

Evaluation of Healing Process and Blood Sugar Level Following Local Anesthetic Infiltration with and Without Vasoconstrictor for Extraction of Maxillary Teeth in Diabetic Patients: Double Blind Randomized Controlled Clinical Trial

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ABSTRACT

Background: Dental extractions are routinely performed in dental offices, and the local anesthetics most frequently employed are combined with vasoconstrictors, which have undeniable benefits. Vasoconstrictors boost the quality of anesthesia, lessen toxic effects, reduce the concentration required, and reduce blood loss during surgical operations.

Objective: The aim of the current study was to evaluate healing of the extraction socket and the glycemic levels before, and after injection of local anesthesia with and without vasoconstrictor in diabetic patients.

Patients and methods: A total of 40 patients with controlled diabetes requiring dental extraction were randomly and equally allocated to either **group A** (anesthetized with Mepivacaine hydrochloride 30 mg (3%) without vasoconstrictor) or **group B** (anesthetized with Mepivacaine hydrochloride 20 mg (2%) with vasoconstrictor Levonordefrin hydrochloride 0.06 mg). The involved tooth was extracted in an atraumatic manner. Blood glucose level was recorded prior to and 30 minutes following extraction and healing of extraction socket was assessed at 24 hours, 4-, 7-, 14- and 21-days using Landry wound healing index. **Results:** Regarding healing scores results showed no statistically significant difference between **groups A** and **B** at 24 hour and 21-day period, however **group A** showed a statistically significant faster healing than **group B** at 4, 7, 14 days period with P values 0.091, 0.027 and 0.035, respectively. While results for blood glucose level showed statistically significant difference in the same group before and after local anesthesia injection ($P < 0.001$); moreover, after administration of local anesthesia **group B** showed statistically significant higher blood glucose level than did **group A** ($P = 0.04$).

Conclusion: Vasoconstrictor present in local anesthetic elevate blood glucose level and may retard extraction socket wound healing with in the first 2 weeks following extraction; however, it is still safe to use local anesthesia with vasoconstrictor with controlled diabetic patients.

Keywords: Healing process, Blood sugar level, Local anesthetic infiltration, Vasoconstrictor for extraction, Maxillary teeth, Diabetic patients.

INTRODUCTION

Most frequently, local anesthetics are combined with vasoconstrictors, which have undeniable benefits. Vasoconstrictors help anesthesia last longer, lessen toxic effects by delaying anesthetic absorption, improve the quality of anesthesia, reduce the minimum concentration of anesthetic required, reduce the peak plasma concentration of the local anesthetic agent, and reduce blood loss during surgical procedures⁽¹⁾.

Numerous studies have shown that local anesthetics with adrenaline as a vasoconstrictor cause blood glucose levels to rise^(2,3). For these individuals, 3% mepivacaine without a vasoconstrictor or 3% prilocaine with 0.03 IU/mL felypressin may be advised^(4,5). The use of local anesthetic with vasoconstrictor may not be a safety issue for healthy patients however researchers have raised concerns in case of medically compromised patients.

A prevalent metabolic illness known as diabetes mellitus (DM) is characterized by an inability to control blood glucose levels as a result of insulin resistance or deficiency. Diabetes patients frequently require extractions due to the high prevalence of periodontal diseases in this population. However, there is no clear protocol in the literature for such operations^(6,7). In these situations, oral surgery necessitates specific safety measures, including the management of

stress and the use of a strong and secure anesthetic solution. Furthermore, there is no agreement on the safety of various local anesthetic treatments^(8,9,10).

Microvascular, macrovascular, and neuropathic problems have been classified as being predisposed to by diabetes. Deficits in microcirculation in particular have a big impact on how well wound heals after surgery. Changes in capillaries, such as thickening of the basement membrane, affect permeability, obstruct leukocyte migration, and worsen hyperemia in diabetes patients, resulting in reduced perfusion during tissue stress and hypoxia. Infection and delayed wound healing are the results of these alterations. The use of vasoconstrictor may further impair healing⁽¹¹⁾.

The aim of the current study was to evaluate healing of the extraction socket and the glycemic levels before, and after injection of local anesthesia with and without vasoconstrictor in diabetic patients. There for the null hypothesis was that there is no difference in blood glucose level and healing of extraction socket when using local anesthetic with and without vasoconstrictor.

PATIENTS AND METHODS

Study design: A 1:1 parallel armed, randomized, controlled, clinical trial comparing the effect of presence and absence of vasoconstriction in local anesthesia on blood glucose level and healing

following simple tooth extraction in type II diabetic patients.

Sample size calculation: In order to apply a statistical test to the null hypothesis that there is no difference between the various examined groups with regard to blood glucose level and extraction socket healing, a power analysis was created. By using an effect size (f) of (0.542) computed based on the findings of a prior research⁽¹²⁾, an alpha (α) level of 0.05 (5%), a beta (β) level of (0.2) (i.e., power=80%), and an effect size (f) of (0.2), the anticipated sample size (n) was a total of (40) instances (i.e., 20 cases per group). G*Power 3.1.9.7 was used to calculate the sample size.

Participant recruitment: Patients were enrolled from the Department of Oral and Maxillofacial Surgery at the Faculty of Dentistry's outpatient clinic, Minia University and out-patient clinic of the Dental Department, Faculty of Medicine, Minia University.

Eligibility criteria: The following inclusion criteria were used to choose participants: patients had to be over 20 and under 60, have their diabetes under oral control, and need a maxillary tooth extraction for periodontal reasons. Only those individuals who agreed to monitor and record their blood sugar levels during the course of the trial. Patients with any significant medical conditions (aside from diabetes mellitus), people who consume alcohol, those taking medications that affect the central nervous system, those who disclosed using medications that might impair pain sensitivity, and those who disclosed pregnancy, lactation, or a sensitivity to local anaesthetic were excluded.

Randomization and blinding: A random sequence was generated using Microsoft Excel software where both groups A and B were denoted and randomly and equally distributed. Sequential numbers were on the cards. Each card was given a unique number before being placed inside of sealed, opaque envelopes. Each participant picked an envelope the day of procedure. This step was done by co-supervisor. The study group intervention was hidden from both participants and outcome judges.

Grouping: A total of 40 controlled diabetic participants were randomly divided into 2 groups: **Group A** ($n=20$), were anesthetized with Mepivacaine hydrochloride 30mg (3%) without vasoconstrictor, (Alexandria Co. for Pharmaceuticals, Egypt). **Group B** ($n=20$) were anesthetized with Mepivacaine hydrochloride 20 mg (2%) with vasoconstrictor Levonordefrin hydrochloride 0.06 mg. (Alexandria Co. for Pharmaceuticals, Egypt).

Intervention: Along with post-surgical guidelines, oral hygiene teaching was reiterated for all participants. All participants received local anesthetic injection according to the assigned group and the involved tooth was extracted in an atraumatic manner

while performing a Stress reduction protocol during the procedure. Finally, all participants were prescribed 500mg amoxicillin (Misr Co. October pharma. S.A.E., Egypt.) to be taken 3 times per day for 7 days and brufen 400mg (Abbott laboratories limited, UK) to be taken 3 times per day for 5 days.

Outcome: Glycemic level was recorded before local anesthesia administration and 30 minutes following local anesthesia injection, while Healing score of the extraction socket was assessed following extraction at 24 hours, 4, 7, 14 and 21 days using the Landry wound healing index to evaluate the rate of tissue recovery after surgery^(13,14). Specific factors, such as tissue color, bleeding response to probing, the existence of granulation tissue, the features of the incision edges, and the presence of suppuration at follow-up dates, were evaluated throughout the evaluation. The index divides the healing pattern into five groups according to the soft tissue color (pink or red), the quantity of bleeding, the presence of granulation tissue, and the exposure of connective tissue. 1-Very poor, 2-poor, 3-good, 4-very good and 5-excellent are listed in that order.

Ethical consideration:

The Faculty of Dentistry at Minia University's Ethics Committee evaluated and approved the study's procedure (committee no. 94; 714), the study protocol was then registered on clinicaltrials.gov with an identification number NCT05875519. All patients signed a written informed consent form after being informed about the steps, benefits, risks and the possible adverse effects of the proposed intervention. The study was conducted out in line with the Helsinki Declaration.

Statistical analysis

A Microsoft Excel spreadsheet was used to capture all the data, and statistical analysis was carried out using commercial software SPSS version 23.0 (SPSS Chicago, IL, USA). Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD). Independent sample t-test was used for comparison between groups. The analysis of pair scores also employed the two-sample Wilcoxon rank-sum test. P value ≤ 0.05 was considered to be statistically significant.

RESULTS

Results showed that both age and gender have no statistical significant difference between **groups A and B (table 1)**.

Table (1): Demographic data between the two groups

Variable		Group A	Group B	P value
Age	Range	(29-60)	(30-59)	0.448
	Mean ± SD	46.5±10	48.7±8.4	
Gender	Male	8(40%)	7(35%)	0.744
	Female	12(60%)	13(65%)	

Regarding healing scores (**Table 2** and **Figure 1**) results showed no statistical significant difference between **groups A** and **B** at 24 hours and 21 days period where $p = 1$; however **group A** showed a statistical significant faster healing than **group B** at 4, 7, 14 days period where p value recorded (0.091, 0.027, 0.035) respectively .

Table (2): Healing score between the two groups at different times

Healing score		Group A	Group B	P value
At 24h	Very Poor	17 (85%) ^a	17 (85%) ^a	1
	Poor	3 (15%)	3 (15%)	
	Good	0 (0%)	0 (0%)	
	Very good	0 (0%)	0 (0%)	
	Excellent	0 (0%)	0 (0%)	
At 4 days	Very Poor	0 (0%) ^b	0 (0%) ^b	0.091
	Poor	6 (30%)	12 (60%)	
	Good	12 (60%)	8 (40%)	
	Very good	2 (10%)	0 (0%)	
	Excellent	0 (0%)	0 (0%)	
At 7days	Very Poor	0 (0%) ^c	0 (0%) ^c	0.027*
	Poor	0 (0%)	0 (0%)	
	Good	7 (35%)	14 (70%)	
	Very good	13 (65%)	6 (30%)	
	Excellent	0 (0%)	0 (0%)	
At 14 days	Very Poor	0 (0%) ^d	0 (0%) ^d	0.035*
	Poor	0 (0%)	0 (0%)	
	Good	0 (0%)	0 (0%)	
	Very good	16 (80%)	20 (100%)	
	Excellent	4 (20%)	0 (0%)	
At 21days	Very Poor	0 (0%) ^e	0 (0%) ^e	1
	Poor	0 (0%)	0 (0%)	
	Good	0 (0%)	0 (0%)	
	Very good	0 (0%)	0 (0%)	
	Excellent	20 (100%)	20 (100%)	
<i>P value (between 5 times)</i>		<0.001*	<0.001*	

Chi square test for qualitative data between the two groups. Wilcoxon’s Signed Rank test for comparison between each two times within each group. Superscripts with different small letters between two times within each group.

*: Significant level at P value <0.05.

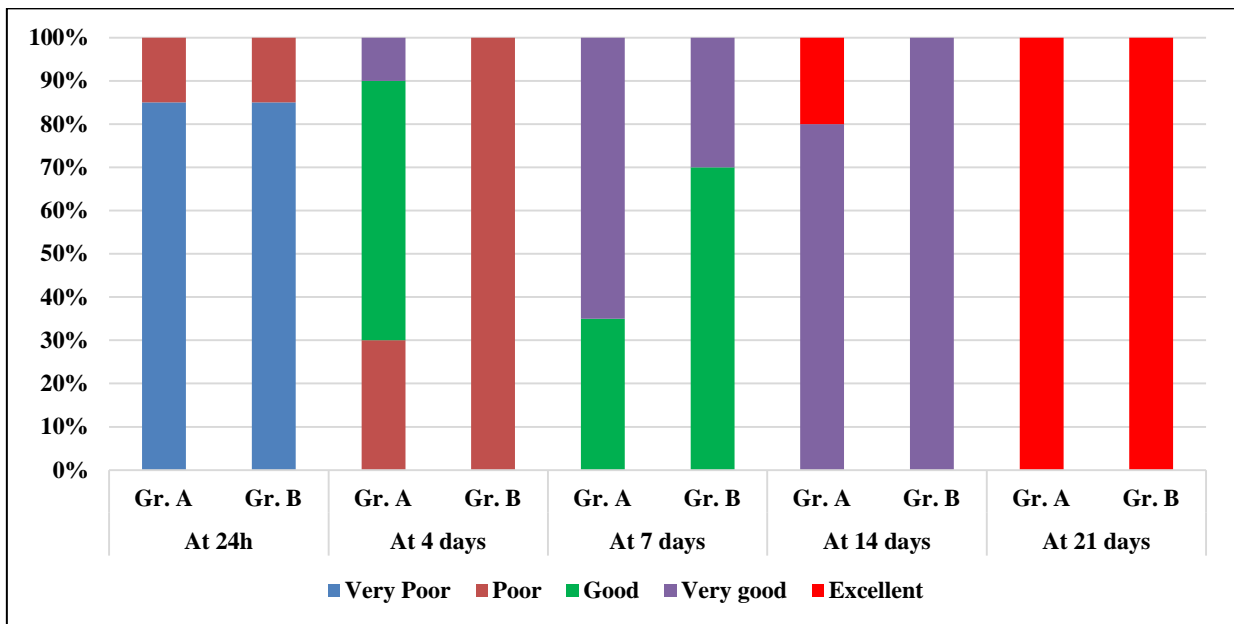


Figure (1): Healing score between the two groups at different times.

Results also showed statistically significant difference in blood glucose level in the same group before and after local anesthesia injection with $p < 0.001$; moreover, after administration of local anesthesia **group B** showed statistically significant higher blood glucose level than did **group A** with $p = 0.004$ (Table 3, Figure 2).

Table (3): Blood glucose level between the two groups before and after anesthesia

Blood sugar level		Group A	Group B	P value
Before anesthesia	Mean \pm SD	183.3 \pm 13.5	181.5 \pm 13.9	0672
After anesthesia	Mean \pm SD	187 \pm 13.3	201 \pm 15.4	0.004*
P value (before vs after)		<0.001*	<0.001*	

*: Significant level at P value <0.05.

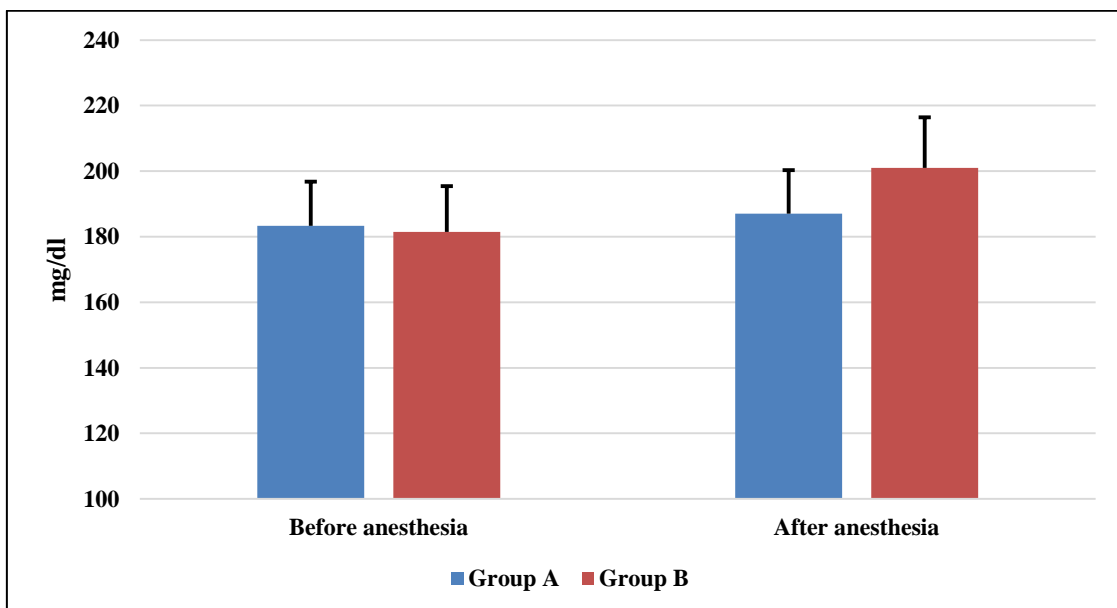


Figure (2): Blood glucose level between the two groups before and after anesthesia.

DISCUSSION

Dental extractions are routinely performed in dental offices, and the local anesthetics most frequently employed with vasoconstrictors, which have undeniable benefits. Vasoconstrictors boost the quality of anesthesia, lessen toxic effects, reduce the lowest concentration of anesthetic required, and reduce blood loss during surgical operations⁽¹⁾.

One of the main causes of dental socket extraction recovery being delayed is diabetes. A complex pathophysiology comprising vascular, neuropathic, immunological, and metabolic elements contributes to the impaired repair in diabetic individuals. More inflexible blood vessels associated with hyperglycemia result in microvascular dysfunction, sluggish circulation, and ultimately less tissue oxygenation. These individuals' blood vessel changes also prevent leukocytic migration into the wound, which raises the risk of infections^(15,16).

A double-blind design was followed in the present trial to ensure minimizing bias. This was accomplished by making both injection solutions seem identical. Additionally, neither the patient nor the blood glucose level and healing- assessors were aware of the anesthetic solution assigned. This tactic was employed to lessen validity risks and, in addition, to prevent any situational and operator variability from having an impact on the results of the study⁽¹⁷⁾.

Regarding the present study healing scores in **group A** showed a statistical significant faster healing than **group B** at 4, 7, 14 days period. This may be explained by the presence of the vasoconstrictor in **group B** which aggravates the already present impairment in the tissues on a histological level as a thickening of the capillaries' basement membrane that causes the cell wall to become more stiff and change permeability^(18,19).

This comes in accordance with studies by **Politis et al.**⁽²⁰⁾ found that elevated glucose levels in diabetes patients' tissues lead to toxic sorbitol buildup, pericapillary albumin deposition, which obstructs nutrition and oxygen passage, and tissue changes that interfere with collagen synthesis and maturation.

Roy et al.⁽²¹⁾ stated that the inflammatory phase is prolonged in diabetics due to macrophage dysfunction. They all significantly affect how quickly a wound heals.

Results also showed statistically significant difference in blood glucose level in the same group before and after local anesthesia injection; moreover after administration of local anesthesia in **group B** showed statistically significant higher blood glucose level than did **group A** indicating that **group B** participants that were anesthetized with Mepivacaine hydrochloride 20 mg (2%) and vasoconstrictor Levonordefrin hydrochloride 0.06 mg, caused a significant and transient increase in blood glucose level which comes in agreement with **Meechan**⁽²²⁾,

Meechan and Welbury⁽²³⁾, **Nakamura et al.**⁽²⁴⁾ and **Kalra et al.**⁽²⁵⁾ all of those detected a substantial rise in glucose levels when epinephrine was used during oral surgery. This can be explained that the vasoconstrictor probably leaked in to the systemic circulation resulting in increase of the blood glucose level. In the present study, the null hypothesis is rejected, as there was a significant difference among the two study groups.

CONCLUSION

Vasoconstrictor present in local anesthetic elevates blood glucose level and may retard extraction socket wound healing with in the first 2 weeks following extraction; however it is still safe to use local anesthesia with vasoconstrictor with controlled diabetic patients. Further studies were needed to determine the effect of larger doses of local anesthetic with vasoconstrictor in diabetic patients in surgical extractions and their effect on healing.

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