

A New Era of Local Anaesthetic Agent: Centbucridine

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ABSTRACT

One century after the clinical introduction of cocaine, local anesthesia remains the most important method of pain control in dentistry. Many local anesthetics have been marketed since 1884, and it is likely that attempts to produce drugs that enhance anesthetic efficacy, reduce systemic and local toxicity, and increase nociceptive selectivity, will continue. Centbucridine is a non-ester, non-amide group LA and has not been comprehensively studied in the dental setting and the objective was to compare it to Lignocaine. This was a randomized study comparing the onset time, duration, depth and cardiovascular parameters between Centbucridine (0.5%) and Lignocaine (2%). The study was conducted in the department of oral and maxillofacial surgery of our dental college in on patients attending for the extraction of lower molars.

Keywords: centbucridine, lidocaine, anesthesia

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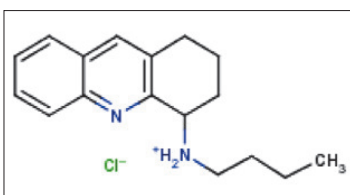
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Introduction

Today Lignocaine is the most commonly used local anesthetic agent in dentistry and is referred to as the "gold standard" for dental procedures[1]. Although its properties resemble an ideal LA agent, it is not completely free from cardiovascular toxicity and has an inherent vasodilating property[1, 2, 3]. As a result of the vasodilating characteristic, it has to be combined with a vasoconstrictor, such as adrenaline, to decrease its rate of absorption at the injection site and hence prolong the duration and depth of anesthesia. The use of adrenaline as a vasoconstrictor is sometimes contraindicated for medically compromised patients. To overcome these disadvantages, other LAs have been developed over the past few years, including Centbucridine.

Centbucridine, chemically known as 4-N-butylamino-1,2,3,4-tetrahydroacridine hydrochloride, is a new quinoline derivative with local anesthetic action (synthesized at the Central Drug Research Institute, Lucknow, India).



In animal experiments the drug is 5-8 times as active as

lidocaine, being highly effective for infiltration anesthesia at a concentration of 0.5%. In mice, rats, and monkeys given graded doses of centbucridine (subcutaneously in rats and monkeys and intraperitoneally in mice), the LD50 was one-fourth that of lidocaine[4]. Centbucridine does not cause local irritation on infiltration in animals[3]. Preliminary Studies [5-7] in human volunteers have confirmed its safety and effectiveness as a local anesthetic. Most of the clinical work on centbucridine has been published in Indian medical journals. Centbucridine does not affect the central nervous or central vascular system except when administered at very large doses [8]. Centbucridine has been used in subarachnoid and extradural anesthesia[9] and in intravenous regional anesthesia[10].

Vacharajani et.al[11], compared the efficacy of 0.5% centbucridine to 2.0% lidocaine for dental extractions in 120 patients. Centbucridine is five to eight times as potent as lidocaine, with an equally rapid onset of action and an equivalent duration of action. Significantly, centbucridine does not affect the central nervous or cardiovascular systems adversely except when administered in very large doses. They reported that the degree of analgesia attained with centbucridine compared well to that obtained with lidocaine. Centbucridine was well tolerated, with no significant changes in cardiovascular parameters and no serious side effects.

Objectives

The aim was to compare the efficacy of 0.5% Centbucridine HCl to 2% Lignocaine HCl with Adrenaline (1:200000) for various parameters required in the dental field.

1. To assess and compare the onset (in seconds), duration (in minutes), and depth (using a visual analogue score) of anesthesia in healthy adults between Lignocaine and Centbucridine.
2. To monitor and compare the cardiovascular response (pulse and blood pressure) in patients on the two LAs.
3. To identify any side effects/allergic reactions to Centbucridine.

Material and Methods

All patients who attended as outpatients for dental extractions and met the criteria were asked to participate in the study. Patients were examined clinically and routine laboratory data were performed. All of the patients attended for the extraction of lower

molars. All patients were healthy adults according to ASA I classification and aged between 18 and 60 years old. Subjects received either centbucridine or lidocaine (neither with epinephrine) according to a randomization chart. Both drugs were supplied in equal amounts in identical vials labeled only with a code number. An intradermal sensitivity test was performed on each individual with 0.1 ml of the respective drug. None of the 322 patients studied showed any abnormal reaction to the intradermal test injection. The onset, duration, depth, and cardiovascular measurements were carried out by a qualified medical nurse. The time taken for the onset and duration of local anesthesia was measured using a stopwatch.

The study population was divided into two groups: **Group I** (Centbucridine) and **Group II** (Lignocaine).

Assessment Criteria

- Onset of Anesthesia** (Measured in Seconds). This was measured both objectively, by a pinprick test using a 20 gauge sterile needle which was applied over the attached gingiva of the tooth to be extracted and subjectively when the patient first described symptoms of anesthesia for example numbness or tingling sensation over lower lip.
- Duration of Anesthesia** (Measured in Minutes). This was the time interval between the onset of anesthesia and when the patient reported subjective feelings of normal sensation. This was confirmed objectively by the pinprick test as described above.
- Depth of Anesthesia.** This was judged subjectively by the patient using a standardized visual analogue score (VAS). The score ranged from "0" to "5" with "0" being "no pain" and "5" being the most severe intense pain, which the patient could not bear. Each patient was asked to score the "amount" of pain he/she felt during the extraction of the tooth.

A low score (0) meant that the patient felt no pain at all; a moderate score (1 and 2) meant that the patient felt mild pain; a score of (3 and 4) meant that the patient felt moderate pain; a high score (5) meant that the patient felt excruciating and unbearable pain [Table I].
- To Monitor and Compare CVS Response Using Blood Pressure, Heart Rate and Spo2.** The systolic and diastolic blood pressure (BP) was measured in mm of mercury, and the pulse rate was measured using beats per minute. The measurements were done preoperatively (base line), and then at 10, 20, 30, and 60 minute intervals after the administration of the LA. All patients were seated and in the resting position when the measurements were recorded [Table II].
- Side Effects/Allergic Reaction.** Any signs of an allergic reaction including itching, redness, and localized swelling were recorded.

Result

Of the 322 patients, 170 received 0.5% centbucridine and 152 had 2% lidocaine. 72 women and 98 men received centbucridine; 68 women and 84 men received lidocaine. Their ages ranged from 18-60 years (Table III). Table IV gives the onset of action and the duration of anaesthesia. The onset of action was rapid with both the drugs (Table IV). Statistical analysis showed no significant differences between centbucridine and lidocaine with respect to onset of action and duration of surgery performed (Table IV).

In the concentrations and volumes used, both centbucridine and lidocaine were generally well tolerated. Six patients who received lidocaine had changes in blood pressure. One of these had a marked decrease in blood pressure from 120/80 to 100/60 mm Hg 45 min after infiltration, with an increase in pulse rate from 84 to 96 beats/min. This patient felt vertigo and vomited. The other five subjects, who had changes in blood pressure after lidocaine had mild hypertension initially and showed transitory increases of 10-20 mm Hg in systolic blood pressure, lasting for 15-20 min. However, none had any symptoms and no other treatment was administered. Another patient given lidocaine also complained of giddiness but had no changes in blood pressure and did not require treatment. One hypertensive patient given centbucridine had an increase in blood pressure from 180/100 mm Hg before injection to 190/100 mm Hg 60 min after infiltration but without symptoms. Another hypertensive patient given centbucridine, whose blood pressure was 180/100 mm Hg, showed no change in blood pressure. Also, no decrease in blood pressure was observed in patients given centbucridine.

Table I: Depth of Anesthesia

VAS score	Group 1	Group 2	Statistical analysis
0	138(81.2%)	125(82.2%)	P=0.132
1	32(18.8%)	27(17.8%)	P=0.133
Total	170	152	

Table II: Comparison of mean heart rate at various time intervals using Centbucridine and Lignocaine

Heart rate Base line	Centbucridine 75.5	Lignocaine 76.6	Statistical analysis
10 min after LA	75.99±1.911	77.1±1.02	p=0.000
20 min after LA	75.41±1.53	76.12±1.53	p=0.000
30 min after LA	75.5±1.50	76.05±1.51	p=0.001
60 min after LA	75.6±1.55	75.7±1.49	p=0.556

Table III: Age and Gender Distribution

Group	Mean age	Men	women	Total
I	36.3	98(58%)	72(42%)	170
II	37.1	84(55%)	68(45%)	152

Table IV: Onset and Duration of Anesthesia

Parameters	Group 1(mean±SD)	Group 2(mean±SD)	Statistical analysis
Onset (seconds)	158.80±1.89	175.44±1.70	p=0.00
Duration of anesthesia(minutes)	150.59±1.52	110.62±1.65	p=0.00

No adverse effects were observed and the wounds healed without complications in both groups.

Discussion

Each group had almost equal numbers of patients with equal age and gender distribution. Neither the demographical characteristics had any significant differences, so the groups could be compared to each other. The average time required for onset of anesthesia was just under three minutes, and Centbucridine was significantly shorter. On average, patients felt the anesthetic effect of Centbucridine about 14 seconds quicker than that of Lignocaine which is clinically not significant. These results are within the reported range of initiation of anesthesia as reported by others to be between 1 and 6 minutes [11,12]. This could be due to the inherent vasoconstrictive effect of Centbucridine as compared to Lignocaine. The mean duration of anesthesia was significantly higher for Centbucridine compared to Lignocaine. Patients reported an average anesthesia of 2.5 hours (151 minutes) for Centbucridine compared to less than 2 hours (111 minutes) for Lignocaine. A possible reason could be the fact that since Centbucridine has a natural vasoconstrictive effect; the LA solution remained close to and around the nerve tissue for a longer period of time. The solution was prevented from being absorbed and dispersed, and this could have resulted in the longer duration of anesthetic time that was obtained. Both LAs showed similar results in terms of depth of anesthesia. No patients reported a score of more than 1 (mild annoying pain), and all patients were sufficiently anesthetized to carry out the procedures. This was similar to other studies [13]. There was mild and transient elevation of heart rate in both the groups at the 10 minute interval. However, at all subsequent evaluations, the heart rate had returned to the preanesthesia value. In all of the cases, the tooth was extracted and treatment was complete within 10 minutes. Therefore, after the 10 minute interval, the patients were much more relaxed, the fear had decreased, and their anxiety had been reduced. It was therefore understandable that their heart rate was high at the 10 minute mark but reduced and returned to normal by the 20 minute interval and at all subsequent evaluations. This has been also reported in other studies [12]. and considered normal. There was no difference between the blood pressure parameters of both the LAs. Mild elevation of this parameter during initial time was attributed due to anxiety and fear as discussed above. This has also been reported by other authors [1,12,13]. Lignocaine has an inherent vasodilating property, which in turn requires adrenaline. This has been shown to increase the blood pressure and heart rate in some studies [1,13]. and is contraindicated to some medically compromised patients. In this study, although there were no medically compromised patients, Lignocaine did not significantly increase the blood pressures and heart rate. There were no adverse or allergic reactions to either of the LAs in our sample population. Earlier episodes of an allergy to Lignocaine have been reported but are very rare [14-16]. Since the

sample population in the study consisted of about 200 patients, it is not surprising that there were no patients who reported adverse reactions. Centbucridine has showed an antihistaminic activity by blocking the H1 histamine receptors which makes it an ideal LA agent in patients with known allergy to other conventional LAs [12,17]. However, it must be noted that the sample population in the study was relatively small.

Conclusion

The field of local anesthesia has burgeoned in its first century. Techniques and drugs have blossomed that can ease suffering and support operative procedures that might otherwise have been impossible without rendering the patient unconscious. Investigations of the pharmacology and physiology of local anesthesia is providing a rational basis for drug use and will serve as the soil from which new advances will sprout. It can be concluded that Centbucridine produced a significantly longer duration of anesthesia. It worked just as effectively as the "gold standard" Lignocaine, matching it in terms of time of onset, depth of anesthesia, and cardiovascular effects. It produced no side effects or toxic reactions and confirmed its safety for use in this sample population. We can recommend Centbucridine as a LA agent for dental procedures which may last up to 2 hours. It is also recommended that Centbucridine could be confidently used in medically compromised patients where Lignocaine or adrenaline is contraindicated.

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