Comparison of Ropivacaine 0.75 % and Lignocaine 2 % with 1:200,000 Adrenaline in Dental Extractions: Single Blind Clinical Trial

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Abstract

Introduction The aim of this study was to evaluate the efficacy, safety and clinical acceptability of the local anaesthetic agent ropivacaine 0.75 % in comparison with lignocaine 2 % with adrenaline 1:200,000 in minor oral surgical procedures.

Methods Forty-seven patients, who required bilateral extractions in a single arch, were included in this study. One hundred and sixty-six extractions were performed and all the patients were administered nerve blocks/infiltration. Pre and postoperative pulse, blood pressure, random blood sugar, electrocardiogram and partial oxygen pressure were recorded at specified time intervals. Pain score by visual analogue scale, onset of action and depth of anesthesia were also observed. Duration of anaesthesia was assessed by feeling of numbness and first sign of pain.

Results Statistical analysis revealed insignificant difference between both the groups in terms of pulse, blood pressure, random blood sugar, and partial oxygen pressure.

The depth of anesthesia was evaluated by pain, comfort during the procedure with visual analog scale and showed no significant difference between the two groups. The onset of action for maxillary infiltration was 33.29 ± 9.2 (ropivacaine), 32.12 ± 6.8 s (2 % lignocaine with adrenaline 1:200,000) and for pterygomandibular nerve block was 181.0 ± 87.5 (ropivacaine), 32.12 ± 6.8 s (2 % lignocaine with adrenaline 1:200,000). Duration of anesthesia when compared was 411.7 ± 66.11 min (ropivacaine) and 107.87 ± 16.54 (2 % lignocaine with adrenaline 1:200,000). On maxillary buccal vestibule infiltration it was also observed that in ropivacaine group there was no requirement of palatal infiltration suggestive of good diffusion property.

Conclusion Ropivacaine is a safe, clinically acceptable long acting local anaesthetic agent with added advantage of effective diffusion property.

Ethical Committee Approval Number SDC/MISC/2013/239.

Keywords Ropivacaine · Lignocaine with adrenaline · Cardiovascular system · Central nervous system · Random blood sugar · Diffusion property

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Abbreviations

LA	Local anaesthesia
LAdr	Local anaesthesia with adrenaline
CVS	Cardiovascular system
CNS	Central nervous system
RBS	Random blood sugar
BP	Blood pressure
SPO ₂	Partial oxygen pressure
ECG	Electrocardiograph
VAS	Visual analog scale

Introduction

Anaesthetic agents have been in use for dental pain management since early 1844, when nitrous oxide was first used for sedation during tooth extraction. The first chemical local anaesthetic came with discovery of cocaine in 1860 but was widely misused resulting in local tissue sloughing, addiction and death. Modern chemical local anaesthetic agents came in 1904–1905 when Alfren Einhorn discovered procaine, but with the discovery of Lidocaine in 1943 by Lofgren, the field for local anaesthesia (LA) entirely changed [1]. Its onset of action is 2–3 min with sufficient potency and is commonly available as plain Lignocaine hydrochloride or with adrenaline in different concentrations (LAdr).

The higher doses of LAdr may cause cardiovascular system (CVS) and central nervous system (CNS) effects such as talkativeness, apprehension, excitability, slurred speech, vomiting, elevated heart rate, elevated blood pressure (BP) and elevated respiratory rate. These are major concerns while managing the patients with CVS or CNS disorders.

Bupivacaine, a long acting local anesthetic was invented in 1956 and is widely used for spinal anesthesia. However studies have reported adverse effects of bupivacaine on CNS and CVS. The latest discovery in field of local anaesthesia is ropivacaine, which was introduced in 1996 for clinical use and was found to be equivalent to bupivacaine which is considered as gold standard amongst long acting anaesthetic agents [2]. Ropivacaine is preferred as a spinal anaesthetic due to its lower toxicity to CVS and CNS in comparison to bupivacaine. Ropivacaine is an amide type local anaesthetic i.e. monohydrate of hydrochloride salt and is an enantiomerically (non-super imposable mirror image) pure structural homologue of bupivacaine. A number of studies in biomedical field have reported that ropivacaine has lower potential for CVS and CNS toxicity than bupivacaine, so ropivacaine can replace bupivacaine if clinical studies proved its anaesthetic efficacy [3]. Maximum plasma concentrations of ropivacaine averaged $0.69 \pm 0.08 \mu\text{g/ml}$ after 90 min administration and mean elimination half-life of ropivacaine was found to be $2.83 \pm 0.51 \text{ h}$ [2].

Ropivacaine a long acting anaesthetic compared to LAdr has a duration of onset of action almost similar to lignocaine hydrochloride and is safer for cardiac patients as its toxic effect on CVS is much lesser than lignocaine hydrochloride [2]. According to latest study by world health organization the population suffering from diabetes mellitus is greatest among Indian population and incidence of ischemic heart disease is also increasing, so the judicious use of adrenaline is to be considered in current scenario. Diffusion is another

important property of local anesthesia in which drug moves from extra neural site towards nerve endings. Factors affecting diffusion of LA agent are keratinized or nonkeratinized type of mucosa, mucosal vessels and porosity of bone. Hasan et al. [4] reported that 4 % articaine has good quality of diffusion compared to 2 % lignocaine. Although lignocaine has a poor diffusion property, it is already established and there is limited available data regarding the diffusion property of ropivacaine.

The aim of this study was to investigate local and systemic effect of LAdr and ropivacaine in terms of random blood sugar (RBS), blood pressure (BP), partial oxygen pressure (SPO_2), electrocardiograph (ECG) changes if any, diffusion property and also compare the efficacy of both these drugs in dental pain management. LAdr is an established, widely used local anesthetic with duration of action lasting for about 120–150 min, therefore it was considered as the control group anesthetic in the present study.

Materials and Methods

This in vivo, randomized, single blind, prospective study, included patients above the age of 13 years, who required extraction of bilateral teeth under local anesthesia. A total of 166 extractions were carried out in 47 patients (24 males and 23 females) requiring extraction of bilateral premolars for orthodontic purpose or total extraction due to adult periodontitis or extraction of bilateral impacted 3rd molars. The study protocol was explained to patients in detail and informed consent was obtained. Drugs used in present study were LAdr 1:200,000 (Astrazeneca) and ropivacaine 0.75 % (Neon).

All patients were unaware of the drug being used and were asked to record data of pain score, duration of anesthesia and need of post operative analgesics. Pulse, SPO_2 , blood pressure were recorded pre-operatively, intra-operatively and post-operatively. RBS and ECG were recorded pre-operatively and 45 min post-operatively. After sensitivity test for anaesthetic agent, nerve block and/or infiltrations were performed in aseptic condition. The quantity of drug used was kept constant at 0.5 ml for buccal infiltration, 0.2 ml for palatal infiltration (if required), 1.2 ml for IAN block, 0.5 ml for lingual block, 0.5 ml for long buccal block and after achieving satisfactory anesthesia extraction was carried out. Initially palatal infiltration was avoided in all patients to know diffusion property of both LA solutions, which was assessed from 30 s to 5 min for effectiveness over palatal mucosa and requirement of palatal anesthesia. Intra operative monitoring of pulse, SPO_2 and pain score on VAS were recorded before injecting the drugs, on injecting and same parameters were

recorded after injection at intervals of 1, 2, 3, 4, 5, 10, 15, 20, 30 and 40 min. All the patients were assessed for level of comfort and depth of anaesthesia intra-operatively via VAS immediately after extraction, for both the agents to assess the depth of anesthesia achieved. For duration of postoperative analgesia patients were asked to note the time at which sensation or pain returns in the anesthetized area. For need of postoperative analgesics, patients were instructed to note the time and number of analgesics required. All patients were recalled on 1st post operative day for follow up and data collection. Further patients were also recalled on 7th post operative day for suture removal if trans-alveolar procedure was performed.

The operator and observer were same for all the patients and data collected was recorded for statistical analysis. The mean and standard deviation was calculated for each interval for both the groups. The unpaired 'Z' test was used to evaluate any difference between the data obtained for each observation of both agents and paired 't' test for comparison within the group.

Results

None of the patients were found allergic to any of these anaesthetic agents.

The onset of action for maxillary infiltration was 33.29 ± 9.2 (ropivacaine), 32.12 ± 6.8 s (2 % LAdr 1:200,000) and for pterygomandibular nerve block was 181.0 ± 87.5 (ropivacaine), 32.12 ± 6.8 s (2 % LAdr 1:200,000). There was no significant difference in pre and post operative pulse for the two groups, it was observed that mean pulse rate increased for both the groups post injection from 81.68 ± 10.81 to 87.72 ± 13.4 in LAdr group and from 81.65 ± 14.06 to 84.48 ± 16.7 in ropivacaine group. However when paired 't' test was applied to individual drugs pre and postoperatively (45 min) pulse rate data, then we found it to be highly significant for LAdr from 81.68 ± 10.81 to 87.72 ± 13.4 . Mean SPO₂ in both the groups were statistically insignificant.

The value of mean systolic and diastolic pressure pre and postoperatively 45 min after deposition of both the agents were interpreted insignificant, although there was an increase in mean systolic pressures for both the groups (Table 1). However the increase in mean systolic pressure for LAdr was statistically significant which was not so in ropivacaine group. The mean diastolic BP of the LAdr was decreased post injection (45 min) in comparison to the mean diastolic BP pre-injection, whereas it increased in ropivacaine group (Table 2).

The diffusion property of ropivacaine and LAdr was also observed for the patients by evaluating the anesthetic effect on palatal mucosa after administering maxillary

Table 1 Depicts the mean pre and post-operative systolic and diastolic pressure for the two groups and the *P* value on application of 'Z' test

Time	LAdr	Rop	<i>P</i> value
Preop systolic	120.1 ± 15.9	120.3 ± 15.6	0.327 ^{NS}
Preop diastolic	75.1 ± 12.1	73.3 ± 10.3	0.439 ^{NS}
Postop systolic	123.6 ± 15.8	122.9 ± 15.8	0.830 ^{NS}
Post op diastolic	73.8 ± 11.3	75.02 ± 10.9	0.595 ^{NS}

Table 2 Depicts the comparison between mean systolic and diastolic pressure for the two groups when compared individually and the *P* value on application of paired 't' test

Drug used	Preop	Postop 45 min	<i>P</i> value
LAdr-systolic	120.1 ± 15.9	123.6 ± 15.8	0.009 significant
LAdr-diastolic	75.1 ± 12.1	73.8 ± 11.3	0.248 ^{NS}
Rop-systolic	120.3 ± 15.6	122.9 ± 15.8	0.072 ^{NS}
Rop-diastolic	73.3 ± 10.3	75.02 ± 10.9	0.099 ^{NS}

Table 3 Depicts the mean random RBS for the two groups and the *P* value on application of 'Z' test

Time	LAdr	Rop	<i>P</i> value
Preop	105.4 ± 13.4	106.5 ± 12.3	0.679 ^{NS}
Postop	104.2 ± 13.2	107.1 ± 12.6	0.278 ^{NS}
	<i>P</i> -0.039 significant	<i>P</i> -0.37 ^{NS}	

buccal infiltration. It was observed that palatal anesthesia was achieved within 3–8 min post injection in 41 patients, in whom only ropivacaine was administered buccally, whereas in LAdr group none of the patients achieved palatal anesthesia as subjective and objective sign.

It was noticed that the mean RBS at post injection (45 min) for the LAdr group decreased in comparison to mean pre-injection values, whereas it increased in ropivacaine group. However there was no significant difference for mean RBS values in both the groups after 45 min of injection (Table 3).

Cardiovascular effects of the two anesthetic agents was observed by recording the ECG preoperatively and post-operatively (45 min after deposition of anesthetic). No significant difference between the two anaesthetic agents was observed.

The potency of ropivacaine as an anaesthetic agent in maxillofacial surgery was evaluated by observing the pain by VAS, at various time intervals during the extraction and comparing it with that of pain scores at the same time

Table 4 Depicts the mean pain score for the two groups and the *P* value on application of 'Z' test

Time interval	Lignocaine with adrenaline	Rop	<i>P</i> value
On injection	2 ± 0	2.04 ± 0.29	0.346 ^{NS}
30 s	0.042 ± 0.29	0 ± 0	–
1 min	0.29 ± 0.71	0.08 ± 0.40	0.082 ^{NS}
2 min	0.89 ± 1.08	0.55 ± 0.92	0.071 ^{NS}
3 min	1.91 ± 0.92	1.14 ± 1.08	0.003 significant
4 min	1.70 ± 1.24	1.70 ± 1.17	1 ^{NS}
5 min	1.36 ± 1.32	1.40 ± 1.24	0.880 ^{NS}
10 min	0.55 ± 1.29	0.85 ± 1.42	0.292 ^{NS}
15 min	0.25 ± 0.79	0.29 ± 0.93	0.822 ^{NS}
20 min	0.08 ± 0.4	0.21 ± 0.74	0.292 ^{NS}
30 min	0 ± 0	0.08 ± 0.40	–
40 min	0 ± 0	0 ± 0	–

intervals for the LAdr group (Table 4). There was no significant statistical difference between the two groups.

The efficacy and clinical acceptability of ropivacaine was evaluated by comparing its mean duration of anesthesia with that of the LAdr, which was statistically significant as it was 411.7 ± 66.11 min for ropivacaine and 107.8 ± 16.5 min for LAdr.

Discussion

Ropivacaine elicits nerve block via reversible inhibition of sodium influx into nerve fibers, resulting in decreased membrane permeability to sodium and increased threshold for electrical excitability. Ropivacaine has a biphasic vascular effect as other long-acting local anesthetics. Low concentrations of ropivacaine (0.063–0.5 %) injected intradermally (0.1 ml) caused vasoconstriction, but at higher concentration (1 %) did not have same effect [5, 6]. Earlier studies on animals and humans have shown that addition of vasoconstrictive agent to ropivacaine did not result in any additional benefit [7]. The vasoconstrictive effect at low concentrations is likely to contribute to its duration of action in dental anesthesia, but the question of its influence on cardiovascular parameters remains as studies on volunteers and animals have reported contradictory results for the cardiovascular effect of ropivacaine [8].

Effect of ropivacaine on pulse rate was similar to the results of study by Stewart et al. [9], where there was no statistically significant difference between the pre and postoperative phase.

A study conducted by Oliveira et al. [2] in 2006, found no difference in pre and postoperative systolic and diastolic pressure which is very similar to our observation. They focused on CVS effects of ropivacaine and found that ropivacaine alone did not cause any changes, but ropivacaine with epinephrine caused a transient increase in

systolic BP (6 %) and heart rate (11 %) 2 min after injection [2]. This may be due to adrenaline's action on alpha and beta receptors which causes increase in heart rate and rise in systolic pressure. Similarly in the present study also there was a significant difference in pre and postoperative systolic BP for the LAdr group. An increase in the mean pulse rate was also recorded for the ropivacaine group though statistically insignificant.

Another study conducted by Knudsen et al. [10], to assess the effect of ropivacaine and bupivacaine with IV infusion, concluded that bupivacaine increases QRS width during sinus rhythm and reduced both ventricular systolic and diastolic function compared with ropivacaine; whereas a study done by Atanassoff et al. [11] did not find any changes. In present study, we found insignificant effect of LAdr and ropivacaine on CVS, which were assessed by pre and post operative ECG. With these observations it can be concluded that LAdr and ropivacaine do not have adverse effects over CVS in limited dental dosage.

LAs exert a dual effect on respiration, direct relaxant action on bronchial smooth muscle occur in normal dosage level, whereas due to over dosage respiratory depression to arrest can occur. These actions can be assessed by recording SPO₂ while injecting these drugs. Similar to the studies of Oliveira et al. [2] in present study also there was no significant change in SPO₂ from pre-injection to post injection values for both the drugs. These observations show that both the drugs do not have significant respiratory depressant action in limited doses.

Adding of sympathomimetic drugs in LA solution is very well established in literature. Adrenaline is commonly used among this group with lidocaine. Hyperglycemic effect of adrenaline may be due to reduction in insulin secretion by the action of α_2 adrenergic receptors causing inhibition of β cells of the islets of Langerhans, stimulation of glycogenolysis resulting in cyclic AMP-dependent activation of phosphorylation, decrease in glucose

utilization, increase in glucagon concentration by glycogenolysis and gluconeogenesis, which causes skeletal muscles glycogenolysis thereby increasing the lactate concentration [12].

The change in RBS pre and post injection were observed in our study, which were different from those of Kalra et al. [12], where they found significant difference in blood glucose level post injection of LAdr 1:80,000. Another study conducted by Meechan et al. [13] reported the increase in mean blood glucose level from 82.08 to 94.32 mg/dl. In our study we did not observe any significant changes in RBS, probably due to lesser concentration of adrenaline. Secondly other studies have included diabetic group where as only healthy individuals were included in the present study. Although mild hypoglycemia in LAdr group and mild hyperglycemia in ropivacaine group were observed but were statistically insignificant.

Observations from the present study in terms of effects of ropivacaine on CVS, indicate it to be safe as a long acting anesthetic agent in minor oral surgical procedures where adrenaline is contraindicated.

The present study focused on onset of anesthesia also for both the drugs used. It was observed that mean onset for LAdr for maxillary infiltration was 32.12 ± 6.8 s and for mandibular block 115.31 ± 29.32 s, whereas for ropivacaine maxillary infiltration was 33.29 ± 9.22 s and mandibular block was 181.06 ± 87.58 s. These are similar to observations as in study by Axelsson and Icsacsson [14] who observed that mean onset time for pulpal anesthesia was 126 s for 1 ml volume of solution and 96 s for 2 ml. Oliveira et al. [2] reported 120 s as onset time with 1.8 ml plain ropivacaine (0.75 %) and 0.75 % ropivacaine with epinephrine when used for the lingual and inferior alveolar nerve blocks anesthesia. Although in this study, electric pulp tester was not used to access the pulpal anesthesia, but it can be considered that both core and mental fibers were anesthetized in this time as none of the patients suffered any pain or discomfort during extraction. According to Malamed [1] the onset of action by ropivacaine ranges from 120–240 s.

Pain or burning sensation on injecting a LA drug is also a concern in dental anesthesia, which may occur due to needle prick or injecting an acidic solution. The pH for ropivacaine ranges from 4.0 to 6.0 whereas it is more acidic for LAdr which ranges between 3.5 and 5.5. In present study we did not find any significant difference in terms of pain or burning sensation while injecting both the drugs, which may be due to slow rate of injection.

Hassan et al. [4] conducted an in vivo study to assess the effectiveness of LAdr and articaine in bilateral maxillary premolars extraction. They found in their study that for all the patients in articaine group they did not require palatal injection because of its remarkable diffusion property,

whereas in lignocaine group they required an additional palatal injection for palatal soft tissue anesthesia. Lima et al. [15] carried out a study to investigate onset of anesthesia over the palatal mucosa after infiltrating 4 % articaine with different concentrations of adrenaline in buccal vestibule for impacted maxillary 3rd molar surgery and found success rate of 68–78 % after 5 min, and 72–94 % after 10 min. In present study we also found poor depth of diffusion in lignocaine group, whereas in ropivacaine group, all cases did not require palatal injection, which may be due to its appropriate diffusion property. In this study it was also observed that palatal soft tissue anesthesia was achieved within 3–8 min on buccal infiltration. This variation in range can be due to age of patient, as in geriatric group there is more of dense bone and endarteritis obliterans. The mean time taken for diffusion in this study was 297.0 ± 72.4 s in ropivacaine without adrenaline. These results are similar to that of 4 % articaine in terms of diffusion property. According to other study by Kumaresan et al. [16], they had noticed that overall success rate of palatal anaesthesia with a single buccal infiltration of LAdr 1:80,000 was found to be 81.3 % in maxillary anterior region. However to the contrary in our study in none of the cases we could achieve palatal anaesthesia with single buccal infiltration, the possible reasons may be greater density of bone in maxillary premolar (which were majority of cases in our study) as compared to anteriors and another reason could be because of variation in concentration of adrenaline. Although present study does not have a large sample size to establish diffusion property of ropivacaine, it definitely not only avoids another painful injection for palatal infiltration but also prevents complication like persistent paraesthesia due to injury to nerve ending as reported by Malamed [1].

Addition of sympathomimetic drug to LA agent not only reduces the toxicity but also enhances the potency and depth of anesthesia which leads to pain free surgical procedure. On comparison of LAdr and ropivacaine without adrenaline for depth of anesthesia, which was assessed by VAS scale from beginning to end of the procedure, at specific intervals of time, no significant difference among both the groups in terms of intra-operative pain and discomfort were observed. These findings suggest that plain ropivacaine is equally potent, and has similar quality in depth of anesthesia as compared to lignocaine with adrenaline.

Another important factor for any LA to be efficacious is its duration of action, which should be long enough for operative procedure to be completed. Though longer duration of anesthesia in pediatric age group is not desired because of self inflicted injuries like lip/cheek/tongue biting, however they are beneficial for adult patients, because of required need of analgesics can be prolonged and reduced. According to Malamed [1] LAdr is intermediate

acting with duration of action 60 min for pulpal and 180–300 min for soft tissue, whereas Kennedy et al. [17] found that anesthetic efficacy of ropivacaine on maxillary anterior infiltration, results in pulpal anesthesia for an average of 12.43 and 362.25 min for soft tissue. The duration of action for both groups was recorded and need of postoperative analgesic were also assessed and we observed that duration of soft tissue anesthesia with LAdr was 107.87 ± 16.54 min and for ropivacaine it was 411.7 ± 66.11 min. Observations from present study indicate that duration of soft tissue anesthesia with LAdr was less compared to work performed by Malamed [1], whereas it was more with ropivacaine compared to study of Kennedy et al. [17]. The duration of anesthesia was much longer for ropivacaine compared to LAdr and the result of anesthetic efficacy, potency achieved was similar in all age groups, gender as already proven by Ernberg et al. [18].

In the present study we have also observed that required postoperative analgesics were minimal in ropivacaine group compared to the lignocaine group. This may be due to longer duration of anesthesia of ropivacaine, thus minimizing need of postoperative analgesics. This can be of advantage in patients suffering from GERD, peptic ulcer or having intolerance to NASIDs.

Ropivacaine a newer LA agent developed after evidence of bupivacaine related toxicity, is a well-tolerated regional anesthetic effective for surgical anesthesia as well as for relief of postoperative pain. The efficacy of ropivacaine is similar to that of bupivacaine for peripheral nerve blocks with lesser cardiotoxicity, neurotoxicity and has greater degree of separation between sensory and motor block as compared to bupivacaine [19].

Conclusion

Ropivacaine is a safe, efficacious, clinically acceptable and equally potent local anesthetic agent when compared to LAdr in dental pain management with an added advantage of longer duration of action and effective diffusion property.

Compliance with Ethical Standards

The study was approved by institutional Ethical committee vide letter no. SDC/MISC/2013/239 dated 24.01.2013.

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