, the rabbits' ears were split in three flaps. Each flap was nourished by just one end artery (Figure 1). This study was done on 54 ear flaps from 9 rabbits [9 (rabbits) x 2 (ears) x 3 (splits) =54]. Then these were divided into three groups of 18 ear flaps each. Nine of the ear flaps were randomized as control and 9 of them were randomized as study groups (manipulation groups). The different concentrations of epinephrine and lidocaine 1% were injected in the study groups but only lidocaine 1% was injected in control groups. The different concentrations of epinephrine were 1/200000, 1/100000, and 1/50000 given study groups 1, 2, and 3 respectively. The rabbits were named by numbers. Also, were marked the splits of the right ear (ear flaps) as ABC and the left as A'B'C' symmetrically (Figure 1).

Two syringes were prepared for each stage of injection. One was filled with only lidocaine 1% and the other was a mixture of lidocaine 1% and epinephrine. The two syringes were encoded by numbers. One was injected to a split ear flap, e.g. A and the other to its symmetrical split (e.g. A') randomly. The injection was performed by

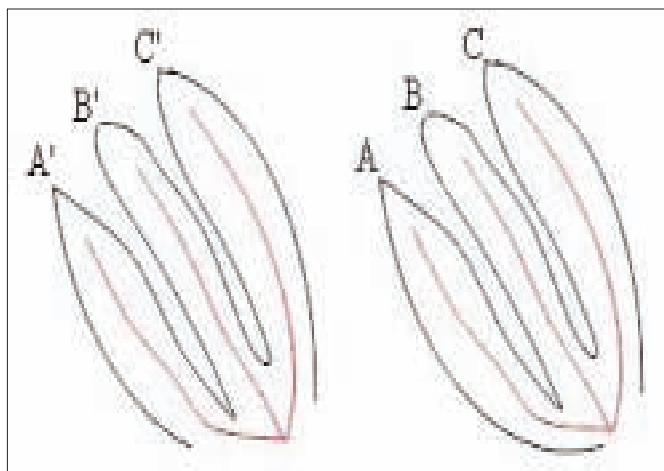


Figure 1: Marking the rabbit's ears and splitting a rabbit's ear in three.

an insulin needle in a circular fashion around the artery. The volume of the dosage for both was 0.9 cc.

The injection was first done by injecting epinephrine with 1/200000 concentration for study group 1, and then with 1/100000 concentration for study group 2 and lastly with 1/50000 concentration for study group 3. Finally, the emergence of necrosis and the viability of the end organs were evaluated 48 hours after the injection by physical examination (eye appearance, loop magnification 4.5, plus touching and tissue cutting). All the procedures were performed in 15 Khordad Hospital's Animal Laboratory. The study was approved by Shahid Beheshti University of Medical Sciences Ethics Committee.

The gathered data were analyzed with SPSS 16 and Fisher's exact test.  $P < 0.05$  was considered as significant level difference between groups.

### RESULTS

Comparison was done between two symmetrical splits of one rabbit's ears (ear flaps), in which one had received epinephrine and the other not. All the rabbits were of the same race and weight. All the rabbits were taken care of in the same way and in the same condition. The only variable factor was epinephrine. This epinephrine was injected in three concentrations. There were no evidence of tissue necrosis in control groups and study groups 1 and 2. However, 4 out of 9 ear flaps showed clear evidence of tissue necrosis in study group 3 (Figure 2).

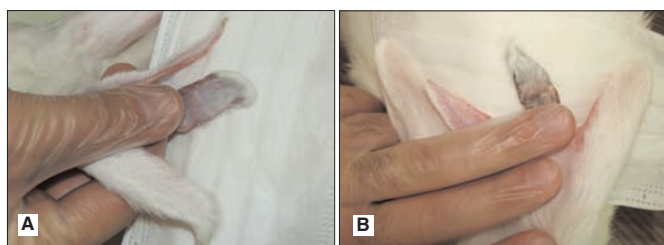


Figure 2: A Pre-necrosis was seen after injection and B necrosis happened after 48 hours of injection with 1/50000 epinephrine concentration.

Table I shows the comparison of tissue necrosis frequency between the ear flaps that had received lidocaine 1% only, i.e. control groups, (from the three groups,  $n=27$ ) and the ear flaps in study group 3 which had received lidocaine 1% with epinephrine 1/50000 concentration ( $n=9$ ). There was a significant difference between them with  $p=0.002$ .

Table I: Frequency of necrosis between lidocaine 1% and lidocaine 1% + epinephrine 1/50000.

	Necrosis	No necrosis	Number of cases
Lidocaine 1% + epinephrine 1/50000	4 (44%)	5 (56%)	9
Lidocaine 1%	0 (0%)	27 (100%)	27
Total	4	32	36

Table II shows the comparison of tissue necrosis frequency between the ear flaps that had received epinephrine 1/200000 and 1/100000 concentration (from two study groups,  $n=18$ ) and the ear flaps in study group 3 which had received epinephrine 1/50000 concentration ( $n=9$ ). There was a significant difference between them with  $p=0.007$ .

Table II: Frequency of necrosis between epinephrine 1/200000 and 1/100000 and epinephrine 1/50000.

	Necrosis	No necrosis	Number of cases
Epinephrine 1/50000	4 (44%)	5 (56%)	9
Epinephrine 1/200000 and 1/100000	0 (0%)	18 (100%)	18
Total	4	23	27

### DISCUSSION

In this study, it was found that epinephrine is not harmful in 1/200000 and 1/100000 concentrations on the end artery. However, epinephrine in 1/50000 concentration can be harmful for the end organs.

Since 1939 epinephrine is an agent known to have a great vasoconstrictive potential effect and it has a great stimulatory effect on both  $\alpha$  and  $\beta$  adrenergic receptors. The greatest vasoconstrictive effect is on the pre-capillary vessels. However, when it is administered in low doses (0.1  $\mu\text{g}/\text{kg}$ ) blood pressure will decrease due to its greatest effect on  $\beta_2$  adrenergic receptors in comparison to its effects on  $\alpha$  receptors.<sup>8</sup>

Several medical textbooks have prohibited the application of epinephrine in the end organs, such as penis, finger, nose tip and external ear.<sup>2,9-11</sup> Local asphyxia distal to tourniquets is well tolerated for several hours by humans, provided that the skin under the tourniquet is anaesthetized. The local changes of acidosis and hyperkalemia that occur in tissues distal to tourniquets are generally not adverse, since dilution prevents systemic acidosis and hyperkalemia, even with tourniquet deflation. Moreover, several digital tourniquet techniques have been described and safely used.<sup>2,3,7</sup> Of the several techniques described, the volar and dorsal approaches are the most common in digital block. The

dorsal approach, which involves only one injection site, over the less painful dorsum of the finger is favoured by the authors; recently, their experience of no complications with this technique using lidocaine with epinephrine in a retrospective series was published.<sup>3,6, 5</sup> However, it was found in our study that epinephrine is not harmful in 1/200000 and 1/100000 concentrations on the end artery. Also, there were evidence in the literature that injecting epinephrine with 1/200000 concentration to the finger tip caused no necrosis.<sup>3,4,13-15</sup>

In this sense, it should be noted that the recommendations are based on some theory regarding the constrictive effects that epinephrine will have on the vessels and the possibility of ischemia and gangrene without any practical proof.<sup>2,9-12</sup>

The risk for bilateral digital vessel injury, in single end artery and thermal injury may be increased with the circular technique or injection of excessive volume of a local anaesthetic.<sup>1</sup>

Again, it is important to carefully perform the end artery block (distal of the organ) procedure with a small-caliber needle and an appropriate volume of local anaesthetic to minimize the risk of vessel injury. The end artery block is discouraged for patients with disease processes potentially involving the vessels (i.e. infection or trauma). Furthermore, the use of epinephrine is cautioned for patients with pheochromocytoma, hyperthyroidism, severe hypertension, cardiac disease, and peripheral vascular disease.<sup>1,9</sup>

Necrotic tissue becomes fragile, black in colour, and without any fresh bleeding which was all visible with naked eye. Histopathology for microscopic tissue diagnosis was not performed which is a limitation of this study.

Finally, this study was distinguished from the similar previous studies in two aspects. Firstly, those studies were done on human fingers as an end organ which has two arteries. This study was done on a split of rabbit's ear which had only one artery. Secondly, those studies were done by just 1/200000 concentration of epinephrine but this study set out to try three different concentrations, i.e. 1/200000, 1/100000, and 1/50000.

## CONCLUSION

This study shows that injecting epinephrine with 1/200000 and 1/100000 concentrations has no harmful effect for an end artery, but 1/50000 concentration is shown to be harmful. Although epinephrine 1/50000 concentration can cause tissue necrosis in a single end artery, the human end organs, such as nose, fingers and ears, have more than one end artery. So it might not lead to necrosis as it did in a split of rabbit's ear flap. In addition, using epinephrine with more than 1/100000

concentration is discouraged in human end organs which have a damaged end artery. Further studies need to be done in order to find out the effects of epinephrine with the same concentrations on the human end artery.

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## REFERENCES

1. Waterbrook AL, Germann CA, Southall JC. Is epinephrine harmful when used with anesthetics for digital nerve blocks? *Ann Emerg Med* 2007; **50**:472-5.
2. Brunnicardi F, Andersen D, Billiar T, Dunn D, Hunter J, Pollock RE. Schwartz's principles of surgery. 8th ed. New York: *McGraw-Hill*; 2004.
3. Wilhelmi BJ, Blackwell SJ, Miller JH, Macoll JS, Dardano T, Tran A, et al. Do not use epinephrine in digital blocks: myth or truth? *Plast Reconstr Surg* 2001; **107**:393-7. Comment in: *Plast Reconstr Surg* 2001; **108**:1831-2.
4. Krunic AL, Wang LC, Soltani K, Weitzel S, Taylor RS. Digital anesthesia with epinephrine: an old myth revisited. *J Am Acad Dermatol* 2004; **51**:755-9.
5. Rammamurthy S, Hickey R. Anesthesia. In: Green DP, editor. *Operative hand surgery*. 3rd ed. New York: *Churchill Livingstone*; 1993. p. 40-51.
6. Sims NS. Upper extremity anesthesia. In: McCarthy JG, editor. *Plastic surgery*. Philadelphia: *W. B. Saunders*; 1990. p. 4302-28.
7. Wilhelmi BJ, Blackwell SJ, Miller J, Mancoll JS, Phillips LG. Epinephrine in digital blocks: revisited. *Ann Plast Surg* 1998; **41**:410-4. Comment in: *Ann Plast Surg* 1999; **43**:572.
8. Brunton LL, Lazo JS, Parker KL. Goodman and Gilman's, the pharmacological basis of therapeutics. 11th ed. New York: *McGraw-Hill*; 2006.
9. Scott DB. Techniques of regional anesthesia. Norwalk: *Medi-Globe*; 1989.
10. Erickson G. Digital nerve block. In: Malamed SF, editor. *Handbook of local anesthetics*. Philadelphia: *W.B. Saunders*; 1980. p.50-2.
11. Raj M, Pai U. Techniques of nerve blocking in handbook of regional anesthesia. New York: *Churchill Livingstone*; 1990.
12. Auletia MJ, Grekia RC. Local anesthesia for dermatologic surgery. New York: *Chuchill Livingstone*; 1985.
13. Barnett A, Pearl RM. Readily available, inexpensive finger tourniquet. *Plast Reconstr Surg* 1983; **71**:134-5.
14. Sylaidis P, Logan A. Digital blocks with adrenaline: an old dogma refuted. *J Hand Surg Br* 1998; **23**:17-9.
15. Altinyazar HC, Ozdemir H, Koca R, Hosnuter M, Demirel CB, Gundogdu S. Epinephrine in digital block: color Doppler flow imaging. *Dermatol Surg* 2004; **30**:508-11.

