

Hemodynamic and Glycaemic Safety of Two Local Anaesthetic Agents during Intra-Alveolar Tooth Extraction: A Comparison

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ABSTRACT

Introduction: There have been some controversies in the literature about the effect of Local Anesthetic (LA) solutions with and without adrenaline on plasma glucose and hemodynamics during dental treatment. The purpose of this study was to investigate and compare the hemodynamic and metabolic effects of two local anesthetic agents in patients undergoing intra-alveolar tooth extraction.

Methods: All medically fit normotensive and nondiabetic patients were included and randomized into two groups. Participants had breakfast before coming in for tooth extraction. The blood pressure, pulse rate, respiratory rate, and temperature were measured pre-anesthesia and 10 and 15 minutes post administration of local anesthesia and blood glucose was measured before and 30 min after administration of local anesthetic agents.

Results: Both groups showed a modest increase in their blood glucose and systolic pressure post administration of local anesthesia, while there was neither statistically significant increase nor decrease in the pulse rate, respiratory rate, and temperature in both groups. There was an increase in the systolic pressure at 10 minutes post-extraction, after which a gradual downward trend towards the baseline value was observed in both.

Conclusion: Adrenaline containing bupivacaine and lidocaine appears to have minimal hemodynamic and glycemic effect when used as LA agents in patients undergoing intra-alveolar tooth extraction.

Keywords: Hemodynamic; Local anesthetic; Blood glucose; Tooth extractions

INTRODUCTION

The effects of local anesthetic solutions with or without adrenaline on plasma glucose and hemodynamics during dental treatment have generated a lot of controversies in the literature. Although many studies have been conducted previously with regard to this issue, no conclusive evidence has been reached [1-6].

No significant changes in the plasma concentration of glucose pre and post-operatively was observed when Tily and Thomas compared the effect of local anesthetic agents containing adrenaline on blood glucose concentration in healthy and diabetic patients, they concluded that dental local anesthetics containing adrenaline can be safely used in healthy and diabetic patients Also did not find any significant difference in plasma

glucose between pre and post administration of local anesthetic agents for extraction [7,8].

However, some studies have shown that there are changes in blood glucose after administering clinical doses of dental local anesthetics containing epinephrine.

Increased systemic blood pressure, heart rate and plasma glucose concentration when they investigated the effects of local anesthetic agents on systemic blood pressure, plasma catecholamine, plasma glucose, and insulin concentration in eleven normotensive patients during dental surgery, this they attributed to activation of sympathetic adrenal outflow by local anesthetic solution and extraction [2].

Similarly, Meechan also reported a significant increase in blood glucose at 10 and 20 min following the injection of a local

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anesthetic solution containing epinephrine when this is compared with the baseline and epinephrine-free solution [9].

Naveed in another study did not observe any glycemic change in healthy as well as diabetic patients who had taken their hypoglycemic medication but observed an increase in plasma glucose of diabetic patients who were not compliant with their hypoglycemic medication [6].

While some studies reported no change in blood pressure with the administration of adrenaline-containing local anesthetics some studies, however, showed that there was a decrease in heart rate between 15 and 30 minutes which was statistically significant for both Bupivacaine and Lidocaine.

This reduction in heart rate has been attributed to the result of the decrease in endogenous catecholamine associated with the termination of the surgical procedure [1,10-14].

MATERIALS AND METHODS

The study was approved as a prospective, randomized, double-blind, clinical trial by UI/UCH Ethical Review Committee. It was carried out at the maxillofacial surgery department of the University College Hospital Ibadan between September 2015 and August 2016.

Consecutive adult patients (18 years and above) who presented to the department for intra-alveolar tooth extraction and who did not have a history of any reaction to local anesthetic agents and showed willingness and has given consent to participate in the study were included.

Exclusion criteria included pregnancy, uncontrolled underlying systemic disease like; diabetes mellitus, cardiovascular disease, liver or renal disease, uncontrolled major depression and any other psychiatric disorders as well as inability to understand the demands of the study.

The sample size was calculated using the formula:

$$n = (Z \alpha / 2 + Z \beta)^2 [P1 (1-P1) + P2 (1-P2)] / (P1 - P2)^2$$

According to this, the sample size was calculated as 120 patients per group (i.e. a total of 240 subjects)

The subjects were randomly assigned to 2 groups: (A and B) (Those who received one cartridge (1.8 ml) of either 0.5% Bupivacaine with 1:200,000 epinephrine or 2% Lidocaine with 1:100,000 epinephrine as the local anesthetic agent for the extraction) using Computer-generated randomization method (Winpepi 235, version 11.4).

The details of the study including, the extraction procedure, measurement of vital signs and blood glucose were explained to the subjects pre-operatively. Double blinding in which both the subjects and the surgeon (researcher) performing the extraction was blinded was used. The local anesthetic labels were removed and the cartridges were then re-labeled A or B under aseptic condition. The patient and surgeon performing the extraction

were not aware of the local anesthetic agent in A or B. The procedure (tooth extraction) was carried out between the hours of 8:00 am and 11:00 am to subject the participant to almost the same environmental condition.

The same standard protocol and technique were used for all the extractions, the only 1.8 ml of 0.5% Bupivacaine with 1:200000 adrenaline and 1.8 ml of 2% Lidocaine with 1:100000 adrenaline was used. All subjects who received more than 1.8 ml were excluded.

Measurement of Blood pressure, Pulse rate, Respiratory rate, and Temperature was carried out at three-time points; immediately before the administration of the local anesthetic agent, and at 10 and 15 minutes respectively after the administration of local anesthetic agents.

Blood glucose was also measured immediately before the administration of a local anesthetic agent and 30 minutes after the administration of a local anesthetic agent.

RESULTS

A total of 252 subjects participated in the study between September 2015 and August 2016 with an average of two subjects per day.

The subjects were randomly allocated into two groups; One hundred and twenty-six subjects each were allocated to Lidocaine and Bupivacaine groups respectively.

Only 240 subjects were included in the analysis, 12 subjects did not meet up with the criteria for inclusion (Use of more than 1.8 ml local anesthetic agent, uncontrolled diabetics, uncontrolled hypertension, and history suggestive of allergy to any of the L.A).

There was an increase of 1-13 mg/dl in the blood glucose 30 minutes after the administration of local anesthetic agents (Table 1).

An increase in the systolic blood pressure was observed at 10 minutes (just before the extraction) and 15 minutes (just after the extraction) after the administration of local anesthetic agents (Table 2).

There was no change in diastolic pressure in 196 and 210 subjects at 10 minutes (just before the extraction) and 15 minutes (just after the extraction) respectively after administration of local anesthetic agents (Table 3).

No change in the respiration was observed in 174 and 199 subjects at 10 minutes (just before the extraction) and 15 minutes (just after the extraction) respectively after administration of local anesthetic agents (Table 4).

There was no change in pulse rate in 201 and 199 Subjects (Table 5) and body temperature in 222 and 229 subjects at 10 minutes (just before the extraction) and 15 minutes (just after the extraction) respectively after administration of local anesthetic agents (Table 6).

Table 1: Difference between pre-anesthetic random plasma glucose and random plasma glucose 30 minutes after administration of local anesthetic agents.

Increase in blood glucose	Local anesthetic agents		Total N (%)	X ²	p-value
	Lidocaine	Bupivacaine			
	n (%)	n (%)			
-6	0 (0.0)	1 (0.8)	1 (0.4)		
-3	0 (0.0)	6 (5.0)	6 (2.5)		
-2	0 (0.0)	2 (1.7)	2 (0.8)		
0	3 (2.5)	5 (4.2)	8 (3.3)		
1	9 (7.5)	1 (0.8)	10 (4.2)		
2	4 (3.3)	15 (12.5)	19 (7.9)		
3	0 (0.0)	7 (5.7)	7 (2.9)		
4	13(10.8)	9 (7.5)	22 (9.2)		
5	0 (0.0)	3 (2.5)	3 (1.2)		
6	6 (5.0)	8 (6.7)	14 (5.8)		
7	18 (15.0)	6 (5.0)	24 (10.0)		
8	9 (7.5)	15 (12.5)	24 (10.0)		
9	10 (8.3)	5 (4.2)	15 (6.3)		
10	8 (6.7)	12 (10.0)	20 (8.3)		
11	11 (9.2)	0 (0.0)	11 (4.6)		
12	3 (2.5)	0 (0.0)	3 (1.3)		
13	13 (10.8)	8 (6.7)	21 (8.8)		
14	6 (5.0)	3 (2.5)	9 (3.8)		
15	2 (1.7)	4 (3.3)	6 (2.5)		
16	3 (2.5)	0 (0.0)	3 (1.3)		
17	0 (0.0)	1 (0.8)	1 (0.4)		
18	2 (1.7)	5 (4.2)	7 (2.9)		
20	0 (0.0)	2 (1.7)	2 (0.8)		
27	0 (0.0)	2 (1.7)	2 (0.8)		
Total	120 (100.0)	120 (100.0)	240 (100.0)	87.034*	0.000*

*Likelihood Ratio

Table 2: Difference between pre-anesthetic systolic pressure and systolic pressure 10 minutes (just before the extraction) and 15 minutes (just after the extraction), after administration of local anesthetic agents.

Differences in the systolic pressure after administration of local anesthetics	Local anesthetic agent		Total	X ²	p-value
	Lidocaine	Bupivacaine	N (%)		
	n (%)	n (%)			
10 minutes	-9	0 (0.0)	3 (2.5)	3 (1.3)	
	-6	1 (0.8)	3 (2.5)	4 (1.7)	
	0	2 (1.7)	1 (0.8)	3 (1.3)	
	1	3 (2.5)	5 (4.2)	8 (3.3)	
	2	24 (20.0)	16 (13.3)	40 (16.6)	
	3	5 (4.2)	5 (4.2)	10 (4.2)	
	4	22 (18.4)	9 (7.5)	31 (12.8)	
	5	13 (10.8)	5 (4.2)	18 (7.5)	
	6	15 (12.5)	31 (25.8)	46 (19.2)	
	7	8 (6.7)	10 (8.3)	18 (7.5)	
	8	5 (4.2)	9 (7.5)	14 (5.8)	
	9	4 (3.3)	6 (5.0)	10 (4.2)	
	10	0 (0.0)	1 (0.8)	1 (0.4)	
	11	1 (0.8)	0 (0.0)	1 (0.4)	
	12	2 (1.7)	0 (0.0)	2 (0.8)	
	13	0 (0.0)	3 (2.5)	3 (1.3)	
	14	1 (0.8)	6 (5.0)	7 (2.9)	
	15	6 (5.0)	0 (0.0)	6 (2.5)	
	16	3 (2.5)	2 (1.7)	5 (2.1)	
	17	4 (3.3)	2 (1.7)	6 (2.5)	
	18	0 (0.0)	3 (2.5)	3 (1.3)	
21	1 (0.8)	0 (0.0)	1 (0.4)		
Total	120 (100.0)	120 (100.0)	240 (100.0)	52.846*	0.0001*
15 minutes	-4	0 (0.0)	3 (2.5)	3 (1.3)	
	-2	0 (0.0)	3 (2.5)	3 (1.3)	

0	9 (7.5)	16 (13.3)	25 (10.4)		
1	37 (30.8)	26 (21.7)	63 (26.2)		
2	28 (23.4)	14 (11.7)	42 (17.5)		
3	12 (10.0)	16 (13.3)	28 (11.6)		
4	0 (8.3)	8 (6.6)	18 (7.5)		
5	7 (5.9)	11 (9.2)	18 (7.5)		
6	9 (7.5)	9 (7.5)	18 (7.5)		
7	1 (0.8)	0 (0.0)	1 (0.4)		
8	0 (0.0)	7 (5.8)	7 (2.9)		
9	2 (1.7)	3 (2.5)	5 (2.1)		
10	1 (0.8)	2 (1.7)	3 (1.3)		
11	4 (3.3)	0 (0.0)	4 (1.7)		
12	0 (0.0)	2 (1.7)	2 (0.8)		
Total	120 (100.0)	120 (100.0)	240 (100.0)	38.634*	0.0001*

*Likelihood Ratio

Table 3: Difference between pre-anesthetic diastolic pressure and diastolic pressure 10 minutes (just before the extraction) and 15 minutes (just after the extraction), after administration of local anesthetic agents.

Differences in the diastolic pressure after administration local of anesthetic agents	Local anesthetic agents		Total	X2	p-value
	Lidocaine	Bupivacaine	N (%)		
	n (%)	n (%)			
10 minutes	-3	4 (3.4)	0 (0.0)	4 (1.7)	
	-2	1 (0.8)	6 (5.0)	7 (2.8)	
	-1	7 (5.8)	6 (5.0)	13 (5.4)	
	0	99 (82.5)	97 (80.8)	196 (81.6)	
	1	3 (2.5)	5 (4.2)	9 (3.7)	
	2	4 (3.3)	3 (2.5)	7 (2.8)	
	3	2 (1.7)	3 (2.5)	5 (2.0)	
Total		120 (100.0)	120 (100.0)	240 (100.0)	19.855* 0.047*
15 minutes	-4	1 (0.8)	0 (0.0)	1 (0.4)	
	-300	2 (1.7)	0 (0.0)	2 (0.8)	
	-2	2 (1.7)	2 (1.7)	4 (1.7)	

	-1	3 (2.5)	5 (4.1)	8 (3.3)		
	0	102 (85.0)	108 (90.0)	210 (87.5)		
	1	5 (4.1)	2 (1.7)	7 (2.9)		
	2	2 (1.7)	2 (1.7)	4 (1.7)		
	3	3 (2.5)	1 (0.8)	4 (1.7)		
Total		120 (100.0)	120 (100.0)	240 (100.0)	17.93*	0.118*

*Likelihood Ratio

Table 4: Difference between pre-anesthetic respiratory rate and respiratory rate 10 minutes (just before the extraction) and 15 minutes (just after the extraction), after administration of local anesthetic agents.

The difference in the respiration 10 and 15 minutes after administration of local anesthetic agents		Local anesthetic agents		Total N (%)	X2	p-value
		Lidocaine	Bupivacaine			
		n (%)	n (%)			
10 minutes	-2	10 (8.3)	9 (7.5)	19 (7.9)		
	-1	3 (2.5)	6 (5.0)	9 (3.8)		
	0	89 (74.2)	85 (70.8)	174 (72.5)		
	1	9 (7.5)	9 (7.5)	18 (7.5)		
	2	9 (7.5)	11 (9.2)	20 (8.3)		
Total		120 (100.0)	120 (100.0)	240 (100.0)	1.345	0.854
15 minutes	-2	3 (2.5)	8 (6.7)	11 (4.6)		
	-1	2 (1.6)	3 (2.5)	5 (2.1)		
	0	101 (84.2)	98 (81.7)	199 (82.9)		
	1	9 (7.5)	4 (3.3)	13 (5.4)		
	2	5 (4.2)	7 (5.8)	12 (5.0)		
Total		120 (100.0)	120 (100.0)	240 (100.0)	18.723	0.157

Table 5: Difference between pre-anesthetic pulse rate and Pulse rate 10 minutes (just before the extraction) and 15 minutes (just after the extraction), after administration of local anesthetic agents.

The difference in the respiration 10 and 15 minutes after administration of local anesthetic agents		Local anesthetic agents		Total N (%)	X2	p-value
		Lidocaine	Bupivacaine			
		n (%)	n (%)			
10 minutes	-2	3 (2.5)	3 (2.5)	6 (2.5)		
	-1	6 (5.0)	5 (4.2)	1 (4.5)		

	0	101 (84.2)	100 (83.3)	201 (83.8)		
	1	4 (3.3)	6 (5.0)	10 (4.2)		
	2	4 (3.3)	4 (3.3)	8 (3.3)		
	3	2 (1.7)	2 (1.7)	4 (1.7)		
Total		120 (100.0)	120 (100.0)	240 (100.0)	0.496	0.992
	-2	4 (3.3)	3 (2.5)	7 (2.9)		
	-1	5 (4.2)	6 (5.0)	11 (4.6)		
15 minutes	0	100 (83.4)	99 (82.5)	199 (82.9)		
	1	7 (5.8)	7 (5.8)	14 (5.8)		
	2	4 (3.3)	5 (4.2)	9 (3.8)		
Total		120 (100.0)	120 (100.0)	240 (100.0)	0.35	0.986

Table 6: Difference between pre-anesthetic temperature and temperature 10 minutes (just before the extraction) and 15 minutes (just after the extraction), after administration of local anesthetic agents.

Difference between pre-anesthetic temperature and temperature 10 minutes after administration of local anesthetic agents	Local anesthetic agents		Total	X2	p-value	
	Lidocaine	Bupivacaine	N (%)			
	n (%)	n (%)				
	-0.2	1 (0.8)	2 (1.7)	3 (1.3)		
	-0.1	3 (2.5)	2 (1.7)	5 (2.1)		
10 minutes	0	110 (91.7)	112 (93.3)	222 (92.5)		
	0.1	4 (3.3)	3 (2.5)	7 (2.9)		
	0.2	2 (1.7)	1 (0.8)	3 (1.3)		
Total		120 (100.0)	120 (100.0)	240 (100.0)	1.028	0.906
	-0.2	1 (0.8)	1 (0.8)	2 (0.8)		
	-0.1	2 (1.7)	1 (0.8)	3 (1.3)		
15 minutes	0	115 (95.8)	114 (95.0)	229 (95.4)		
	0.1	1 (0.8)	3 (2.5)	4 (1.7)		
	0.2	1 (0.8)	1 (0.8)	2 (0.8)		
Total		120 (100.0)	120 (100.0)	240 (100.0)	1.338	0.855

DISCUSSION

We found an average of 7.7 ± 5.3 mg increase in plasma glucose 30 minutes after the administration of both anesthetic agents. This increase is most likely due to enhanced hepatic glycogen breakdown orchestrated by the epinephrine in the local

anesthetic solutions and not pain, as all the subjects were pain-free as at the time of plasma glucose measurement. However, we cannot exclude the role of initial injection pain on catecholamine and subsequently on blood glucose in this study. We did not find any statistically significant difference between

Lidocaine and Bupivacaine group in this study ($p=0.157$), their glycemic effect was similar.

Our findings are similar to that of Meechan who reported a significant increase in blood glucose following the injection of an anesthetic solution containing epinephrine at 10 and 20 minutes [9]. It is also similar to that of Nakamura and colleagues who investigated the changes in plasma glucose and insulin concentration in normotensive patients during dental procedures under local anesthesia and reported increased plasma glucose concentration [2].

However, the finding is at variance with that of Akinmoladun et al. [3] that reported no significant increase in the plasma glucose in another similar study using Lidocaine and also different from that of Tily and coworkers who did not find any significant change in the plasma concentration of glucose pre and post-operatively when they compared the effect of adrenaline administration in the dental local anesthesia solution on blood glucose in healthy and diabetic patients [7].

About 95.8% and 87.1% of all the subjects had increased systolic pressure at 10 minutes and 15 minutes respectively, this is similar to the findings of Mohammad et al. [15] and the Bible who observed increase in systolic pressure following administration of both local anesthetic agents and there is no significant difference between Bupivacaine and Lidocaine in this study [15-17]. The increase observed in this study may be due to the vasoconstrictor effect of adrenaline on systolic blood pressure via increased heart rate and myocardial muscle contractility. Different observation to ours was made in similar studies in which there was no change in blood pressure with the administration of adrenaline containing local anesthetic agents [10,11,17].

We did not find any difference in diastolic pressure at measurement between Bupivacaine and Lidocaine as the presentation was similar. There was neither significant increase nor decrease in the diastolic pressure at 10 minutes (just before extraction) and 15 minutes (immediately after extraction) after the administration of local anesthetic agents in this study. This is similar to the findings of Ogunlewe and colleagues who did not find any change in diastolic blood pressure and thus concluded that local anesthetic agents with or without vasoconstrictor had no significant effect on patients [18].

However, our finding is at variance with that of Mohammad and colleagues, Ezmek and Bible (meta-analysis) who reported a statistically significant increase in diastolic pressure [15,16,19] and these changes have been attributed to either the agents themselves or to the dental anxiety in the patients.

We did not observe any change in the pulse rate both at 10 minutes (just before extraction) and 15 minutes (immediately after extraction) in both local anesthetic agents. This is an agreement with the findings of Ogunlewe and colleagues who did not observe any significant change in the pulse rate following the use of local anesthetic agents containing epinephrine [18]. Vijay, however, reported a statistically significant decrease in heart rate between 10 and 15 minutes for both Bupivacaine and Lidocaine [12] while Bible observed an increase in heart rate [16]. There is no significant difference in

pulse rate between the Lidocaine group and the Bupivacaine group ($p=0.992$ and 0.986 at 10 and 15 minutes respectively).

CONCLUSION

Hemodynamic effects of bupivacaine and lidocaine were similar to each other as there was no difference between their glycemic and hemodynamic effects. Both Local anesthetic agents caused an increase in plasma glucose, the only hemodynamic effect of Bupivacaine and Lidocaine was an initial rise in the systolic pressure at 10 minutes after injection which was returning to baseline measurement by 15 minutes. Both local anesthetic agents appear to be hemodynamically safe, at the tested percentage, to be used in a dental procedure.

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