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EFFECT OF LIGNOCAINE & ADRENALINE COMBINATION AS LOCAL ANESTHETIC ON ECG PARAMETERS

Annasaheb Gagare[1], Sinare B. R.*[2], Prashant Patel[3], Rahul Kunkulol[4] and Narwane Sandeep[5]

[1,2]Assistant Professor**,** Department of General Medicine.

[3]Assistant Professor, [4]Professor, [5]Associate Professor, Department of Pharmacology, Rural Medical College of Pravara Institute of Medical Sciences (Deemed to be University), Loni, Maharashtra, India.

***Corresponding Author: Dr. Sinare B. R.**

Assistant Professor, Department of General Medicine.

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ABSTRACT

Background: The effect of Ligocaine-Adrenaline combination as local anesthetic during dental procedures on healthy individuals has been scarcely studied. The objective of the study was to study effects of Lignocaine 2% & Adrenaline 1:80000 combination on various ECG parameters in dental patients without other co morbidities undergoing dental procedures. **Methods:** This was a prospective, observational clinical study done in collaboration with the Department of Oral & Maxillofacial Surgery, Rural Dental College & Hospital, Loni. Patients scheduled for oral surgeries under local anesthesia with Lignocaine and adrenaline combination of age 18 years or above of either gender willing to give written informed consent were included in the study. A standard 12-lead ECG (25 mm/s) was recorded for each patient before administration of drugs (Basal), during dental procedure (Intraoperative) and immediately after completion of surgical procedure. **Results:** Total 75 patients were included in the study. The increase in heart rate from basal (88.84 ± 7.77 beats per minute) to intra operative (89.52 ± 7.50) and postoperative (90.16 ± 7.41) was statistically significant. There was statistically significant decrease seen in the PR and RR interval when the basal, intra operative and post operative values were compared. There was statistically significant decrease in QT and QTc interval, QT and QTc dispersion. **Conclusion:** Effects of lignocaine-adrenaline combinations on electrocardiographic parameters are minimal and clinically irrelevant in healthy individuals.

KEYWORDS: Lignocaine & Adrenaline combination, Local anesthetic, ECG parameters.

INTRODUCTION

Local anesthetics are chemicals that reversibly block action potentials in all excitable membranes. The central nervous system and cardiovascular system are especially susceptible to their depressant actions.[1,2] Following systemic absorption, local anesthetics act on the cardiovascular system.[3,4] Local anesthetics decrease the electrical excitability of the myocardium, conduction rate, and force of contraction.[2] In addition, most local anesthetics cause arteriolar dilation. Local anesthetics are known to cause cardiovascular collapse and death, either due to its action on the pacemaker or the sudden onset of ventricular fibrillation.[3] Acceleration of the ventricular rate has been reported in patients with atrial arrhythmias.[5] Adrenaline is absorbed from the site of injection, just as is the local anesthetic. Resting plasma adrenaline levels are increased after administration of 1.8 ml of Lignocaine with 1:100000 adrenaline.[6,7,8] The effects of local anesthetics and sympathomimetic amines on human ECG have been extensively studied. The effects of the combinations, however, have not been studied well in healthy individuals. The present study was planned to evaluate the effects of Lignocaine and adrenaline combination on the ECG of healthy individuals.

The aim of the present study was to study the effects of Lignocaine 2% and Adrenaline 1:80000 combinations on various ECG parameters in patients undergoing dental procedures.

MATERIAL AND METHODS

This was a prospective, observational clinical study done in collaboration with the Department of Oral & Maxillofacial Surgery, Rural Dental College & Hospital, Loni. Patients planned for various oral surgeries under local anesthesia were enrolled for the study according to eligibility criteria. All patients scheduled for oral surgeries under local anesthesia with Lignocaine and adrenaline combination of age 18 years or above of either gender willing to give written informed consent were included in the study. Patients with history of hepatic, renal, cardiovascular and thyroid disorders were excluded from the study. Total 75 patients planned for dental surgeries under anesthetic cover of Lignocaine 2% & Adrenaline 1:80000 fixed dose combinations were

included in the study. The Demographic Profile of patients was recorded. A standard 12-lead ECG (25 mm/s) was recorded for each patient before administration of drugs (Basal), during dental procedure (Intraoperative) and immediately after completion of surgical procedure. ECG was recorded by same individual and same machine for a patient. The ECGs were analyzed qualitatively and quantitatively including measurements of the PR, RR and QT Interval. QTc interval was calculated by using the formulae of Bazett.[9] Any adverse effect in terms of cardiovascular morbidity was also noted.

RESULTS

Table 1: Age wise Distribution of Patients.

Age (in yrs)	No. of participants
18-40	28 (37.33%)
41-60	32 (42.67%)
> 60	15 (20.00%)

It was seen from **Table 1** that most of the patients (32 of 75) belonged to age group of 41-60 years age group, followed by 28 patients in 18-40 years age group. Forty patients were males while 35 patients were females.

Table 2: Dental procedures performed using Lignocaine and Adrenaline combination.

Procedure	No. of patients
Dental Extraction	14 (18.67%)
Impaction	14 (18.67%)
Alveoplasty	26 (36.67%)
Incision & Drainage of Abscess	9 (12.00%)
Mandibular Fracture Fixation	12 (16.00%)
Total	**75**

It was seen from **Table 2** that the patients undergoing the following dental procedures, viz. Dental extraction (14), Impaction (14), Alveoplasty (26), Incision & drainage of abscess (9) and Mandibular fraction fixation (12).

Table 3: Recordings of Mean Heart Rate, Mean PR Interval & Mean RR Interval from ECG at Basal, Intraoperative & Postoperative period.

	Heart Rate (per min) Mean ± SD	PR Interval (in seconds) Mean ± SD	RR Interval (in seconds) Mean ± SD
Basal	88.84 ± 7.77	0.150 ± 0.019	0.681 ± 0.060
Intraoperative	89.52 ± 7.50$	0.147 ± 0.018*	0.675 ± 0.057*
Postoperative	90.16 ± 7.41@	0.144 ± 0.018#	0.670 ± 0.056#

$: Significant, p<0.0001 (Basal vs. Intraoperative),
@: Significant, p<0.0001 (Basal vs. Postoperative)
*: Significant, p<0.0001 (Basal vs. Intraoperative),
#: Significant, p<0.0001 (Basal vs. Postoperative)

As shown in Table 3 that Basal, Intraoperative and Postoperative mean heart rate, mean PR interval & mean RR interval of patients. By applying Friedman test (Non-parametric Repeated Measures ANOVA test), there was highly significant increase in mean values of Heart rate when Basal compared to Intraoperative and Postoperative (p<0.0001). By applying Friedman test (Non-parametric Repeated Measures ANOVA test), there was highly significant decrease in mean values of PR Interval and RR Interval when Basal compared to Intraoperative and Postoperative (p<0.0001).

Table 4: Recordings of Mean QT Interval, Mean QTc Interval, Mean QT Dispersion & Mean QTc Dispersion at Basal, Intraoperative & Postoperative period.

	QT Interval (in seconds) Mean ± SD	QTc Interval (in seconds) Mean ± SD	QT Dispersion(in seconds) Mean ± SD	QTc Dispersion(in seconds) Mean ± SD
Basal	0.358 ± 0.032	0.434 ± 0.032	0.047 ± 0.016	0.057 ± 0.020
Intraoperative	0.353 ± 0.031$	0.430 ± 0.030$	0.044 ± 0.015*	0.053 ± 0.019*
Postoperative	0.349 ± 0.029@	0.427 ± 0.028@	0.041 ± 0.015#	0.050 ± 0.018#

$: Significant, p<0.0001 (Basal vs. Intraoperative),

@: Significant, p<0.0001 (Basal vs. Postoperative)
*: Significant, p<0.0001 (Basal vs. Intraoperative),
#: Significant, p<0.0001 (Basal vs. Postoperative)

As shown in Table 4 that the mean QT Interval, mean QTc Interval, mean QT dispersion & mean QTc dispersion at Basal, Intraoperative & Postoperative period. By applying Friedman test (Non-parametric Repeated Measures ANOVA test), there was highly significant decrease in mean values of QT Interval and QTc Interval when Basal compared to Intraoperative and Postoperative (p<0.0001). By applying Friedman test (Non-parametric Repeated Measures ANOVA test), there was highly significant decrease in mean values of QT Dispersion and QTc Dispersion when Basal compared to Intraoperative and Postoperative (p<0.0001). Out of 75 patients, 10 complained of palpitation, whose heart rate were found to be more than 100 heart beats per minute.

DISCUSSION

It is currently thought that the cardiovascular effects of conventional adrenaline doses are of little practical concern, even in patients with heart disease.[10] However, even following usual precautions (e.g., aspiration, slow injection), sufficient adrenaline can be absorbed to cause sympathomimetic reactions such as apprehension, tachycardia, sweating and palpitation.[11]

Dental practitioners use local anesthetic injections with various concentration of adrenaline. The basal mean heart rate in our study was 88.84 beat per minute. This increased to 89.52 beats per minute intraoperative & 90.16 beats per minute post-operative, which was highly statistically significant.

The basal PR interval observed was 0.150 sec which decreased to 0.147 sec intraoperative and 0.144 postoperative. Similarly the RR interval before drug administration was 0.681 sec which decreased to 0.675 sec intraoperative and 0.670 sec postoperative. By applying Friedman test (Non-parametric Repeated Measures ANOVA test), there was highly significant decrease in mean values of PR Interval and RR Interval when Basal compared to Intraoperative and Postoperative (p<0.0001).

The mean QT interval was 0.358 sec before drug administration, this decreased to 0.353 sec intraoperative and 0.349 sec postoperative. Similarly QTc interval was 0.434 sec before drug administration and decreased to 0.430 sec intraoperative and 0.427 sec postoperative. By applying Friedman test (Non-parametric Repeated Measures ANOVA test), there was highly significant decrease in mean values of QT Interval and QTc Interval when Basal compared to Intraoperative and Postoperative (p<0.0001).

The mean QT dispersion decreased from basal 0.047 sec to 0.044 sec intraoperative and 0.041 sec postoperative, while the QTc dispersion was 0.057 sec before drug administration and decreased to 0.053 sec intraoperative and 0.050 sec postoperative. By applying Friedman test (Non-parametric Repeated Measures ANOVA test), there was highly significant decrease in mean values of QT Dispersion and QTc Dispersion when Basal compared to Intraoperative and Postoperative (p<0.0001).

The results in terms of ECG parameters revealed significant decrease in PR interval, RR interval, QT interval, QTc interval, QT dispersion and QTc dispersion which appears to be due to adrenaline 1:80000 administered along with 2% lignocaine.

Various studies have shown that there is a swift absorption of adrenaline resulting in direct or indirect increase in heart rate which can be confirmed from the results of earlier studies.[12-14] Salonen et al confirms that there is approximately 5 fold increase in plasma adrenaline levels and approximately 2 fold increase in noradrenaline levels during dental surgery, indicative of sympathetic activity.[14] The statistical minimal rise in heart rate in present study may be due to the above stated theory of rise in endogenous adrenaline and noradrenaline. There was no clinically significant relevance of the above theory demonstrated in present study as the changes in the ECG parameters were within normal limits.

There had been infrequent reports of serious complications associated with use of lignocaine-adrenaline combinations in various dental procedures.15 The adverse effects were noted in terms of cardiovascular morbidities in present study. The only morbidity was found to be palpitation and the heart rate in all the patients having palpitation was never more than 105 beats/min. None of the patients showed any electrocardiographic changes relevant to cardiac arrhythmias which can be determined by QT interval, QTc interval, QT dispersion and QTc dispersion. This signifies the safety of lignocaine-adrenaline combinations in all apparently healthy, non-cardiovascular compromised patients. Godzieba et al recommended ECG monitoring during use of local anesthetic with vasoconstrictor in cardiac compromised patients, taking into consideration compication rate of as high as 15.5%.[16]

While in a study by Laragnoit et al, there were no differences in blood pressure, heart rate and pulse oximetry values before, during and after local anesthesia injection.[17] Results of the present study showed similar findings but with increase in heart rate without any clinical significance. Conrado et al also suggested that dental extractions performed under anesthesia with

adrenaline (1:100000) does not imply additional ischemic risks, as long as performed with good anesthetic technique and maintenance of the pharmacological treatment prescribed by the cardiologist.[18]

Concern is always over the use of the combination in cardiovascular compromised patients. Majority of the studies for safety of lignocaine adrenaline combination was done on cardiovascular compromised patients.[16-19] Present study was focused on effects of lignocaine adrenaline combination on apparently healthy, non-cardiovascular compromised patients. Emphasize was given to the effects of the drug combination on electrocardiogram. ECGs were analyzed for effects of the drug combination in patients receiving 1.8 ml of Lignocaine 2% with Adrenaline 1:80000.

There was significant decrease in all the ECG parameters studied from baseline to postoperative period. Based on the results it becomes evident that use of adrenaline along with lignocaine have shown increase in heart rate which is in concurrence with earlier studies. The mean increase in heart rate may be due to increase sympathetic activity and indirect release of endogenous catecholamines. The vagal tone and baroreceptor sensitivity differ in each individual and may interfere with dose response relationship of adrenaline.[20] This explains the lack of correlation between so called endogenously released plasma adrenaline and its clinical manifestations which were revealed in present study showing no any clinically significant changes in ECG parameters and heart rate. It can be very well stated that effects of lignocaine-adrenaline combinations on ECG remains irrelevant clinically.

Limitations

Plasma concentrations of adrenaline were not measured and evaluation of these effects should be done on a larger scale in terms of larger sample size to draw conclusive results.

CONCLUSION

This study was undertaken primarily to find out the safety of Ligocaine-Adrenaline combination as local anesthetic in various dental operative procedures in Pravara Rural Hospital in terms of Electrocardiography. The increase in heart rate although was statistically significant, it was always within normal limits suggestive of no clinical significance. There was statistical significant decrease in QT and QTc interval, QT and QTc dispersion. The change in all these parameters was within physiologic range. All these relevant parameters for cardiac arrhythmias did not show any arrhythmogenic potential of lignocaine-adrenaline combination. The change in the heart rate and ECG parameters might be attributed to the presence of adrenaline in the combination. No cardiovascular morbidities were observed except palpitation. Thus "effects of lignocaine-adrenaline combinations on electrocardiographic parameters are minimal and clinically irrelevant in healthy individuals."

REFERENCES

1. Katzung BG, Masters SB, Trevor AJ. Basic and Clinical Pharmacology. 11th ed. The McGraw-Hill Companies; 2009.
2. Malamed SF. Handbook of Local Anesthesia. 6th ed. Elsevier Inc.; 2013.
3. Brunton LL, Chabner BA, Knollmann BC. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12th ed. The McGraw-Hill Companies, 2011.
4. Covino BG. Toxicity and systemic effects of local anesthetic agents. In: Local Anesthetics. Strichartz GR, editor. Handbook of Experimental Pharmacology, vol. 81. Springer-Verlag, Berlin, 1987; 187–212.
5. Kapitanyan R, Su M, Tarabar A. Local Anesthetic Toxicity. Available from: http://emedicine.medscape.com/article/167309-overview [updated 2014 Jan 8; cited on 2014 Feb 27].
6. Tolas AG, Pflug AE, Halter JB. Arterial plasma epinephrine concentrations and hemodynamic responses after dental injection of local anesthetic with epinephrine. J Am Dent Assoc., 1982; 104: 41–43.
7. Cryer PE. Physiology and pathophysiology of the human sympathoadrenal neuroendocrine system. N Engl J Med., 1980; 303: 436–44.
8. Yagiela JA: Epinephrine and the compromised heart. Orofac Pain Manage, 1991; 1: 5–8.
9. Bazett HC, An analysis of time relation of electrocardiograms. Heart, 1920; 7: 353–67.
10. Jastak, JT, Yagiela, JA, Donaldson D, editors. Local anesthesia of the oral cavity. Philadelphia: WB Saunders, 1995.
11. de Jong RH: Uptake, distribution, and elimination. In: de Jong RH, editor: Local anesthetics. St Louis: Mosby, 1994.
12. Knoll-Köhler E, Frie A, Becker J, Ohlendorf D. Changes in plasma epinephrine concentration after dental infiltration anesthesia with different doses of epinephrine. J Dent Res., 1989; 68(6): 1098-101.
13. Troullos ES, Goldstein DS, Hargreaves KM, Dionne RA. Plasma Epinephrine Levels and Cardiovascular Response to High Administered Doses of Epinephrine Contained in Local Anesthesia. Anesthesia Progress, 1987.
14. M. Salonen, H. Forssell and M. Scheinin: Local dental anaesthesia with lidocaine and adrenaline: Effects on plasma catecholamines, heart rate and blood pressure. Int. J. Oral Maxillofac. Surg., 1988; 17: 392-94.
15. Rosen E, Tsesis I. Surgical Anesthesia: When a Tool Becomes a Weapon. In: Tsesis I, editor. Endodontic Surgery: Prevention, Identification and Management. Springer, 2014: 53-60.

16. Godzieba A, Smektala T, Jedrzejewski M, Sporniak-Tutak K. Clinical assessment of the safe use local anaesthesia with vasoconstrictor agents in cardiovascular compromised patients: A systematic review. Med Sci Monit., 2014; 20: 393-98.
17. Laragnoit AB, Neves RS, Neves ILI, Vieira JE. Locoregional anesthesia for dental treatment in cardiac patients: A comparative study of 2% plain lidocaine and 2% lidocaine with epinephrine (1:100,000). Clinics., 2009; 64(3): 177-82.
18. Conrado VC, de Andrade J, de Angelis GA, de Andrade AC, Timerman L, Andrade MM, et al. Cardiovascular Effects of Local Anesthesia with Vasoconstrictor during Dental Extraction in Coronary Patients. Arq Bras Cardiol, 2007; 88(5): 446-52.
19. Neves RS, Neves IL, Giorgi DM, Grupi CJ, Cesar LA, Hueb W, et al. Effects of Epinephrine in Local Dental Anesthesia in Patients with Coronary Artery Disease. Arq Bras Cardiol, 2007; 88(5): 482-87.
20. Taggart E, Hedworth-Whitty R., Carruthers M., Gordon E. Observations on electrocardiogram and plasma catechol-amines during dental procedures: the forgotten vagus. Br. Med. J., 1976; 2: 787-89.