Comparative Evaluation of Local Anaesthesia with Adrenaline and Without Adrenaline on Blood Glucose Concentration in Patients Undergoing Tooth Extractions

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Abstract

Background Lignocaine hydrochloride is the most widely used and easily available local anaesthetic agent. Adrenaline is frequently combined with lignocaine to enhance the duration of anaesthesia, decrease toxicity, to achieve vasoconstriction and to provide a bloodless field.

Aim and Objective This study was conducted to do the comparative evaluation of local anaesthesia with adrenaline and without adrenaline on blood glucose concentration in patients under going tooth extraction.

Materials and Method The study was conducted on 120 patients comprising of 60 healthy and 60 diabetic patients. All these patients were in need of multiple extractions. The patients were in the age group of 18–50 years. On their first visit the patients were given plain lignocaine and tooth extraction was carried out. One week later the same patient was given lignocaine with 1:80,000 adrenaline to carry out tooth extraction. Serial blood glucose estimations were done at definite intervals (prior to administration of local anaesthetic, immediately after injecting the LA, 10 and 20 min following the injection of LA) on both the occasions.

Results The mean blood glucose concentration increased from the base line level of 84.81 to 85.09 mg/dl in healthy patients and from 206.82 to 207.09 mg/dl in diabetic patients 10 min following the injection of 2% plain lignocaine. This increase in blood glucose concentration following the administration of plain lignocaine was statistically not significant ($P > 0.05$). There was statistically significant ($P < 0.005$) increase in the blood glucose concentration from 88.81 to 105.55 mg/dl in healthy, and 208.77 to 242.46 mg/dl in diabetic patients 20 min following the injection of lignocaine with adrenaline.

Interpretation and Conclusion While assessing the generalized effects of local anaesthetic solutions, metabolic as well as haemodynamic responses should be investigated. Adrenaline containing LA should be used with caution in Type 2 diabetics as adrenaline causes suppression of insulin release.

Keywords Adrenaline · Blood glucose concentration · Diabetic · Lignocaine

Introduction

Pain is a nearly ubiquitous phenomenon—a fact of everyday life. Pain is the chief symptom that brings patients to dental or medical attention. Local anaesthetics are frequently used by the dental surgeon to control intra-operative pain. An oral surgeon has to use local anaesthetics for most minor surgical procedures. Increase in stress, decrease in physical activity, irregular food habits, consumption of nutritionally poor food have a detrimental effect on a person's health. All these factors and many more have increased the incidence of juvenile and maturity onset

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diabetes on one hand and the use of hypoglycemics on the other [1]. Since lignocaine with or without adrenaline is one of the most commonly used local anaesthetics in our country, we decided to undertake a study to observe its effects on blood glucose concentration in patients undergoing tooth extraction. Most dental treatments are performed under local anaesthesia, and an increase in blood pressure is common even in normotensive patients. This increase is influenced by many factors, such as psychological and physical stress, painful stimuli and the action of catecholamine present in local anaesthetic [2]. There is considerable information available concerning the haemodynamic effect of vasoconstrictors in dental local anaesthetic solutions, in both healthy and medically compromised individuals. There is, however, little data on systemic metabolic effects attributable to the injection of local dental anaesthetics. Before the start of the study, a clear clinical protocol was designed and ethical clearance was obtained from the committee constituted by the institute (SDM College of Dental Sciences and Hospital, Dharwad). Each patient was informed about the study protocol and a written informed consent was obtained.

Materials and Methods

A total of 120 patients between 18 and 50 years of age, requiring multiple extractions in different quadrants seen in the Oral and Maxillofacial Surgery department of SDM College of Dental Sciences and Hospital, Dharwad were included in the study. Of these, 60 were controlled Type 2 diabetic patients, while the remaining 60 were healthy controls.

Armamentarium:

1. Glucometer.
2. Sterile lancet.
3. 2% lignocaine (plain).
4. 2% lignocaine (adrenaline 1:80000).
5. Disposable syringe (5 ml).

Selection criteria for healthy patients:

1. Healthy patients without any systemic disorders.
2. Patients requiring multiple extractions.
3. Patients should not have been on any medications for a medical problem.

Selection criteria for controlled diabetics:

1. Patients with controlled Type 2 diabetes (non-insulin dependent).
2. Patients requiring multiple extractions.
3. Patients should not have been receiving any other medication other than oral hypoglycemics.

The procedures were divided into two groups, namely:

Group A: Plain lignocaine.

Group B: lignocaine with adrenaline (1:80000).

Study Design

For each patient, the treatment was carried out in two appointments, with a gap of 1 week between appointments. The patients were scheduled in the morning between 10 and 10.30 AM. The patients were advised to have their normal breakfast, identical in content and quantity, on both appointments.

At the first treatment appointment, tooth extraction was carried out under plain lignocaine (Group A). At the second treatment appointment, scheduled 1 week later, the remaining extractions were carried out under lignocaine with adrenaline (Group B). Serial blood glucose estimations were carried out at identical intervals on both occasions.

Procedure for Blood Glucose Estimation

The patient was seated comfortably and first reading of blood glucose concentration was taken before administration of local anaesthesia. Blood was drawn by pricking the finger tip with a sterile lancet and peripheral blood glucose was estimated by using a glucometer. At each appointment a maximum of 2 ml local anaesthetic solution was administered to each patient in the form of nerve blocks.

Immediately after local anaesthetic administration, peripheral blood glucose estimation using the glucometer was repeated. Further readings were obtained 10 and 20 min after local anaesthetic administration (a total of four readings per procedure).

Blood Glucose Analysis

The device used for blood glucose analysis was One Touch Ultra™ 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. This glucometer is able to read a minimal sample of 1 µl. The result ranges from 20 to 600 mg/dl.

Reagent Composition

Each One Touch Ultra Test Strip contains: Glucose oxidase (*Aspergillus niger*). The vial cap contains approximately 1.4 silica gel or 2.8 g of molecular sieve.

Results and Observations

The present study compared the blood glucose concentration in 60 healthy and 60 controlled diabetic patients in Group A (2% plain Lignocaine) and Group B (2% Lignocaine with 1:80000 adrenaline).

The blood glucose, irrespective of stress, rose during the dental extraction procedure when performed under lignocaine with adrenaline.

Healthy Individuals

Table 1 shows comparison of blood glucose concentration between plain lignocaine and lignocaine with adrenaline in healthy patients. Statistically significant difference was found ($P < 0.005$) at the 10 min reading. Highly significant mean difference was found in the blood glucose level at 20 min ($P < 0.001$) (Fig. 1).

Controlled Diabetics

Table 2 shows a comparison of blood glucose concentration between plain lignocaine and lignocaine with adrenaline in controlled diabetic patients.

The blood glucose concentration was higher in lignocaine in adrenaline when compared to plain lignocaine with a mean difference of 24 mg% at 10 min. This was statistically significant ($P < 0.05$). When comparing baseline value with the value at 20 min interval, statistically highly significant difference in the blood glucose concentration was observed ($P < 0.005$) (Fig. 2).

Plain Lignocaine

Table 3 shows the blood glucose levels for the healthy and diabetic patients with plain lignocaine recorded at four intervals.

A rise in blood glucose levels was observed from the baseline level at 2 intervals in healthy patients, i.e. immediately after injecting the LA and 10 min after injecting the LA (0.19 and 0.10 mg%, respectively). The magnitude of increase was, however, not statistically significant.

Fig. 1 Comparison of blood glucose concentration in healthy patients in Group A and Group B

In diabetic patients too, a difference in the blood glucose level from the baseline level was seen at each interval, but the difference was not statistically significant (0.30 and 0.20 mg%) (Fig. 3).

Lignocaine with Adrenaline

Table 4 shows variations in blood glucose levels for the healthy and diabetic patients when treated under lignocaine with adrenaline.

Statistically highly significant difference was observed in the level of blood glucose from the base line level measured at two intervals (10 and 20 min after anaesthetic injection) in both healthy (10.3 and 16.7 mg%) and diabetic patients (21.0 and 33.7 mg%) (Fig. 4).

Discussion

Vasoconstrictors are used in local anesthetic solutions to retard their systemic absorption. This enhances the local anesthetic effect by localizing it to the site of injection, decreases toxicity by retarding systemic absorption, prolongs the duration of anaesthesia, and may decrease the total dose of the local anaesthetic drug required [3]. Another secondary advantage to the use of vasoconstrictors in local anesthetic solutions is in the control of bleeding or

Table 1 Comparison of blood glucose concentration in healthy patients in Group A and Group B

	Group A		Group B		Unpaired <i>t</i> -value	<i>P</i> -value	Sig.
	Mean	SD	Mean	SD			
Bld. sug. before LA	84.9953	10.8482	88.8127	13.0584	−1.2316	0.2231	NS
Bld. sug. after LA	85.1800	10.8789	90.3283	13.0544	−1.6594	0.1024	NS
10 min after LA	85.0913	10.8740	99.1237	13.0229	−4.5302	0.0000	S
20 min after LA	84.6670	10.8114	105.5583	12.9136	−6.7942	0.0000	HS

Table 2 Comparison of blood glucose concentration in diabetic patients in Group A and Group B

	Group A		Group B		Unpaired <i>t</i> -value	<i>P</i> -value	Sig.
	Mean	SD	Mean	SD			
Bld. sug. before LA	206.8227	29.4542	208.7780	29.1464	−0.2585	0.7970	NS
Bld. sug. after LA	207.1393	29.4505	213.3190	28.9664	−0.8194	0.4159	NS
10 min after LA	205.8907	29.4317	229.7770	28.6754	−3.1839	0.0023	S
20 min after LA	205.6157	29.3536	242.4623	32.8689	−4.5797	0.0000	HS

Fig. 2 Comparison of blood glucose concentration in diabetic patients in Group A and Group B **Fig. 3** Comparison of blood glucose concentration in healthy and diabetic patients in Group A**Table 3** Comparison of blood glucose concentration in healthy and diabetic patients in Group A

	Healthy				Diabetes			
	Mean	SD	Diff. from baseline	Sig.	Mean	SD	Diff. from baseline	Sig.
Bld. sug. before LA	84.9953	10.8482	–	–	206.8227	29.4542	–	–
Bld. sug. after LA	85.1800	10.8789	0.1900	NS	207.1393	29.4505	0.3000	NS
10 min after LA	85.0913	10.8740	0.1000	NS	207.0907	29.4317	0.2000	NS
20 min after LA	84.6670	10.8114	−0.3300	NS	205.6157	29.3536	−1.2000	NS

haemostatic effect that the vasoconstrictor provides [3]. Meehan JG recorded the rise in blood glucose following the injection of 30 ml of local anesthetic solution containing 1:200,000 adrenaline as crural blocks [2].

However, it has been reported that the hyperglycaemic effect of adrenaline occurs at plasma adrenaline concentration 4–5 times basal levels, i.e. at values of 150–200 pg/ml [4].

Such concentrations may be obtained shortly after the injection of clinical doses of adrenaline containing local anesthetic [5].

In the present study, an attempt was made to evaluate the blood glucose levels in both healthy and diabetic patients undergoing extractions in the age group 18–50 years under local anesthesia. A standard protocol was followed for the dental extractions. The procedures were completed within 20–30 min. The procedures were

divided into two groups, Group A and Group B (plain lignocaine, and lignocaine with adrenaline) and each patient was subjected to similar procedure under both the groups, but 1 week apart.

With 2% lignocaine without adrenaline, though there was hyperglycemia, it was clinically insignificant (Table 3) and maybe attributed to endogenous catecholamine release, whereas the values observed 20 min after administration of plain lignocaine were less than baseline values. The blood glucose level increased from mean baseline value of 84.99 to 85.18 in healthy patients and from 206.82 to 207.13 in diabetic patient (obtained immediately after LA administration). Though not significant this slight increase may be attributed to the stress induced catecholamine release.

In lignocaine with adrenaline, however, there was a highly significant increase in blood glucose concentration observed 10 and 20 min after administration, in both

Table 4 Comparison of blood glucose concentration in healthy and diabetic patients in Group B

	Healthy				Diabetes			
	Mean	SD	Diff. from baseline	Sig.	Mean	SD	Diff. from baseline	Sig.
Bld. sug. before LA	88.8127	13.0584	–	–	208.7780	29.1464	–	–
Bld. sug. after LA	90.3283	13.0544	1.5000	NS	213.3190	28.9664	4.6000	S
10 min after LA	99.1237	13.0229	10.3000	HS	229.7770	28.6754	21.0000	NS
20 min after LA	105.5583	12.9136	16.7000	HS	242.4623	32.8689	33.7000	NS

Fig. 4 Comparison of blood glucose concentration in healthy and diabetic patients in Group B

healthy and diabetic patients. In healthy patients blood glucose concentration increased from 88.8 (baseline value) to 105.5 (mean value) at 20 min. In controlled diabetic patients, the blood glucose concentration increased from 208.77 (baseline value) to 242.46 (mean value) after 20 min. These observations indicate a highly significant increase in blood glucose concentration in both healthy and controlled Type 2 diabetic patients when adrenaline containing local anaesthetic was administered.

When extractions of a similar complexity were carried out under plain lignocaine (Group A), a decrease in blood glucose levels from baseline values was observed in both the healthy and diabetic patients, except in the period immediately after injection of local anaesthesia.

The difference between treatments can confidently be attributed to the local anaesthetic solution as all other parameters were carefully controlled. Thus, the increase in the blood glucose level in the patient receiving local anaesthesia with adrenaline can be contributed to the adrenaline present in the local anaesthetic. This finding coincides with the results published by Meechan et al. [2] and Markku et al. [6]. Physical and emotional stress is also known to increase blood glucose levels and theoretically, it has been proven that pain from injection, per se, can stimulate endogenous epinephrine release, which might, in turn, increase the blood glucose level. Dionne et al. studied the circulating adrenaline levels in sedated and non sedated

patients having third molar surgery under local anesthesia without adrenaline and found that diazepam attenuates the sympatho adrenal response to surgical stress, while adrenaline containing local anaesthetics result in increased circulating adrenaline levels.

Since the same patient was treated at both the appointments and procedures were carried out under local anaesthesia without any sedation, the effect of stress on the projected result has been controlled in our study. This finding supports the findings of Dionne et al. [4].

Adrenaline increases blood glucose levels probably due to the following reasons:

1. Reduction in insulin secretion by the action of $\alpha 2$ adrenergic receptors causing inhibition of β cells of the islets of langerhans in the pancreas [7].
2. Stimulation of glycogenolysis via adrenergic stimulation of β receptors resulting in cyclic AMP-dependent activation of phosphorylation.
3. Decrease in glucose utilisation both directly by affecting peripheral tissue glucose uptake and indirectly by decreasing insulin release [7].
4. β -Adrenergic mediated increase in glucagon concentration. Glucagon increases glucose production by stimulating glycogenolysis and gluconeogenesis and inhibiting hepatic glycolysis [8].
5. β -Adrenergic stimulation causes skeletal muscles glycogenolysis thereby increasing the lactate concentration, which thus become available for hepatic gluconeogenesis.

Since we have subjected the same patients under the same sets of circumstances, time, nutrition and environment to injections of plain lignocaine and lignocaine with adrenaline, the settings can be considered to be standardized.

The hyperglycemic responses to lignocaine with adrenaline can therefore be safely attributed to the action of adrenaline, probably through the mechanisms that are outlined above. Therefore, 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, especially those on insulin, as it is

transient, but would definitely be a cause of concern to patient with Type 2 diabetics. The results suggest that when considering the systemic effects of local anaesthetic injections metabolic as well as hemodynamic changes should be investigated.

Hypoglycaemia is a common problem that arises on the dental chair and is one of the causes for vasovagal syncope [9]. As a corollary to this finding, it is logical to infer that vasovagal syncope could also be prevented by injecting local anesthetic with adrenaline as significant increase in blood glucose (mean 33 mg%) after injecting local anesthetic with adrenaline was observed in the present study.

Summary and Conclusion

The present study was undertaken to evaluate and compare changes in blood glucose concentration in two groups, Group A (plain lignocaine) and Group B (lignocaine with adrenaline, 1:80,000). The study comprises of 120 patients divided under two categories:

1. Healthy patients under going dental extractions.
2. Controlled Type 2 diabetic patients undergoing dental extractions.

It was observed that:

1. In patients receiving plain lignocaine, there was a decrease in blood glucose concentration except mild hyperglycemia observed immediately after injection in both healthy and diabetic patients. The use of local anaesthetic with adrenaline produced a significant increase in blood glucose concentrations among both healthy and controlled diabetic subjects.
2. Initial increase in blood glucose concentration during the operative procedures under plain local anaesthesia (immediately and after 10 min) can be attributed to the stress related hormonal response and endogenous catecholamine release which invariably results in hyperglycaemic episode.
3. In the adrenaline containing local anaesthesia group, the levels of blood glucose were found to be

comparatively higher. This added response can only be due to the adrenaline content of local anaesthesia.

From the results of the present study we conclude that:

1. Local anaesthetic solutions injected in clinical doses can exert systemic metabolic responses and that these effects are still apparent in patients under some degree of stress.
2. While assessing the generalized effects of local anaesthetic solutions, metabolic as well as hemodynamic responses should be investigated.
3. Lignocaine containing adrenaline should be used with caution in Type 2 diabetic patients.

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