

Comparing hemodynamic and glycemic response to local anesthesia with epinephrine and without epinephrine in patients undergoing tooth extractions

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ABSTRACT

Introduction: Lignocaine with epinephrine as local anesthetic (LA) provides hemostasis and decreases the risk of systemic toxicity. The purpose of the present study was to investigate and compare the response of lignocaine with and without epinephrine to evaluate hemodynamic and metabolic response in normotensive and type II controlled diabetic patients. **Material and Methods:** A total of 50 patients (25 healthy and 25 controlled type II diabetics) undergoing multiple tooth extractions (age group of 20–80 years) were included in this prospective, randomised, clinical study. On their first visit, the patients were given 2% lignocaine HCl with 1:200,000 epinephrine, and 2% lignocaine HCl was given on the second visit, to carry out tooth extractions. Blood pressure (BP), pulse rate, oxygen saturation, and blood glucose estimations were done at definite intervals (before, immediately after, and 20 min after the administration of LA) on both the visits. **Results:** The increase in blood glucose concentration following the administration of 2% lignocaine HCl with 1:200,000 epinephrine was statistically significant ($P < 0.05$) in controlled diabetic patients. Statistically significant variability in diastolic BP (DBP) was also noted in controlled diabetic patients. Both systolic BP and DBPs were statistically significantly elevated after the administration of 2% lignocaine HCl. **Conclusion:** 2% lignocaine HCl with 1:200,000 epinephrine in type II diabetics and 2% lignocaine HCl should be used with caution in normotensive as well as type II controlled diabetic patients.

Key words: Epinephrine, lignocaine HCl, local anesthesia, normotensive, tooth extractions, type II diabetes

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INTRODUCTION

Exodontia is routinely done under local anesthesia (LA). Most commonly used LA agent is 2% lignocaine hydrochloride with epinephrine as a vasoconstrictor. Role of epinephrine is to increase the depth and duration

of LA as well as to decrease the systemic absorption and toxicity of both the LA agent and vasoconstrictor.

Studies have revealed that epinephrine affects hemodynamic response of body and blood glucose

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levels.^[1-27] The present study was done to comparatively evaluate the effects of 2% lignocaine and 2% lignocaine with 1:200,000 epinephrine on blood glucose level and hemodynamics in patients undergoing multiple tooth extractions.

MATERIALS AND METHODS

The study was conducted in outpatients' department. A total of 50 patients comprising 25 healthy and 25 type II controlled diabetic patients in need of multiple tooth extractions were included in this prospective, randomized, clinical study. The patients were in the age group of 20–80 years.

Before the start of the study, a clear clinical protocol was designed, and routine tooth extraction patients were selected who were normotensive and controlled type II diabetic patients. Informed consent was obtained from all individual participants included in the study.

Armamentarium^[6]

For blood glucose estimation (in mg/dl), the following were needed:

- Caresens II™ blood glucose meter (mg/dl)
- Lancing device
- Sterile lancets (28-gauge).

For hemodynamics, the following were needed:

- Blood pressure (BP) apparatus - Diamond LED regular (mmHg)
- Stethoscope
- Pulse oximeter-model™: 50 (pulse rate [PR] in number of beats per minute and oxygen saturation [PO₂] in percentage) 2 × 1.5 V AAA, Technocare Medisystems (units for PR: Number of beats per minute; unit for PO₂: %).

Selection criteria for healthy patients were as follows:^[6]

- Healthy patients without any systemic disorders
- Patients requiring multiple extractions
- Patients should not have been on any medication for a medical problem.

Selection criteria for controlled diabetics were as follows:^[6]

- Patients with controlled type II diabetes (noninsulin dependent)
- Patients requiring multiple extractions
- Patients should not have been receiving any other medication other than oral hypoglycemics.

The procedure was divided into two groups, namely:

- Group A: Healthy patients
- Group B: Type II controlled diabetic patients.

Study design^[6]

For each patient, the treatment was carried out in two appointments. The patients were advised to have

their normal breakfast on both appointments. At each appointment, a maximum of 2 ml LA solution was administered to each patient in the form of nerve blocks. Parameters were recorded before LA administration. Further readings were obtained immediately after and 20 min after LA administration (a total of three readings per procedure).

At one treatment appointment, tooth extraction was carried out under 2% lignocaine HCl in each group (Groups A and B). At the second treatment appointment, scheduled on the next visit, another tooth extraction was carried out under 2% lignocaine HCl with 1:200,000 epinephrine in the same patients of each group (Groups A and B). Serial blood glucose and hemodynamic estimations were carried out at identical intervals (prior to administration of LA, immediately after injecting the LA, and 20 min following the injection of LA) on both the occasions. Peripheral blood glucose was estimated by using a glucometer from the blood drawn by pricking the fingertip with a sterile lancet. Systemic BP was measured with auscultatory method using a stethoscope and BP apparatus. Peripheral finger PR and PO₂ were estimated with a pulse oximeter. The same armamentarium was used in all the patients.

RESULTS AND OBSERVATIONS

The study comprised 50 patients divided into two groups (Group A of healthy and Group B of controlled type II diabetic patients) of 25 each. The age of the patients in this study was 50 ± 13 years in Group A and 60 ± 7 years in Group B. Male: female ratio was 17/8 in healthy and 18/7 in type II controlled diabetic patients. All the patients included in the study met the inclusion criteria.

Quantitative data were presented as mean ± standard deviation [Tables 1 and 2]. Normality of data was checked by measures of Kolmogorov–Smirnov tests of normality. As data were normally distributed, means of two groups (Groups A and B) were compared by independent *t*-test [Tables 3 and 4]. There was no significant difference in random blood sugar (RBS), PR, and PO₂ recorded after the administration of either 2% lignocaine with 1:200,000 epinephrine or 2% lignocaine HCl. However, systolic BP (SBP) was significantly elevated immediately after and 20 min after the administration of 2% lignocaine HCl with 1:200,000 epinephrine. Both SBPs and diastolic BPs (DBPs) rose immediately after and 20 min after the administration of 2% lignocaine HCl.

There was a significant difference in RBS levels in type II controlled diabetic patients who were treated under 2% lignocaine HCl with 1:200,000 epinephrine

Table 1: Mean ± standard deviation of measurements taken for random blood sugar, pulse rate, oxygen saturation, systolic blood pressure, and diastolic blood pressure in Group A patients

Test	2% lignocaine with 1:200,000 epinephrine			Test	2% lignocaine		
	Time				Time		
	Before LA, mean ± SD	After LA, mean ± SD	After 20 min, mean ± SD		Before LA, mean ± SD	After LA, mean ± SD	After 20 min, mean ± SD
RBS	112.24 ± 18.7	110.29 ± 28.37	114.08 ± 24.6	RBS	109.92 ± 25.6	112.52 ± 28.7	111.36 ± 28
PR	80.92 ± 13.7	80.20 ± 13	79.68 ± 11	PR	82.96 ± 14.5	84.16 ± 14	84.44 ± 14
PO ₂	95.96 ± 5.1	95.88 ± 5	94.60 ± 6.8	PO ₂	95.76 ± 4.8	95.56 ± 6.7	93.04 ± 8.6
SBP	120.96 ± 17	121.56 ± 16.7	121.16 ± 16.7	SBP	119.2 ± 16.8	122.3 ± 17	120.36 ± 19.8
DBP	76.4800 ± 12.7	76.24 ± 11	75.64 ± 9.8	DBP	73.36 ± 9.6	75.52 ± 10	75.68 ± 10.6

SD: Standard deviation, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, PR: Pulse rate, LA: Local anesthesia, RBS: Random blood sugar, PO₂: Oxygen saturation

Table 2: Mean ± standard deviation of measurements taken for random blood sugar, pulse rate, oxygen saturation, systolic blood pressure, and diastolic blood pressure in Group B patients

Test	2% lignocaine with 1:200,000 epinephrine			Test	2% lignocaine		
	Time				Time		
	Before LA, mean ± SD	After LA, mean ± SD	After 20 min, mean ± SD		Before LA, mean ± SD	After LA, mean ± SD	After 20 min, mean ± SD
RBS	135.36 ± 24.7	118.84 ± 28.5	117.72 ± 29.7	RBS	131.28 ± 25.6	117.96 ± 34	115.64 ± 34.9
PR	83.64 ± 12.7	84.24 ± 13	84.36 ± 13.7	PR	82.60 ± 13.7	81.76 ± 12	80.84 ± 12
PO ₂	96.04 ± 4	95.36 ± 5.8	93.64 ± 7.8	PO ₂	96.40 ± 2.9	96.00 ± 3.7	96.52 ± 2.9
SBP	137.2 ± 17.5	138.8 ± 18	139.3 ± 18.9	SBP	138.9 ± 17.8	138.2 ± 16	135.1 ± 18
DBP	82.1 ± 7	81.1 ± 6.6	80.2 ± 9.6	DBP	84.64 ± 7	82.92 ± 8.6	83.61 ± 8

SD: Standard deviation, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, PR: Pulse rate, LA: Local anesthesia, RBS: Random blood sugar, PO₂: Oxygen saturation

Table 3: Patients treated under 2% lignocaine and epinephrine 1:200,000

Test	Time								
	Before LA			After LA			After 20 min		
	t	df	Significant	t	df	Significant	t	df	Significant
RBS	-30.7	48	0.001**	-10.05	47	0.299	-0.471	48	0.640
PR	-0.726	48	0.471	-10.08	48	0.284	-10.3	48	0.197
PO ₂	-0.06	48	0.951	0.335	48	0.739	0.456	48	0.650
SBP1	-30.3	48	0.002**	-30.49	48	0.001**	-30.58	48	0.001**
DBP1	-10.93	48	0.059	-10.86	48	0.069	-10.65	48	0.105

**For significance. DBP: Diastolic blood pressure, SBP: Systolic blood pressure, PR: Pulse rate, LA: Local anesthesia, RBS: Random blood sugar, PO₂: Oxygen saturation

Table 4: Patients treated under 2% lignocaine

Test	Time								
	Before LA			After LA			After 20 min		
	t	df	Significant	t	df	Significant	t	df	Significant
RBS	-20.942	48	0.005**	-0.6	48	0.546	-0.477	48	0.636
PR	0.090	48	0.929	0.64	48	0.523	0.943	48	0.351
PO ₂	-0.561	48	0.577	-0.28	48	0.777	-10.9	48	0.063
SBP2	-40.016	48	<0.001**	-30.35	48	0.002**	-20.72	48	0.009**
DBP2	-40.074	48	<0.001**	-30.35	48	0.002**	-20.6	48	0.010**

**For significance. DBP: Diastolic blood pressure, SBP: Systolic blood pressure, PR: Pulse rate, LA: Local anesthesia, RBS: Random blood sugar, PO₂: Oxygen saturation

between both the groups ($P = 0.048$, by ANOVA). Paired samples t -test showed statistically significant variability in DBP between patients treated under 2% lignocaine HCl with 1:200,000 epinephrine (DBP1) and 2% lignocaine HCl (DBP2) in type II controlled diabetic patients ($P = 0.020$).

The results of the study and statistical data are shown in Tables 1 and 4, Figures 1-5. All calculations were two sided and were performed using SPSS software version 17 (Technocare Medisystems, Chicago, IL, USA). $P < 0.05$ was considered to indicate statistical significance.

DISCUSSION

Systemic complications during dental treatments are caused by LA, and among these complications, the proportion of cases relating to the circulatory system is the largest.^[1-5] Endogenous catecholamines secreted *in vivo*, caused by psychological stress, accompanied by the injection pain and the added exogenous adrenaline in the LA, which acts as a vasoconstrictor, are cited as the causes of these complications.^[6] Vasoconstrictors are used in LA solutions to retard their systemic absorption. This enhances the LA effect by localizing it to the site of injection, decreases toxicity by retarding systemic

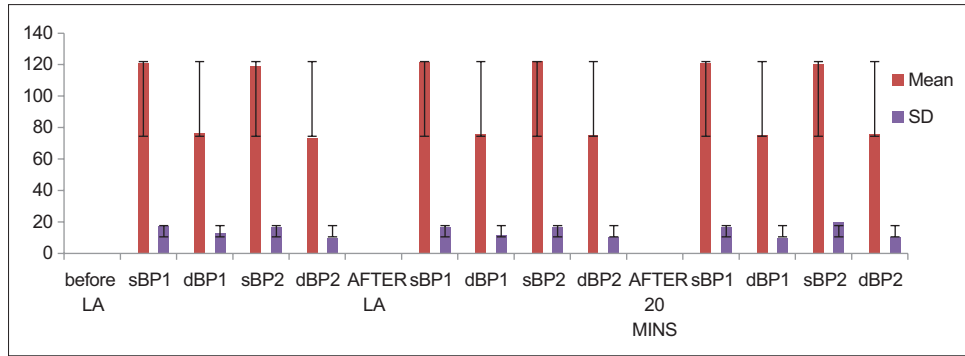


Figure 1: Mean systolic and diastolic blood pressure in healthy patients. SBP1, DBP1: Systolic blood pressure and diastolic blood pressure in patients treated under 2% lignocaine and epinephrine 1:200,000, SBP2, DBP2: Systolic blood pressure and diastolic blood pressure in patients treated under 2% lignocaine. ANOVA score (between groups): SBP1 ($f = 2, df = 0.002, P = 0.992$), DBP1 ($f = 2, df = 0.036, P = 0.965$), SBP2 ($f = 2, df = 0.192, P = 0.826$), DBP2 ($f = 2, df = 0.396, P = 0.674$). Paired samples *t*-test: Pair 1 (SBP1–SBP2): ($t = 0.348, df = 0.74, P = 0.729$), Pair 2 (DBP1–DBP2): ($t = 1.046, df = 0.74, P = 0.299$)

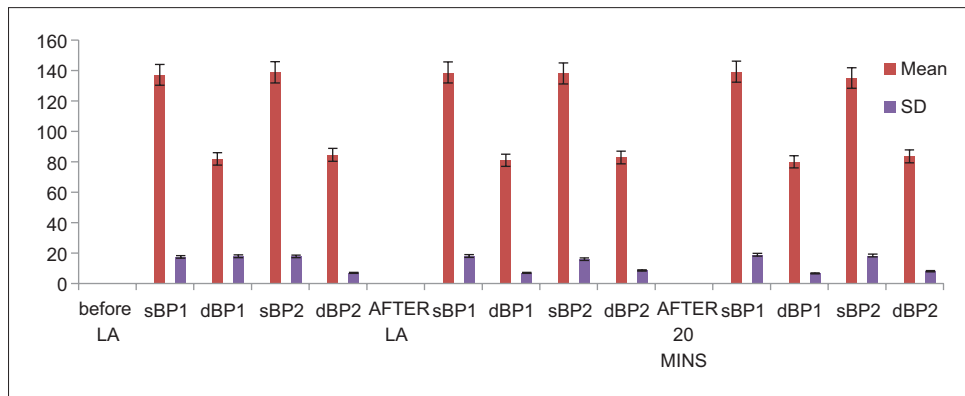


Figure 2: Mean systolic and diastolic blood pressure in controlled diabetic patients. SBP1, DBP1: Systolic blood pressure and diastolic blood pressure in controlled diabetic patients treated under 2% lignocaine and epinephrine 1:200,000, SBP2, DBP2: Systolic blood pressure and diastolic blood pressure in controlled diabetic patients treated under 2% lignocaine. ANOVA score (between groups): SBP1 ($f = 2, df = 0.088, P = 0.916$), DBP1 ($f = 2, df = 0.380, P = 0.685$), SBP2 ($f = 2, df = 0.331, P = 0.719$), DBP2 ($f = 2, df = 0.309, P = 0.735$). Paired samples *t*-test: Pair 1 (SBP1–SBP2): ($t = 0.560, df = 0.74, P = 0.577$), Pair 2 (DBP1–DBP2): ($t = -2.376, df = 0.74, P = 0.020^*$). *Significance

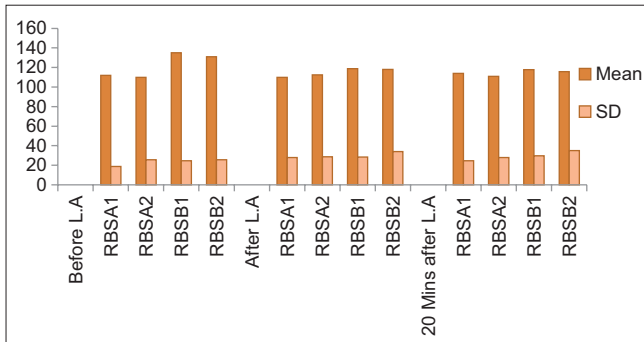


Figure 3: Mean random blood sugar. RBS_A1: Random blood sugar in healthy patients treated under 2% lignocaine and epinephrine 1:200,000, RBS_A2: Random blood sugar in healthy patients treated under 2% lignocaine, RBS_B1: Random blood sugar in controlled diabetic patients treated under 2% lignocaine and epinephrine 1:200,000 adrenaline, RBS_B2: Random blood sugar in controlled diabetic patients treated under 2% lignocaine. ANOVA score (between groups): RBS_A1 ($f = 0.150, df = 2, P = 0.861$), RBS_A2 ($f = 0.056, df = 2, P = 0.946$), RBS_B1 ($f = 3.162, df = 2, P = 0.048^*$), RBS_B2 ($f = 1.751, df = 2, P = 0.181$). *Significance

absorption, prolongs the duration of anesthesia, and may decrease the total dose of the LA drug required.^[6,7] Another secondary advantage to the use of vasoconstrictors in LA

solutions is in the control of bleeding or hemostatic effect that the vasoconstrictor provides.

Meehan recorded the rise in blood glucose following the injection of 30 ml of LA solution containing 1:200,000 adrenaline as crural blocks.^[6,8] However, it has been reported that the hyperglycemic effect of adrenaline occurs at plasma adrenaline concentration 4–5 times basal levels, i.e., at values of 150–200 pg/ml.^[6,9,10] Such concentrations may be obtained shortly after the injection of clinical doses of adrenaline containing LA.^[6,11]

Several hemodynamic studies have been carried out in patients subjected to LA agents with vasoconstrictor.^[1,12-14] Since the administration of LA with epinephrine elicited an increase in blood glucose levels even in patients with normal glucose tolerance, such administration may cause further increases in blood glucose levels in patients with diabetes.^[15,16] In the present study, blood glucose levels between different time periods were significantly increased in controlled type II diabetic patients treated under 2% lignocaine HCl with 1:200,000 epinephrine.

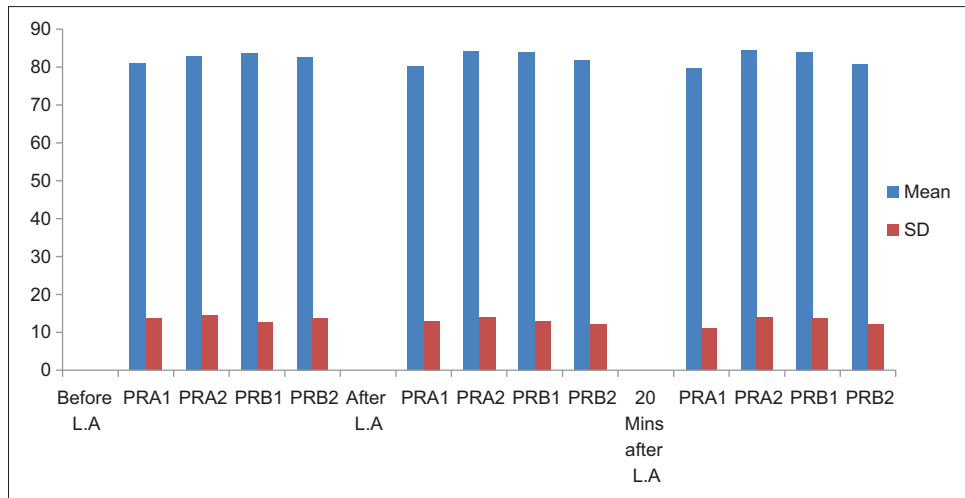


Figure 4: Mean peripheral finger pulse rate. PR_A1: Pulse rate in healthy patients treated under 2% lignocaine and epinephrine 1:200,000, PR_A2: Pulse rate in healthy patients treated under 2% lignocaine and epinephrine 1:200,000, PR_B1: Pulse rate in controlled diabetic patients treated under 2% lignocaine and epinephrine 1:200,000, PR_B2: Pulse rate in controlled diabetic patients treated under 2% lignocaine. ANOVA score (between groups): PR_A1 ($f = 0.060$, $df = 2$, $P = 0.942$), PR_A2 ($f = 0.075$, $df = 2$, $P = 0.928$), PR_B1 ($f = 0.021$, $df = 2$, $P = 0.979$), PR_B2 ($f = 0.118$, $df = 2$, $P = 0.889$)

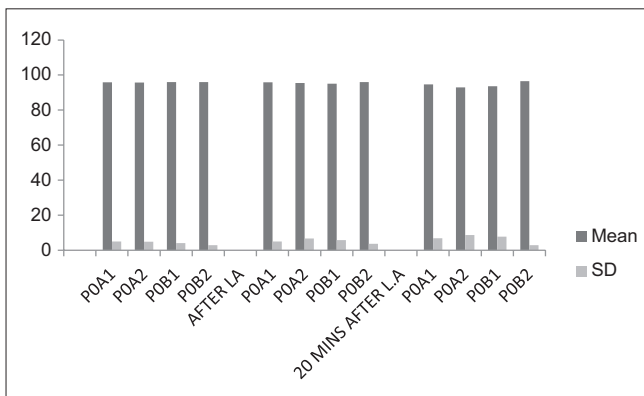


Figure 5: Mean peripheral finger oxygen saturation. PO_A1: Oxygen saturation of healthy patients treated under 2% lignocaine and epinephrine 1:200,000, PO_A2: Oxygen saturation of healthy patients treated under 2% lignocaine, PO_B1: Oxygen saturation of type II diabetic patients treated under 2% lignocaine and epinephrine 1:200,000, PO_B2: Oxygen saturation of type II diabetic patients treated under 2% lignocaine. ANOVA score (between groups): PO_A1 ($f = 0.438$, $df = 2$, $P = 0.647$), PO_A2 ($f = 1.197$, $df = 2$, $P = 0.308$), PO_B1 ($f = 1.007$, $df = 2$, $P = 0.370$), PO_B2 ($f = 0.175$, $df = 2$, $P = 0.840$)

The difference between treatments can confidently be attributed to the LA solution as all other parameters were carefully controlled.

Thus, the increase in the blood glucose level in the patients receiving 2% lignocaine HCl with 1:200,000 epinephrine can be contributed to the epinephrine present in the LA. This finding coincides with the results published by Meechan *et al.*^[6,8] and Salonen *et al.*^[6,17] Variations in glucose plasma levels during dental treatment have been the subject of study and controversy in the literature. Tilly and Thomas^[18] compared the effects of adrenalin administration in the dental LA solution on blood glucose concentrations in healthy and diabetic dental patients after extraction. They observed no significant changes in pre- and post-operative blood glucose levels.^[1,18]

A study by Meral *et al.*^[19,20] used the same anesthetic solution that we used at a similar volume (2.0 mL of plain lidocaine with 1:100,000 epinephrine). These patients also underwent extractions although they were otherwise healthy. There were no significant differences in the BP. With respect to the HR, the authors reported a significant increase in both groups, which differed from the findings of our present study, as there were no significant differences in the changes in heart rate between treatments at any of the times recorded in both the groups. Some studies have suggested that adrenaline injected as a vasoconstrictor is associated with transient effects in normotensive patients; hemodynamic complications could develop in uncontrolled hypertensive patients, with possible cardiovascular accidents, though such problems would be related to the dose of vasoconstrictor administered and to the LA used.^[1] The results from the present study showed that administration of 2 ml of 2% lignocaine with 1:200,000 epinephrine resulted in a statistically significant increase in SBP while DBP and heart rate were largely unaffected. Both SBP and DBPs rose after and 20 min after the administration of 2% lignocaine. Statistically significant variation was noted in DBP in controlled diabetic patients. The increases noted by some authors may have been transient as to have been missed in the current study at 15 min if indeed they occurred.^[1]

Monitoring vital constants is required to rapidly correct possible hypoxia in patients subjected to oral surgery.^[21,22,28,29] Minor fluctuations in vital signs are common during the administration of LA. The results of the present study are in agreement with previous studies that report no statistically significant differences

in PO_2 ^[21,26] and also in heart rate^[23-25] attributable to the type of LA used.

According to Malamed,^[10] most instances of true epinephrine overdosage are of such short duration that little or no formal management is required in an American Society of Anesthesiologists type 1 patient.^[10] One explanation to this could be the shorter half-life of 1–3 min for epinephrine. Further, epinephrine is largely eliminated from the blood within 10 min due to its metabolism by catechol-O-methyl transferase in the blood, liver, lungs, and other tissues.^[26] This is also an explanation of recording parameters of the present study, immediately after and 20 min after the administration of LA with and without epinephrine.

CONCLUSION

Hence, we conclude that the LA with epinephrine causes a slight increase in blood glucose concentration in type II controlled diabetic patients, which is not found to be clinically significant and therefore safe to use on diabetic patients. 2% lignocaine with 1:200,000 epinephrine concentration causes a rise in SBP. Both SBPs and DBPs elevate after the administration of 2% lignocaine. In the present study, LA with and without epinephrine influenced hemodynamic and metabolic parameters without perceptible clinical changes in healthy and type II controlled diabetic patients undergoing tooth extractions.

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Conflicts of interest

There are no conflicts of interest.

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