Original Article - Comparative Study

Effect of Local Anaesthesia with and without Adrenaline on Blood Glucose Concentration in Patients Undergoing Tooth Extractions - A Comparative Study

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Abstract

Introduction: Local anaesthesia (LA) is the usual drug used in dentistry to reduce intraoperative pain. The efficacy of lignocaine is improved by adding adrenaline as a vasoconstrictor. Adrenaline decreases the systemic absorption of LA and reduces blood loss during the surgical procedure. The study was conducted to observe the effect of adrenaline on blood glucose concentration in patients undergoing tooth extraction. **Materials and Methods:** The study was conducted on 100 patients needing multiple teeth extraction. On the first appointment, extraction was done using lignocaine without adrenaline (plain), and for the second appointment, extraction was done using lignocaine with adrenaline (1:200,000). Serial blood glucose estimations were carried out at identical intervals on both occasions. **Results:** Significant difference in blood glucose level was noted when the patients received lignocaine with adrenaline before administration and after 10 min/20 min intervals ($P < 0.05$). **Discussion:** Constant vigilance and prudence are recommended while using lignocaine with adrenaline in patients suffering from diabetes mellitus.

Keywords: Adrenaline, diabetes, extraction, lignocaine, vasoconstrictors

Introduction

The famous novelist George Orwell said that in the face of physical pain, there are no heroes. Visiting a dentist is dreaded even by the bravest of men and women. Thus, painless treatment is undoubtedly the ultimate aim of any dental procedure. Tooth removal is a common dental procedure in dental practice which is considered to be both stressful and painful for the patient. Local anaesthesia (LA) is the usual drug used in dentistry to reduce intraoperative pain. If the pain is controlled in an adequate manner, the outcome is far better with minimal psychological trauma to the patient.

LA is the pharmacological agent which causes reversible loss of sensation in the circumscribed area of the body.[1-4] Lignocaine, which is a habitually used local anaesthetic in dentistry, was introduced by Lofgren in the year 1943. The efficacy of lignocaine is improved by adding adrenaline as a vasoconstrictor. Adrenaline decreases the systemic absorption of the local anaesthetic and reduces blood loss during the surgical procedure.[5]

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In today's times, we are all in the midst of a perpetual rat race that leaves us with no time to pay attention to our mental and physical well-being. The modern lifestyle presents us with innumerable comforts and unhealthy options that make us an easy target for various chronic ailments. An increase in stress, lack of physical activity and modified food habits increase the incidence of diabetes mellitus.[6] Studies found a fivefold increase in serum plasma after injecting the local anaesthetic with adrenaline. Adding to this, stress, trauma, surgery and pain lead to the occurrence of metabolic and

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hormonal changes which increase the glucose level in the blood.[7] Adrenaline increases blood glucose by α-adrenergic inhibition of insulin.[8] Meechan recorded the rise in blood glucose following the injection of 30 ml of a local anaesthetic solution containing 1:200,000 adrenaline as neural blocks.[9] Taylor *et al*. found a significant increase of 400% in circulating plasma adrenaline concentrations in anaesthetised patients, in whom 4 ml lignocaine with 1:200,000 adrenaline was injected locally before rhinoplasty.[10] Since lignocaine with or without adrenaline is one of the most commonly used local anaesthetics, we decided to undertake a study to observe its effects on blood glucose concentration in patients undergoing tooth extraction.

Materials and Methods

A single-centre, prospective, comparative clinical study was conducted in the Department of Oral and Maxillofacial Surgery. Approval from the institutional research and ethical committee was obtained to conduct this study (Approval No: 290/MGPGI/ACA-1/2019-20/437). All procedures performed in the study were conducted in accordance with the ethical standards given in the 1964 Declaration of Helsinki as revised in 2013. One hundred patients were selected from the outpatient department of the institute. Individuals undergoing simple multiple extractions of teeth and who were willing to give informed consent were included in the study. The study was conducted between June 2018 and June 2019.

Patients with systemic disorders, requiring surgical extractions, pregnant women and patients with pre-operative blood glucose levels of more than 150 mg/dl were excluded from the study.

Confounding variables in the study were the other effects of adrenaline on the blood vessels and blood pressure like an increase in the rate and force of contraction of the heart and a rise in blood pressure.

For each patient, the treatment was carried out in two appointments. The patients were scheduled in the morning. The patients were advised to have their normal breakfast, identical in content and quantity, on both appointments.

First appointment

- **Technique** I – extractions under lignocaine without adrenaline (plain).

Subsequent appointment

- **Technique** II – extractions under lignocaine with adrenaline (1:200,000).

Serial blood glucose estimations were carried out at identical intervals on both occasions.

Procedure for blood glucose estimation

The patient was seated comfortably and the first reading of blood glucose concentration was taken before administration of LA. Blood was drawn by pricking the finger tip with a sterile lancet and peripheral blood glucose was estimated using a glucometer.

At each appointment, a maximum of 2.5 ml of local anaesthetic solution was administered to each patient. After 10 min of local anaesthetic administration, peripheral blood glucose estimation using the glucometer was repeated. Further, reading was obtained 20 min after local anaesthetic administration (a total of three readings per procedure).

Blood glucose analysis

The device used for blood glucose analysis was the Accu-Chek system which uses the latest blood glucose monitoring technology. It measures the glucose content of a blood sample by means of an electrical current produced in the test strip and sent to the meter for measurement. Test results are 'plasma-calibrated'. This glucometer can display results in two different units of measurement – milligrams per decilitre and millimoles per litre. Their result ranges from 10 to 600 mg/dl.

An unpaired *t*-test was used for finding the statistically significant relationship between adrenaline in LA and blood sugar levels.

Results

The present study compared the blood glucose concentration in 100 healthy individuals undergoing multiple extractions. During the first appointment, extraction was done using lignocaine without adrenaline (plain) and for the second appointment, extraction was done using lignocaine with adrenaline (1:200,000). The blood glucose, irrespective of stress, rose during the dental extraction procedure when performed under lignocaine with adrenaline. An unpaired *t*-test was used for statistical analysis.

Table 1 shows that there is a significant difference in blood glucose level when the patients received lignocaine with adrenaline before administration and after 10 min with a mean difference of 3.17 in glucose level and a $P = 0.03$. Similarly, a significant difference was also noted after 20 min of administration with a $P \leq 0.001$ as shown in Table 2. However, the difference is not significant when the patients received lignocaine without adrenaline.

Discussion

Tooth extraction is one of the routine dental procedures which require a pain-control mechanism on an adequate level. LA is commonly used to facilitate pain control. LA produces reversible loss of sensation by blocking nerve impulse transmission.[11] Lignocaine is the gold standard local anaesthetic in dentistry. Lignocaine can be used solitarily as plain LA, or it can be used in combination with adrenaline. Plain lignocaine is a potent vasodilator with the anaesthetic effect being poor and lasting only a short while.[12] Hence, in a bid to increase the efficacy of the local anaesthetic, adrenaline is used as vasoconstrictors in varying concentrations of 1:50,000, 1:80,000, 1:100,000,1:200,000. Adrenaline increases the depth of anaesthesia, shortens its onset, minimises systemic toxicity and reduces blood loss during the procedure. The

Table 1: Blood glucose concentration of patients undergoing tooth extraction under local anaesthesia (before administration and 10 mins after administration of local anaesthesia) with and without adrenaline (*n*=100)

Group	Time points	Mean	SD	95% CI	Test value	*P*
Without adrenaline	Before administration of LA	123.41	16.90	120.06-126.76	1.66	0.09
	10 min after administration of LA	125.98	18.96	122.22-129.74		
With adrenaline	Before administration of LA	122.58	18.19	118.97-126.19	1.02	0.03
	10 min after administration of LA	125.75	19.31	121.92-129.58		

SD: Standard deviation, CI: Confidence interval, LA: Local anaesthesia

Table 2: Blood glucose concentration of patients undergoing tooth extraction under local anaesthesia (before administration and 20 mins after administration of local anaesthesia) with and without adrenaline (*n*=100)

Group	Time points	Mean	SD	95% CI	Test value	*P*
Without adrenaline	Before administration of LA	123.41	16.90	120.06-126.76	2.22	0.02
	20 min after administration of LA	127.40	20.30	123.37-131.43		
With adrenaline	Before administration of LA	122.58	18.18	118.97-126.19	5.14	0.001
	20 min after administration of LA	131.85	21.98	127.49-136.21		

SD: Standard deviation, CI: Confidence interval, LA: Local anaesthesia

maximum advised dose of adrenaline in LA for a healthy patient is 0.2 mg, and in a cardiac patient is 0.04 mg.[13,14] Lignocaine with adrenaline has a duration of action of 2–3 h.

In today's times, diabetes is a quotidian customer that knows no international boundaries. Prolonged hyperglycaemia leads to serious damage that adversely targets organs. Psychological stress and anxiety on account of pain contributed by injections increase endogenous adrenaline secretion. Moreover, adrenaline in the LA acts as exogenous adrenaline.[15,16] Adrenaline contained in one to three cartridges of local anaesthetic (0.018–0.054 mg) may be enough to significantly increase the risk of complications (ketoacidosis and hyperglycaemia) in patients with unstable diabetes.[17]

Adrenaline increases the blood glucose concentration by its action on the α2-adrenergic receptor in beta cells of islets of Langerhans in the pancreas and reduces insulin secretion.[18] It also stimulates glycogenolysis through adrenergic stimulation of β receptors and results in the activation of cAMP-dependent phosphorylation. Adrenaline decreases glucose utilisation by tissues, indirectly by decreasing insulin release.[18] The stimulation of β adrenergic receptor also leads to glycogenolysis and gluconeogenesis as well as inhibition of the hepatic glycolysis mechanism.[19] This study addresses the impact of plain LA and LA with adrenaline (1:200,000) on blood sugar levels. Patients who had to undergo simple tooth extraction requiring multiple sittings were included in this study. The measurements of the abovementioned parameter were performed before and immediately after the administration of the drug, at 10 min and 20 min intervals. Adherence to this was necessitated because epinephrine produces its maximum action 3 min after injection

In our study, the same patients are included in both groups so that the patients experienced the same stress level and control the result of the study.

All 100 patients were included in both groups (lignocaine without adrenaline and lignocaine with adrenaline). The pre-operative blood glucose level and blood glucose levels at 10 min and 20 min after administration of LA were obtained in both groups, and the values were compared.

On comparing the values, it was found that there was a significant disparity in the group which received lignocaine with adrenaline at 10 min with a mean difference of 3.17 and $P = 0.03$, and at 20 min the mean difference was 9.27 and a $P > 0.001$. When comparing the blood glucose level change at 10 min and 20 min after LA administration, a significant level increase in blood glucose was found at 20 min in the lignocaine group with an adrenaline mean difference of 6.1 and $P > 0.001$.

Our study evinces that there is a significant increase in the level of blood glucose concentration when lignocaine with adrenaline 1:200,000 concentration is administered.

However, the mean blood glucose is highest at 20 min among the group with adrenaline in LA.

We have subjected the same patients under the same circumstances, time, nutrition and environment for injections of plain lignocaine and lignocaine with adrenaline. Thus, the settings can be considered to be standardised. Hyperglycaemic responses to lignocaine with adrenaline can therefore be safely attributed to the action of adrenaline; in all probability through the mechanisms that are outlined above. It can be accepted that the injection of lignocaine with adrenaline causes an increase in blood glucose concentration. The effect described should not be a danger to well-controlled diabetics including those on insulin, as it is transient, but would definitely be a cause of concern to patients with Type 2 diabetes. The results suggest that when considering the systemic effects of local anaesthetic injections, metabolic as well as haemodynamic changes should be investigated.

Byakodi *et al*. have observed increased blood sugar levels by the administration of LA with adrenaline.[20]

Khawaja *et al*. while evaluating the effect of adrenaline on blood glucose levels concluded that blood glucose level alterations in the pre-extraction and post-extraction phases are observed only in those diabetic patients who were not on antidiabetic therapy. They found it safer to use adrenaline in healthy persons and those diabetic individuals who are on medicinal therapy.[21]

Meechan[9] in his study found a significant rise in blood glucose concentration after injecting 30 ml of LA with 1:200,000 adrenaline while the hyperglycaemic effect of adrenaline occurred at plasma concentration 4–5 times basal level.[22,23]

Our study buttresses the results published by Meechan[9] and Salonen *et al*. which reveals significant changes in blood glucose level when administering lignocaine with 1:200,000 adrenaline.[24]

Kaur *et al*. study also evince the same imperative change in blood glucose concentration in healthy and controlled Type 2 diabetic patients.[25] Goel *et al*. found that adrenaline-containing local anaesthetic solutions alter the blood glucose levels in those diabetic patients who are not on antidiabetic therapy.[26]

Pradeep *et al*. compared the changes in blood glucose levels associated with the administration of adrenaline-containing local anaesthetic in diabetic and non-diabetic patients undergoing minor oral surgical procedures. The study concluded that it is safe to administer local anaesthetic containing 1:100,000 adrenaline in smaller volumes (single nerve block or infiltration) to well-controlled diabetic patients without causing acute hyperglycaemia.[27]

Qaranizade *et al*. stated that using LA during tooth extraction does not induce hypoglycaemia and could increase the serum blood glucose level in individuals.[28] Similarly, Santos-Paul *et al*. conclude that the use of adrenaline (1:100,000) with local anaesthetics does not increase the risk of hyperglycaemia and haemodynamic repercussions.[29]

From our study, we can conclude that adrenaline (1:200,000) containing local anaesthetic solutions significantly alter the blood glucose levels in normal healthy patients. Thus, precautions have to necessarily be taken while administering the same to diabetic patients. We propose further studies with larger sample sizes, study groups and parameters. This would prove vital in conducting a detailed study to analyse the effect of various components of local anaesthetic solutions on the metabolic status of the body.

It is believed that the presence of epinephrine in local anaesthetic increases the duration of LA, decreases the risk of toxicity and provides haemostasis. However, the unfavourable effects are increased heart rate, raised blood pressure and blood sugar levels. The aim of the study was to evaluate the effect of LA with adrenaline and sans adrenaline on blood glucose levels in patients undergoing the process of routine tooth extraction.

The study conducted on 100 patients, revealed a significant increase in blood sugar levels after the administration of LA with adrenaline in healthy patients, and this increase in a diabetic patient can be hazardous.

Conclusion

We would like to conclude that local anaesthetic solutions with adrenaline injected in clinical doses can exert a systemic metabolic response and these effects are still seen in patients under some stress. While assessing the generalised effects of local anaesthetic solutions, metabolic as well as haemodynamic responses should be investigated. Lignocaine-containing adrenaline should be used with caution in Type 2 diabetic mellitus patients. Constant vigilance and prudence are recommended while using lignocaine with adrenaline in medically compromised patients, the basic nature of which is akin to that of a double-edged sword.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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