A comparative study between 0.5% Centbucridine HCl and 2% Lignocaine HCl with Adrenaline (1:2,00,000)

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Abstract Even today the ability to provide the patient with clinically adequate pain control with minimum systemic side effects is one of the major concerns all over the world. Lignocaine, the most commonly used local anesthetic agent in oral surgery due to its rapid onset & reasonably good potency, does not have adequate duration of action, unless used with Adrenaline, a drug known for its cardiovascular effects. Centbucridine, a non-ester, non-amide group local anesthetic agent developed in India at C D R I Lucknow, has advantage of inherent vasoconstrictor property. This study was planned to compare 0.5% Centbucridine and 2% Lignocaine with Adrenaline, in exodontia patients. The results were recorded for their efficacy and C V S action and statistically analyzed. Centbucridine was found to be an ideal local anesthetic agent with no effects on cardiovascular parameters and exhibiting a sufficient degree of local anesthetic activity suitable for use in routine minor surgery cases. This will be advantageous where Adrenaline is absolutely contraindicated due to systemic problems.

Keywords Centbucridine · Lignocaine · Local anaesthetic

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Introduction

Even today, after more than a century has passed since introduction of synthetic local anesthetic agents in dental/oral surgical practice, the ability to provide the patient with clinically adequate pain control with minimum systemic side effects is one of the major concerns all over the world.

Lignocaine is, today the ‘Gold Standard’ local anesthetic agent against which all new local anesthetics are compared. Though it possesses rapid onset of action & has reasonably good potency Lignocaine has to be used in combination with Adrenaline to produce adequate duration of anesthesia for routine minor oral surgical procedures. Centbucridine, chemically known as 4-N- butylamino-1,2,3,4-tetrahydroacridine hydrochloride, a new quinolone derivative with local anesthetic action, developed in India, was introduced by Patnaik et al. [3]. After a multicentric trial in more than 2700 patients of various age groups, Central Drug

Research Institute of India, concluded that it has inherent vasoconstrictor property and longer duration of action; better cardiovascular stability; possesses antihistaminic activity and is four to five times more potent than lignocaine [2].

The studies regarding pharmacology, toxicology (neurotoxicity and teratogenic) and results of clinical trials of Centbucridine have been reported [4, 5, 6, 7]. The study was planned to find out suitability of Centbucridine in patients where Lignocaine with Adrenaline is contraindicated due to systemic conditions.

Methods

Purpose of study was to compare a) the efficacy (onset, depth and duration of action) and b) cardiovascular stability (Blood pressure and pulse) after administration of Centbucridine/ Lignocaine hydrochloride with Adrenaline (1:2,00,000).

All patients attending the OPD of Department of Oral and Maxillofacial Surgery (BVDC, Pune) were considered for the study during period June 2004 to October 2004. Inclusion criteria was a physically fit (ASA Class I) adult patients of either sex indicated for extractions (surgical/ closed method) of teeth requiring nerve block (upper anterior or lower molar teeth). Highly anxious patients and those patients giving history of allergies to local anesthetic agents and known cardiovascular problems were excluded from study. Also cases with acute infection in orofacial area were not considered.

Investigation was carried out as an open clinical trial. All potential participants were explained the need and design of study and the new drug; and about its advantages and disadvantages. Routine laboratory investigations were carried out. Based on inclusion and exclusion criteria 240 individuals became part of this study. Informed written consent was taken from all agreed patients. Patients were divided into

two groups: Group I (Centbucridine) and Group II (Lignocaine + Adrenaline). The potential candidates were tested for allergy. Local anesthesia was administered by the standard technique. Total 3 ml of anesthetic was injected for nerve blocks and necessary buccal or palatal infiltration. Numbness, was recorded as a subjective sensation of lip paresthesia, and reported on questioning. Presence of pain was determined by using 0.8 mm sterile injection needle prick applied to attached gingiva, in standard manner. Onset of anesthesia was defined as the time required from the end of the injection to the time point when pain to pinprick was abolished and numbness was positive. Duration of anesthesia was measured from the time subjective symptom (Numbness) was positive till the pain in the surgical area was felt. Exodontia procedures were carried out in standardized manner. The depth of anesthesia was determined by visual analogue pain scale while the procedure was being carried out. Operating surgeons used the modified three-point category scale to measure the quality of anesthesia. Duration of surgery was also recorded to assess if the duration of anesthetic is sufficient for minor oral procedures. Side effects to the anesthetic (if any) were noted. Blood pressure and pulse rate was checked and recorded, prior to injection and again at 10, 30 and 60 minutes interval after local anesthesia administration, by trained staff nurse. All patients were provided with analgesic medication and instructed to take medication only when they felt it necessary for pain control. Time for requirement of analgesic was noted by patient and reported the next day. Patients who failed to report the next day were omitted from the study (total forty patients). Of the remaining 200 patients, 120 cases were of group I and 80 cases of group II. Age, sex, type of nerve block and pre-anesthesia pulse and blood pressure were compared statistically to know the homogeneity of the two groups. Intra and post treatment changes in B.P and pulse pressure from baseline to different time intervals were noted and analyzed by paired t-test (Intra group). $P < 0.05$ is considered significant difference.

Results

1) Efficacy of local anesthesia

Difference between onsets of action of two drugs was statistically significant with Centbucridine slower by few seconds.

The difference in mean duration of action (time in minutes) was statistically

Table 1 Onset and duration of action

	Group I	Group II	Statistical analysis
Onset (seconds)	116.54 (35s–300s)	85.9 (25–300s)	Statistically significant
Duration of Anesthesia (minutes)	134.26 (20mn–360mn)	151.68 (50mn–360mn)	Statistically not significant

Table 2 Depth of anesthesia (Checked by modified surgeon's criteria and Visual analogue)

	Surgeons criteria (Table 1)	Visual analogue scale (Patients criteria) (Table 2)		
		0	1	2
Group I	Successful (100%)	112(93.33%)	5(4.16%)	3(2.5%)
Group II	Successful (100%)	80(100%)	0	0

Table 3 Changes in systolic blood pressure

Changes in systolic blood pressure	Group I		Group II	
	mean	p-value	mean	p-value
Pre-anesthesia	122.77	0.30	122.12	0.049
with 10 min. post-anesthesia	123.40	Not significant	123.35	Significant
Pre-anesthesia	122.7	0.50	122.12	0.119
with 30 min. post-anesthesia	123.19	Not significant	121.17	Not significant
10 minutes post-anesthesia	123.4	0.59	123.3	0.00 significant
with 30 min. post-anesthesia	123.19	Not significant	121.17	at 1% [$p < 0.01$]

Table 4 Changes in diastolic blood pressure

Changes in Diastolic Blood Pressure	Group I		Group II	
	mean	p-value	mean	p-value
Pre-anesthesia	77.85	0.39	80.25	0.373
with 10 min. post-anesthesia	78.2	Not significant	88.36	Not Significant
Pre-anesthesia	77.85	0.52	80.25	0.012
with 30 min. post-anesthesia	78.10	Not significant	78.77	significant
10 minutes post-anesthesia	78.2	0.77	88.25	0.291
with 30 min. post-anesthesia	78.1	Not significant	78.77	Not significant

Table 5 Changes in pulse rate

Pulse	Group I		Group II	
	mean	p-value	mean	p-value
Pre-anesthesia	81.42	0.862	80.81	0.00
with 10 min. post-anesthesia	81.49	Not significant	82.81	significant
Pre-anesthesia	81.42	0.938	80.81	0.008
with 30 min. post-anesthesia	81.38	Not significant	81.96	significant

not significant. The average time required for the surgical procedure in the present study was well within the limits of the duration of action of Centbucridine (Table 1).

Some shortcomings regarding the depth of anesthesia, according to patient's criteria were noted in few patients of Centbucridine group and none in Lignocaine group (Table 2).

2) Cardiovascular stability (Blood pressure and Pulse rate)

Since by end of an hour the cardiovascular parameters were same as pre anesthesia they have been omitted from the analysis. Systolic and diastolic blood pressures were analyzed separately and compared within the group.

Group I patients did not show statistically significant changes in blood pressure. While in Group II patients systolic blood pressure changes in first 30 minutes were statistically significant, though it did not cause clinically appreciable symptoms (Table 3, 4).

Pulse rate changes were statistically significant in Group II patients while stable in Group I (Table 5).

3) Side effects

Side effects like headache, dizziness and nausea seen after administration of Centbucridine, which gradually resolved within 10 minutes without any medication.

Discussion

The onset and duration of action of Lignocaine with Adrenaline was comparable to values described by standard textbooks. If the onset and duration of the both the anesthetics is compared there is not much difference this is in accordance reports [4]. In this study Centbucridine had little slower onset of action as compared to Lignocaine with Adrenaline. But few seconds of difference for drug like Local Anesthetic is not necessarily a very important criterion in clinical practice.

Some shortcomings regarding the depth of anesthesia, according to patient's criteria (visual analogue scale) were noted as compared to Lignocaine, but in general operating surgeon had no problems during the procedure. Similar findings are noted Gupta et al. [8]. This may have influence when using in apprehensive patients.

Group I patients showed statistically significant variation in Blood pressure and especially pulse rate though the procedure could be completed in all patients. These changes can, to certain extent, be attributed to Adrenaline in Lignocaine injection; which may become more significant in cardiac cases.

Centbucridine when compared with Lignocaine + Adrenaline had good CVS stability and was devoid of any cardiovascular effects.

Centbucridine had more side effects like nausea vomiting etc., similar findings are reported by Vacharajani et al. [9] and C.D.R.I. [2] study.

One major drawback of Centbucridine is, insufficient data availability on its biotransformation. Central Drug Research Institute did check the vital parameters and hematological and urine tests preinjection and 24 hrs after LA administration, and claimed this drug to be safe. But no information on biotransformation has yet been recorded.

Conclusion

After reviewing the results of the study we can conclude

1. Onset of action of Centbucridine is slower than that of Lignocaine + Adrenaline, but the duration and depth of anesthetic action were comparable to each other and sufficient for both surgical / nonsurgical extractions. It shows sufficient efficacy as local anesthetic agent.

2. Cardiovascular parameters showed, though not much clinically appreciable but, statistically significant changes with Lignocaine + Adrenaline cases which may be attributed to the presence of Adrenaline in Lignocaine injection. While patients injected Centbucridine had good CVS stability. This finding can be significant in known severe cardiac patients.

Hence Centbucridine can be effectively used as an ideal substitute in place of Lignocaine to patients undergoing minor oral surgical procedures, when Adrenaline is absolutely contraindicated due to

systemic problem. Additional study in known cardiac cases needs to be carried out to confirm this.

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