

Comparative Evaluation of Local Anaesthesia with and without Adrenaline on Haemodynamic and Metabolic Responses during Tooth Extraction: A Prospective Study

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ABSTRACT

Introduction: Local Anaesthetic (LA) solutions often incorporate vasoconstrictors to delay the systemic absorption of the drug. This prolongs the duration of anaesthesia, reduces toxicity by slowing systemic uptake, lowers the total required dose of LA and enhances anaesthetic efficacy by localising the drug at the injection site. Despite extensive published literature, the systemic metabolic effects of these agents in diabetic dental patients remain underexplored.

Aim: To evaluate the effect of local anaesthesia with and without adrenaline on blood glucose levels and haemodynamic parameters in patients undergoing routine tooth extractions.

Materials and Methods: This prospective study was conducted at the Department of Oral and Maxillofacial Surgery, Bharati Vidyapeeth Dental College, and Hospital, Sangli, Maharashtra, India, from January 2017 to December 2019. The study included 120 patients aged 17 to 65 years requiring multiple tooth extractions, comprising both medically stable non-diabetic individuals and patients with controlled Type 2 Diabetes Mellitus (T2DM) as the primary inclusion criteria. Each participant received two anaesthetic regimens in separate appointments in randomised order. Haemodynamic parameters (systolic and diastolic blood pressure, heart rate) and random blood glucose levels were recorded before injection (R0), immediately after (R1), and at 10 (R2) and 20 minutes (R3) post-injection. Data were analysed using repeated-measures Analysis of

Variance (ANOVA) with Bonferroni post-hoc tests for intragroup comparisons, Independent t-tests for intergroup change scores, and Chi-square tests for categorical variables ($p \leq 0.05$).

Results: Lignocaine with adrenaline produced significant transient increases in systolic blood pressure, heart rate, and blood glucose levels in diabetic subjects compared with plain lignocaine ($p < 0.001$). Non diabetic patients exhibited smaller, but statistically significant increases in haemodynamic parameters with adrenaline ($p < 0.05$). Blood glucose changes were also statistically significant with adrenaline in non diabetic patients as well (+11.8 mg/dL, $p < 0.001$), although less pronounced than in diabetic subjects. Diastolic blood pressure showed statistically significant but clinically modest increases with adrenaline in both groups ($p < 0.001$), whereas plain lignocaine produced minimal diastolic pressure.

Conclusion: LA solutions can elicit systemic metabolic responses, and caution is warranted when using lignocaine containing adrenaline in patients with T2DM patients. Clinicians should consider plain LA alternatives for diabetic patients when prolonged anaesthesia or enhanced haemostasis is not essential. Patient specific risk assessment is recommended preoperatively, particularly for those with suboptimal glycaemic control despite $HbA1c \leq 7\%$. Future studies should evaluate longer term impact on glycaemic control and incorporate non invasive cardiac output monitoring.

Keywords: Blood glucose, Dental extraction, Epinephrine, Plain lignocaine

INTRODUCTION

Tooth extraction is a common dental procedure that often requires the use of local anaesthesia to minimise pain and discomfort [1]. LAs, namely lidocaine and articaine, are effective in blocking peripheral nerve conduction and thereby producing temporary analgesia and loss of sensation at the operative site [2]. In routine dental practice, these anaesthetic agents are often combined with vasoconstrictors, most notably adrenaline (epinephrine), to enhance the depth and duration of anaesthesia, reduce intraoperative bleeding, and improve visibility in the surgical field.

However, the addition of adrenaline in LA has been a topic of debate among dental professionals [3,4]. Adrenaline is used in varying concentrations such as 1:50,000, 1:80,000, 1:100,000, and 1:200,000. The maximum dosage of adrenaline in healthy patients is 0.2 mg, and in a cardiac patient is 0.04 mg [1,4]. Despite multiple benefits, the inclusion of adrenaline has raised concerns about possible systemic effects, particularly on cardiovascular

and metabolic functions [5-7]. Adrenaline may transiently increase heart rate, blood pressure, and plasma glucose concentration due to its sympathomimetic action. Prior studies have explored haemodynamic fluctuations- such as variations in systolic and diastolic blood pressure and pulse rate- following the administration of local anaesthetics both with and without adrenaline during oral surgical procedures [8,9].

However, there remains a relative paucity of data examining metabolic responses, specifically changes in blood glucose levels, associated with local anaesthetics in dental extractions [10]. The present study, therefore, aimed to systematically compare and analyse the effects of local anaesthesia with and without adrenaline on haemodynamic parameters (blood pressure and heart rate) and metabolic parameters (blood glucose levels) during tooth extraction, thereby providing a more comprehensive understanding of the physiological influence of anaesthetic adjuncts in dental practice.

This study aimed to compare the effects of local anaesthesia with and without adrenaline on blood glucose levels and haemodynamic Changes in patients undergoing routine tooth extraction. Specifically, the objectives were:

1. Measure blood glucose levels and haemodynamic parameters (systolic BP, diastolic BP, heart rate) before, immediately after, and 10/20 minutes following LA administration in non diabetic and controlled T2DM patients.
2. Compare changes in these parameters between LA with vs without adrenaline within each patient group.
3. Assess between-group differences (diabetic vs non diabetic) for both anaesthetic regimens.

The null hypothesis (H_0) of the present study stated that there is no significant difference in blood glucose levels and haemodynamic parameters, specifically blood pressure and heart rate, between diabetic and non diabetic patients receiving local anaesthesia with adrenaline and those receiving anaesthesia without adrenaline during tooth extraction.

Conversely, the alternative hypothesis (H_1) posited that local anaesthesia with adrenaline significantly alters blood glucose levels and haemodynamic parameters compared to anaesthesia without adrenaline between diabetic and non diabetic patients.

MATERIALS AND METHODS

This prospective study was conducted at the Department of Oral and Maxillofacial Surgery, Bharati Vidyapeeth Dental College, and Hospital, Sangli, Maharashtra, India, from January 2017 to December 2019, with prior approval from the Institutional Ethical Committee with number BVDU/DCH IEC/ Dissertation 2016-2017/212. All procedures were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participant before enrolment.

Inclusion criteria: Patients between 17-65 years requiring multiple tooth extractions and medically stable individuals with controlled T2DM (HbA1c $\leq 7\%$) or otherwise healthy patients with no other co-morbidities were included.

Exclusion criteria: Patients with uncontrolled diabetes (HbA1c $> 7\%$), or pre-operative blood glucose level more than 250 mg/dL, patients having cardiovascular disease or hyperthyroidism, pregnant and paediatric patients and also patients on β -blockers, antihypertensives, steroids, or other systemic drugs were excluded.

Sample size calculation: The sample size was calculated based on a repeated-measures design with two within-subject factors (anaesthetic type: with/without adrenaline) and one between-subject factor (diabetic status). Using G*Power 3.1, with an anticipated effect size (partial η^2) [11] of 0.10 for the group $\times$ time $\times$ anaesthetic interaction, $\alpha = 0.05$, power $(1 - \beta) = 0.80$, and correlation among repeated measures of 0.5, the minimum required sample size was 52 participants per group. To account for potential dropouts and enhance statistical power, a total of 120 patients (60 per group) were recruited.

Participants were divided into two groups:

- Group A: Non diabetic patients
- Group B: Controlled T2DM patients

Randomisation determined the sequence of anaesthetic administration for each group. Each subject underwent two extractions in separate appointments:

- First under 2% lignocaine without adrenaline;
- Second under 2% lignocaine with adrenaline (1:80,000).

To reduce bias, both appointments were performed by the same surgeon, at similar times of the day, with identical pre-operative nutritional conditions.

Study Procedure

The procedural details of the study were carried out in a standardised manner. During the preoperative phase (day of procedure), routine blood investigations, including Haemoglobin (Hb%), Bleeding Time (BT), Clotting Time (CT), and Random Blood Glucose, were performed. An Orthopantomogram (OPG) radiograph was obtained for all participants. No pre-treatment medications were prescribed in order to eliminate bias. Participants were allowed to have a light breakfast, standardised approximately two hours before both visits. The second appointment was scheduled seven days after the first extraction. The two sessions were separated by a 7-day washout period, and no dietary or medication adjustments were imposed between visits.

At baseline (R0), participants were seated comfortably, and blood pressure, heart rate (three readings averaged), and finger-stick blood glucose were recorded by a blinded assistant. Local anaesthesia was then administered using a standardised dose of 1.8 mL per session, consisting of a nerve block and infiltration. The sequence of administration was randomised, with either plain local anaesthetic first or adrenaline-containing anaesthetic first, determined using a sealed envelope method. A Lidocaine (LOX 2% injection of lignocaine hydrochloride) manufactured by Neon Laboratories Ltd., was used in all procedures.

The extraction procedure involved only non surgical intra-alveolar extractions, with no use of flaps or elevators. Two to three single-rooted teeth were extracted per session. All procedures were performed by the same operator using an identical technique, and none of the procedures required an unusually prolonged time for completion.

Following the administration of local anaesthesia, post-injection monitoring was carried out at predetermined intervals: R1 (immediately after injection, before extraction), R2 (10 minutes post-injection), and R3 (20 minutes post-injection). During this monitoring period, no analgesics or sedatives were administered. After completion of the procedure, patients were provided with standard postoperative extraction instructions. All procedures complied with ethical standards, and emergency resuscitative equipment was kept ready. No adverse events occurred during the study.

STATISTICAL ANALYSIS

Data were analysed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as mean $\pm$ Standard Deviation (SD) for continuous variables and as frequencies and percentages for categorical variables. For intragroup comparisons (changes over time within the same group), repeated-measures ANOVA was employed with Greenhouse-Geisser correction when sphericity assumptions were violated. Post-hoc pairwise comparisons were performed using Bonferroni correction to adjust for multiple comparisons.

For intergroup comparisons, Independent samples t-tests were used to compare baseline characteristics and change scores (Δ) between diabetic and non diabetic groups. Categorical variables were compared using Chi-square tests.

Effect sizes were reported as partial η^2 for ANOVA results (with values of 0.01, 0.06, and 0.14 representing small, medium, and large effects, respectively) and as Cohen's d for t-tests (with values of 0.2, 0.5, and 0.8 representing small, medium, and large effects, respectively). A 95% Confidence Intervals (CI) was calculated for all mean differences and statistical significance was set at $p \leq 0.05$.

RESULTS

Sociodemographic and baseline characteristics [Table/Fig-1]. A total of 120 patients (60 controlled type 2 diabetics, 60 non diabetics) were enrolled; no participants were lost to follow-up or excluded

Parameters	Non diabetic (n=60)	Diabetic (n=60)	Test statistic	p-value
Age (in years)	45.8±12.4	47.3±11.9	t=0.58	0.56
Male, n (%)	34 (56.7%)	36 (60.0%)	$\chi^2=0.14$	0.71
Female, n (%)	26 (43.3%)	24 (40.0%)		

[Table/Fig-1]: Sociodemographic and baseline characteristics of the study population.

Data presented as mean±standard deviation (SD) or n (%). Age was compared using an independent samples t-test; gender distribution was compared using a Chi-square test. $p \leq 0.05$ is considered statistically significant

post-consent. Groups were comparable in age and gender distribution as seen in [Table/Fig-1].

Non diabetic group A patients receiving lignocaine without adrenaline showed statistically significant but clinically modest increases in haemodynamic parameters over 20 minutes: systolic BP +3.5 mmHg ($p=0.032$), diastolic BP +1.5 mmHg ($p=0.041$), heart rate +2.0 bpm ($p=0.028$). Blood glucose remained stable (+0.85 mg/dL, $p=0.210$) [Table/Fig-2].

Blood glucose levels and haemodynamic parameters of non diabetic patients with adrenaline-containing LA produced marked, progressive increases: systolic BP +18.4 mmHg ($p<0.001$), diastolic BP +2.1 mmHg ($p<0.001$), heart rate +11.4 bpm ($p<0.001$), blood glucose +11.8 mg/dL ($p<0.001$) at 20 minutes [Table/Fig-3].

Controlled diabetics showed minimal haemodynamic changes without adrenaline: systolic BP +1.4 mmHg ($p=0.048$), diastolic

+2.0 mmHg ($p=0.036$), heart rate +1.8 bpm ($p=0.039$). Blood glucose stable (+1.0 mg/dL, $p=0.450$) [Table/Fig-4].

Blood glucose levels and haemodynamic parameters of diabetic patients with adrenaline are shown [Table/Fig-5]. Adrenaline caused pronounced responses in diabetics: systolic BP +13.9 mmHg ($p<0.001$), heart rate +15.1 bpm ($p<0.001$), blood glucose +18.4 mg/dL ($p<0.001$). Diastolic BP increased modestly (+2.7 mmHg, $p<0.001$).

In healthy patients, LA with adrenaline produced significantly greater changes than plain LA across all time points: immediate systolic BP $\Delta+6.1$ mmHg ($p<0.001$), heart rate $\Delta+1.6$ bpm ($p=0.002$), glucose $\Delta+3.1$ mg/dL ($p<0.001$). Diastolic BP differences were non significant except for 10-min ($p=0.022$) [Table/Fig-6].

Diabetics showed exaggerated responses to adrenaline: immediate glucose $\Delta+5.1$ mg/dL ($p<0.001$) vs 4.0 mmHg systolic BP difference ($p<0.001$). All haemodynamic and metabolic parameters were significantly higher with adrenaline (all $p<0.001$ except diastolic BP) [Table/Fig-7].

Under plain lignocaine without adrenaline, non diabetic patients exhibited significantly greater immediate increases in systolic BP ($\Delta+1.5$ mmHg vs. $\Delta+0.8$ mmHg; $p<0.001$), diastolic BP ($\Delta+0.5$ mmHg vs. $\Delta+0.5$ mmHg; $p=0.003$), and heart rate ($\Delta+1.0$ bpm vs. $\Delta+0.5$ bpm; $p=0.006$) compared to diabetic patients. These differences persisted for systolic BP at 10 and 20 minutes ($p<0.001$). However, no significant differences in blood glucose changes were observed between the two groups at any time point ($p>0.05$), as shown in [Table/Fig-8].

Parameters	Before LA (Mean±SD)	After LA (Mean±SD)	10 min after LA (Mean±SD)	20 min after LA (Mean±SD)	F(df)	p-value	Partial η^2
Systolic BP (mmHg)	120.8±8.2	122.3±8.5	123.1±8.7	123.5±8.9	F(3,177)=4.32	0.032*	0.07
Diastolic BP (mmHg)	80.2±6.4	80.7±6.5	81.2±6.6	81.5±6.7	F(3,177)=3.85	0.041*	0.06
Heart rate (bpm)	72.5±7.1	73.5±7.3	73.8±7.4	74.0±7.5	F(3,177)=4.12	0.028*	0.07
Blood glucose (mg/dL)	93.8±10.3	94.2±10.5	94.5±10.6	94.6±10.7	F(3,177)=1.55	0.210	0.03

[Table/Fig-2]: Blood glucose levels and haemodynamic parameters of non diabetic group A (Without Adrenaline).

Note: SD: standard deviation; p-values from repeated-measures ANOVA with Bonferroni correction p less than 0.05 was considered statistically significant and is indicated with an asterisk (*). Partial Eta squared (Partial η^2) is reported as a measure of effect size.*

Parameters	Before LA (Mean±SD)	After LA (Mean±SD)	10 min after LA (Mean±SD)	20 min after LA (Mean±SD)	F(df)	p-value	Partial η^2
Systolic BP (mmHg)	120.5±8.4	128.6±9.2	133.4±9.8	138.4±10.5	F(3,177)=45.7	<0.001*	0.44
Diastolic BP (mmHg)	80.3±6.5	80.0±6.8	82.2±7.1	82.1±7.2	F(3,177)=8.3	<0.001*	0.12
Heart rate (bpm)	72.8±7.3	75.1±7.8	79.2±8.4	83.4±9.1	F(3,177)=52.1	<0.001*	0.47
Blood glucose (mg/dL)	93.7±10.5	97.2±10.8	101.0±11.2	105.5±11.8	F(3,177)=48.6	<0.001*	0.45

[Table/Fig-3]: Blood glucose levels and haemodynamic parameters of healthy patients with adrenaline.

SD: Standard Deviation. p-values from repeated-measures ANOVA (intragroup comparison) with Bonferroni correction. $p \leq 0.05$ is considered statistically significant. Partial Eta squared (Partial η^2) is reported as a measure of effect size.*

Parameters	Before LA (Mean±SD)	After LA (Mean±SD)	10 min after LA (Mean±SD)	20 min after LA (Mean±SD)	F(df)	p-value	Partial η^2
Systolic BP (mmHg)	122.6±12.2	123.2±12.4	123.8±12.5	124.0±12.7	F(3,177)=3.2	0.048*	0.05
Diastolic BP (mmHg)	80.5±7.5	80.8±7.6	81.5±7.7	82.0±7.9	F(3,177)=3.6	0.036*	0.06
Heart rate (bpm)	76.4±8.6	77.2±8.7	77.8±8.8	78.2±9.0	F(3,177)=3.9	0.039*	0.06
Blood glucose (mg/dL)	152.3±24.1	152.8±24.3	153.1±24.5	153.3±24.7	F(3,177)=0.9	0.450	0.02

[Table/Fig-4]: Blood glucose levels and haemodynamic parameters of diabetic patient group B without adrenaline.

SD: standard deviation. p-values from repeated-measures ANOVA (intragroup comparison) with Bonferroni correction. F-values reported. $p \leq 0.05$ is considered statistically significant. Partial Eta squared (Partial η^2) is reported as a measure of effect size.*

Parameters	Before LA (Mean±SD)	After LA (Mean±SD)	10 min after LA (Mean±SD)	20 min after LA (Mean±SD)	F(df)	p-value	Partial η^2
Systolic BP (mmHg)	122.3±12.5	127.1±13.1	130.7±13.8	136.3±14.6	F(3,177)=38.5	<0.001*	0.40
Diastolic BP (mmHg)	80.8±7.6	80.0±7.8	81.3±8.1	82.7±8.4	F(3,177)=7.2	<0.001*	0.11
Heart rate (bpm)	76.3±8.7	80.9±9.2	85.6±9.8	91.4±10.5	F(3,177)=62.3	<0.001*	0.51
Blood glucose (mg/dL)	154.5±25.2	159.7±25.8	164.3±26.5	172.8±27.8	F(3,177)=55.8	<0.001*	0.49

[Table/Fig-5]: Blood glucose levels and haemodynamic parameters of diabetic patients with adrenaline.

SD: Standard Deviation. p-value from repeated-measures ANOVA (intragroup comparison) with Bonferroni correction. $p \leq 0.05$ is considered statistically significant. Partial Eta squared (Partial η^2) is reported as a measure of effect size.*

Parameters	Time point	LA without adrenaline (Mean $\Delta \pm$ SD)	LA with adrenaline (Mean $\Delta \pm$ SD)	Mean difference (95% CI)	t(df)	p-value	Cohen's d
Systolic BP	Immediately	2.5 $\pm$ 3.2	8.6 $\pm$ 4.1	6.1 (4.8, 7.4)	t(118)=9.45	<0.001*	1.73
Diastolic BP	Immediately	0.5 $\pm$ 1.8	0.0 $\pm$ 1.9	-0.5 (-1.0, 0.0)	t(118)=1.96	0.052	0.27
Heart rate	Immediately	1.5 $\pm$ 2.8	3.1 $\pm$ 3.2	1.6 (0.8, 2.4)	t(118)=3.98	0.002*	0.73
Blood glucose	Immediately	0.5 $\pm$ 1.8	3.5 $\pm$ 3.1	3.1 (2.3, 3.9)	t(118)=7.85	<0.001*	1.44
Systolic BP	10 min	3.1 $\pm$ 3.8	13.4 $\pm$ 5.2	10.3 (8.7, 11.9)	t(118)=12.87	<0.001*	2.36
Diastolic BP	10 min	1.2 $\pm$ 2.5	2.2 $\pm$ 3.1	1.0 (0.1, 1.9)	t(118)=2.32	0.022*	0.43
Heart rate	10 min	1.8 $\pm$ 3.2	7.2 $\pm$ 4.5	5.4 (4.1, 6.7)	t(118)=8.24	<0.001*	1.51
Blood glucose	10 min	0.8 $\pm$ 2.2	7.3 $\pm$ 4.3	6.5 (5.3, 7.7)	t(118)=10.75	<0.001*	1.97
Systolic BP	20 min	3.5 $\pm$ 4.2	18.4 $\pm$ 6.5	14.9 (12.9, 16.9)	t(118)=14.52	<0.001*	2.66
Diastolic BP	20 min	1.5 $\pm$ 2.8	2.1 $\pm$ 3.2	0.6 (-0.3, 1.5)	t(118)=1.34	0.182	0.25
Heart rate	20 min	2.0 $\pm$ 3.5	11.4 $\pm$ 5.8	9.4 (7.7, 11.1)	t(118)=10.89	<0.001*	1.99
Blood glucose	20 min	0.9 $\pm$ 2.5	11.8 $\pm$ 6.2	10.9 (9.2, 12.6)	t(118)=12.88	<0.001*	2.36

[Table/Fig-6]: Healthy patients group A comparison of changes (with vs without adrenaline).

Δ : change from baseline (R0). SD: Standard Deviation. p-values from an independent samples t-test (intergroup comparison). t-values reported. $p \leq 0.05$ is considered statistically significant

Parameters	Time point	LA without adrenaline (Mean $\Delta \pm$ SD)	LA with adrenaline (Mean $\Delta \pm$ SD)	Mean difference (95% CI)	t(df)	p-value	Cohen's d
Systolic BP	Immediately	0.8 $\pm$ 3.1	4.8 $\pm$ 2.8	4.0 (3.0, 5.0)	t(118)=5.67	<0.001*	1.04
Diastolic BP	Immediately	0.5 $\pm$ 2.0	0.0 $\pm$ 1.8	-0.5 (-1.1, 0.1)	t(118)=1.67	0.098	0.31
Heart rate	Immediately	0.5 $\pm$ 1.8	4.6 $\pm$ 2.5	4.1 (3.3, 4.9)	t(118)=10.15	<0.001*	1.86
Blood glucose	Immediately	0.1 $\pm$ 0.4	5.2 $\pm$ 2.8	5.1 (4.4, 5.8)	t(118)=14.25	<0.001*	2.61
Systolic BP	10 min	1.3 $\pm$ 4.5	8.3 $\pm$ 5.6	7.0 (5.1, 8.9)	t(118)=7.25	<0.001*	1.33
Diastolic BP	10 min	1.4 $\pm$ 3.2	1.3 $\pm$ 3.4	-0.1 (-1.3, 1.1)	t(118)=0.15	0.882	0.03
Heart rate	10 min	0.8 $\pm$ 2.8	9.3 $\pm$ 3.8	8.5 (7.2, 9.8)	t(118)=13.12	<0.001*	2.40
Blood glucose	10 min	0.2 $\pm$ 0.5	9.8 $\pm$ 4.8	9.6 (8.3, 10.9)	t(118)=14.85	<0.001*	2.72
Systolic BP	20 min	1.8 $\pm$ 5.8	13.9 $\pm$ 9.2	12.1 (9.4, 14.8)	t(118)=8.97	<0.001*	1.64
Diastolic BP	20 min	2.2 $\pm$ 4.5	2.7 $\pm$ 4.8	0.5 (-1.2, 2.2)	t(118)=0.57	0.572	0.10
Heart rate	20 min	1.5 $\pm$ 4.2	15.1 $\pm$ 6.8	13.6 (11.5, 15.7)	t(118)=12.78	<0.001*	2.34
Blood glucose	20 min	0.2 $\pm$ 0.5	18.4 $\pm$ 7.2	18.2 (16.4, 20.0)	t(118)=20.15	<0.001*	3.69

[Table/Fig-7]: Comparison of blood glucose levels and haemodynamic parameters of diabetic patients who underwent extraction under local anaesthesia with and without adrenaline.

Δ : change from baseline (R0). SD: standard deviation. p-values from independent samples t-test (intergroup comparison). t-values reported. $p \leq 0.05$ considered statistically significant

Parameters	Healthy patients (Mean $\Delta \pm$ SD)	Diabetic patients (Mean $\Delta \pm$ SD)	t(df)	p-value
Δ Immediately after LA				
Systolic BP	1.5 $\pm$ 3.2	0.8 $\pm$ 3.1	t(118)=4.89	<0.001*
Diastolic BP	0.5 $\pm$ 1.8	0.5 $\pm$ 2.0	t(118)=3.01	0.003*
Heart rate	1.0 $\pm$ 2.8	0.5 $\pm$ 1.8	t(118)=2.78	0.006*
Blood glucose	0.4 $\pm$ 1.8	0.1 $\pm$ 0.4	t(118)=0.03	0.977
Δ 10 mins after LA				
Systolic BP	3.1 $\pm$ 3.8	1.3 $\pm$ 4.5	t(118)=4.12	<0.001*
Diastolic BP	1.2 $\pm$ 2.5	1.4 $\pm$ 3.2	t(118)=1.48	0.142
Heart rate	1.8 $\pm$ 3.2	0.8 $\pm$ 2.8	t(118)=0.85	0.397
Blood glucose	0.8 $\pm$ 2.2	0.2 $\pm$ 0.5	t(118)=1.29	0.200
Δ 20 min after LA				
Systolic BP	3.5 $\pm$ 4.2	1.8 $\pm$ 5.8	t(118)=3.45	<0.001*
Diastolic BP	1.5 $\pm$ 2.8	2.2 $\pm$ 4.5	t(118)=0.29	0.771
Heart rate	2.0 $\pm$ 3.5	1.5 $\pm$ 4.2	t(118)=1.12	0.266
Blood glucose	0.9 $\pm$ 2.5	0.2 $\pm$ 0.5	t(118)=1.29	0.200

[Table/Fig-8]: Comparison of blood glucose levels and haemodynamic parameters of healthy and diabetic patients who underwent extraction under local anaesthesia without adrenaline.

* Δ : change from baseline (R0). SD: standard deviation. p-values from independent samples t-test (intergroup comparison). $p \leq 0.05$ considered statistically significant.*

When adrenaline containing lignocaine was used, diabetic patients demonstrated significantly exaggerated metabolic and heart rate responses compared to non diabetics. At 20 minutes post-injection,

the increase in blood glucose was substantially higher in diabetics ($\Delta +18.4$ mg/dL) than in non diabetics ($\Delta +11.8$ mg/dL), a difference of $+6.6$ mg/dL ($p < 0.001$). Similarly, the heart rate increase was greater in diabetics ($\Delta +15.1$ bpm) than in non diabetics ($\Delta +11.4$ bpm) ($p < 0.001$). Interestingly, the immediate systolic BP increase was higher in non diabetics ($\Delta +8.1$ mmHg vs. $\Delta +4.8$ mmHg; $p < 0.001$), though this pattern reversed over time. These findings are detailed in [Table/Fig-9].

DISCUSSION

The present study examines and compares the influence of local anaesthesia with adrenaline (1:80,000) vs plain local anaesthesia during tooth extraction on heart rate, blood pressure, and blood glucose levels in subjects with controlled T2DM as well as healthy persons. Measurements at baseline, immediately after injection, and at 10- and 20-minutes post-injection demonstrated that adrenaline containing anaesthetic led to significant elevation in systolic blood pressure, heart rate, and blood glucose, especially in diabetic subjects.

In the diabetic group ($n=60$), the mean baseline random blood glucose was higher before the adrenaline-containing session (154.5 ± 25.2 mg/dL) compared to the plain lignocaine session (152.3 ± 24.1 mg/dL), a difference of 2.2 mg/dL. Although this difference was not statistically significant ($p > 0.05$), it reflects the expected biological variability in day-to-day glycaemic control among T2DM patients, despite all participants having HbA1c $\leq 7\%$. No statistical adjustment was applied because the baseline difference was small and not significant. However, future studies with larger samples may consider using baseline-adjusted models to further minimise any residual confounding.

Parameters	Healthy patients (Mean $\pm$ SD)	Diabetic patients (Mean $\pm$ SD)	t(df)	p-value
Δ Immediately after LA				
Systolic BP	8.1 $\pm$ 4.1	4.8 $\pm$ 2.8	t(118)=9.23	<0.001*
Diastolic BP	0.0 $\pm$ 1.9	0.0 $\pm$ 1.8	—	1.000
Heart rate	3.1 $\pm$ 3.2	4.6 $\pm$ 2.5	t(118)=5.12	<0.001*
Blood glucose	3.5 $\pm$ 3.1	5.2 $\pm$ 2.8	t(118)=4.45	<0.001*
Δ 10 min after LA				
Systolic BP	13.4 $\pm$ 5.2	8.3 $\pm$ 5.6	t(118)=7.89	<0.001*
Diastolic BP	2.2 $\pm$ 3.1	1.3 $\pm$ 3.4	t(118)=1.96	0.053
Heart rate	7.2 $\pm$ 4.5	9.3 $\pm$ 3.8	t(118)=5.67	<0.001*
Blood glucose	7.3 $\pm$ 4.3	9.8 $\pm$ 4.8	t(118)=4.12	<0.001*
Δ 20 min after LA				
Systolic BP	18.4 $\pm$ 6.5	13.9 $\pm$ 9.2	t(118)=3.89	<0.001*
Diastolic BP	2.1 $\pm$ 3.2	2.7 $\pm$ 4.8	t(118)=1.05	0.296
Heart rate	11.4 $\pm$ 5.8	15.1 $\pm$ 6.8	t(118)=4.78	<0.001*
Blood glucose	11.8 $\pm$ 6.2	18.4 $\pm$ 7.2	t(118)=7.12	<0.001*

[Table/Fig-9]: Comparison of blood glucose levels and haemodynamic parameters of healthy and diabetic patients who underwent extraction under local anaesthesia with adrenaline.

* Δ : change from baseline (R0). SD: standard deviation. p-values from independent samples t-test (intergroup comparison). $p \leq 0.05$ considered statistically significant.*

Use of vasoconstrictors in maxillofacial surgery, along with local anaesthesia, to reduce its systemic absorption, which increases the local anaesthesia effect, and hence reduces toxicity simultaneously. So, it prolongs the duration of anaesthesia, which is an advantage in long-duration surgeries, which subsequently reduces the total amount of the local anaesthetic medication needed. A further significant benefit is the haemostatic effect, which is important in the surgical field while operating. While the present study findings confirm that adrenaline enhances anaesthetic efficacy, its sympathomimetic properties also drive transient increases in cardiovascular and metabolic markers. According to previous studies α_2 adrenergic receptors are responsible for suppression of β cells in the pancreatic islets of Langerhans which directly causes decrease in insulin secretion and decrease in glucose affecting peripheral tissue and indirectly causes decrease insulin release which leads to β -Adrenergic mediated increase in glucagon concentration in blood. Glycogenolysis and gluconeogenesis, and glycolysis result in increase in the production of glucose [12,13].

There is a clinically significant interaction between adrenaline and physiologic changes and lead to hypertension with a concomitant reflex bradycardia. Although it is rare in a dental setting, cardiac patients are vulnerable, so caution is taken before and after the procedure [14,15].

Goel M et al., study found that blood glucose levels were stable before and after tooth extraction, with no significant changes in the control group, and the blood glucose levels of diabetic patients taking anti-diabetic drugs remained constant before and after surgery [16]. According to a study by Byakodi S et al., (2017), administering local anaesthesia with adrenaline has been shown to raise blood sugar levels. A comparison was made within the group, but there are no discernible differences in other factors [17]. Rajkumar V et al., similarly noted no marked differences in haemodynamic parameters, suggesting that any transient increases reported in the literature may have been brief and missed due to the timing of post-injection measurements [18].

In a study performed by Akinmoladun VI et al., (2013), it was found that while diastolic blood pressure and heart rates stayed largely unchanged, 3.6 ml of lidocaine 1:100,000 did not significantly raise systolic blood pressure [19].

Khawaja NA et al., found out it is safe to use local anaesthesia with adrenaline in healthy and those with antidiabetic medicine in diabetic patients [20]. Salonen M et al., found out that local anaesthesia with adrenaline (1:200000) has a made significant changes in blood glucose levels [21].

Chernow B et al., conducted a study to define the haemodynamic effects (heart rate, mean arterial pressure, plasma catecholamines) responses. Effect had been recorded for 60 minutes following block and the author noted that there is no change when lidocaine is injected alone and there is a significant but transient change (2 minutes) in haemodynamic parameters [22]. The present study found that healthy patients experienced haemodynamic changes after adrenaline administration, while diabetic patients, even those well-controlled, were more susceptible to significant increases in blood glucose and blood pressure. These effects were most pronounced within the first 20 minutes following anaesthesia. Similarly, Madan S et al., did a study on 100 patients, and concluded that there is a significant increase in blood glucose level in patients with controlled diabetes [23]. Cassidy JP et al., in their study, suggested that epinephrine used in dental practice can cause physiologic changes [24], while Wahl MJ and Brown RS reviewed the safe dosage and anaesthetics toxicity effects [25]. Tolas AG et al., suggested that there is a significant rise in plasma epinephrine concentration in high-risk patients after local anaesthesia with adrenaline and advised to carefully monitor [26].

In diabetic patients, immediately after administration of local anaesthesia, there was a significant difference between all parameters when extraction was performed with or without adrenaline. Ten and 20 minutes after local anaesthesia administration, the systolic BP, heart rate and blood glucose levels showed a significantly higher change when extraction was done under local anaesthesia with adrenaline. There was no significant difference in the change in diastolic BP. After extraction done under local anaesthesia without adrenaline, there was a significant difference in haemodynamic parameters amongst the healthy and diabetic patients immediately after local anaesthesia. Except for systolic blood pressure, there was no discernible difference in the data between the diabetic and healthy patients at 10 or 20 minutes after local anaesthesia. In the diabetic group, the mean baseline random blood glucose was higher before the adrenaline-containing session (154.5 $\pm$ 25.2 mg/dL) compared to the plain lignocaine session (152.3 $\pm$ 24.1 mg/dL), a difference of 2.2 mg/dL. Although this difference was not statistically significant ($p > 0.05$), it reflects the expected biological variability in day-to-day glycaemic control among T2DM patients, despite all participants having HbA1c $\leq 7\%$. The two sessions were separated by a 7-day washout period, and no dietary or medication adjustment was imposed between visits. However, future studies with larger samples may consider using baseline-adjusted models to further minimise any residual confounding.

After extraction done under local anaesthesia with adrenaline, there was a marked difference in systolic BP, Heart rate and blood glucose concentrations amongst the healthy and diabetic patients immediately following local anaesthesia, 10 and 20 minutes after local anaesthesia. In our study standardised conditions by delivering lignocaine injections with adrenaline and lignocaine alone to the same cohort under identical circumstances, including time, nutrition, and environment. This approach allowed us to attribute any observed hyperglycaemic responses specifically to the action of adrenaline. The findings of the present study indicate that lignocaine and adrenaline injections raise blood glucose levels.

For well managed diabetics, particularly those receiving insulin therapy, this brief elevation in blood glucose levels is usually not of concern. However, it may be more significant for patients with T2DM. Therefore, when evaluating the systemic effects of local anaesthetic injections, it is important to consider both metabolic and haemodynamic changes.

Hypoglycaemia is a common issue encountered in dental settings and can lead to vasovagal syncope. Although the present study demonstrates a significant rise in blood glucose following local anaesthetic with adrenaline, the suggestion that this effect may help prevent vasovagal syncope remains speculative and is not robustly supported by clinical trials or large population data. Existing literature notes that vasovagal syncope during dental procedures is typically psychogenic, associated with anxiety and needle phobia, rather than hypoglycaemia alone. The incidence of vasovagal reactions in patients given local anaesthesia with adrenaline is low (approximately 1.8%) and most studies advise caution and thorough patient education rather than promoting adrenaline as a preventive strategy [27].

Consequently, doctors should be cautious in patients planned for dental extraction with a history of T2DM when using lignocaine with adrenaline. These findings highlight how crucial it is to take haemodynamic and metabolic effects into account when giving LAs, especially to diabetic individuals. Thus, it can be concluded from the current study that LA solutions containing adrenaline have a measurable impact on blood glucose levels in controlled T2DM patients, even when they are on antidiabetic therapy.

The clinical implications are notable. Local anaesthetics with adrenaline are generally safe in healthy and well-controlled diabetics but may pose risks for those with poorly controlled diabetes or cardiovascular comorbidities. Also, practitioners should conduct individualised risk assessments, monitor glucose and cardiovascular parameters closely, and consider alternative anaesthetic regimens for high-risk patients.

The null hypothesis (H_0) - that there is no significant difference in haemodynamic parameters (systolic/diastolic blood pressure, heart rate) and blood glucose levels between patients receiving local anaesthesia with versus without adrenaline - was rejected. This was evidenced by statistically significant differences ($p < 0.05$) across multiple timepoints and patient groups, particularly pronounced in controlled T2DM [Table/Fig-6-9]. Conversely, the alternative hypothesis (H_1) - that adrenaline-containing LA significantly alters these parameters - was accepted, confirming its systemic sympathomimetic effects during routine tooth extractions.

Limitation(s)

Major study limitations included a single-centre design. Only T2DM were included, so findings may not extrapolate to insulin-dependent patients or those with co-morbidities. Parameters such as cardiac output and oxygen delivery were not analysed due to equipment constraints, representing an area for future research. The short monitoring period (20 minutes) captured acute effects but not prolonged glycaemic impact. Convenience sampling limits generalisability.

Potential confounding factors like anxiety and stress were partially mitigated by study standardisation, but psychological responses could still influence results. Future studies should include broader cohorts, increased monitoring intervals, and additional cardiovascular/metabolic indices.

To gain a more comprehensive understanding of how different elements of local anaesthetic solutions affect the body's metabolic state, further researches with bigger sample sizes and diverse study groups should be conducted. These findings highlight the need for further studies to fully understand the metabolic effects of local anaesthetic solutions, especially in diabetic patients.

CONCLUSION(S)

It is well established that adding epinephrine to LA solutions prolongs anaesthesia, reduces the risk of systemic toxicity, and improves haemostasis. Conversely, it may increase blood pressure, blood glucose levels, and heart rate. In summary, clinically administered local anaesthetic solutions can elicit systemic metabolic responses,

which may be more pronounced under stress. Therefore, when evaluating the overall effects of local anaesthetic solutions, both metabolic and haemodynamic responses must be considered. Lignocaine with adrenaline should be administered with caution in patients with T2DM.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Aug 23, 2025
- Manual Googling: May 23, 2026
- iThenticate Software: May 25, 2026 (11%)

ETYMOLOGY: Author Origin

EMENDATIONS: 10

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **May 19, 2025**

Date of Peer Review: **Sep 16, 2025**

Date of Acceptance: **May 27, 2026**

Date of Publishing: **Aug 01, 2026**