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ORIGINAL ARTICLE

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Comparative investigations on the efficacy of articaine 4% (epinephrine 1:200,000) and articaine 2% (epinephrine 1:200,000) in local infiltration anaesthesia in dentistry—a randomised double-blind study

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Abstract A randomised double-blind study investigated 155 patients with tooth extractions in the mandibular and maxillary jaws for a loss of anaesthetic potency when reducing the concentration of the active in articaine solutions. Tests were performed on the preparations of articaine 4% with a 1:200,000 addition of epinephrine (Ultracain D-S) and articaine 2% with a 1:200,000 addition of epinephrine (Ultracain 2%-Suprarenin). Local infiltration anaesthesia was the chosen method of anaesthesia. The most noticeable difference observed between the two injection solutions concerned the duration of anaesthesia, which was significantly shortened under the low-dose solution. The 4% articaine solution did not prove superior in local anaesthetic effect. Articaine 2% with epinephrine 1:200,000, therefore, can be considered a suitable local anaesthetic for tooth extractions.

Keywords Local anaesthesia · Articaine · Epinephrine · Tooth extraction

Introduction

Apart from major maxillofacial surgical procedures and the management of non-compliant patients, local anaesthesia is the dominating method used for pain neutralisation in dentistry where general anaesthesia is required [1]. The development of acid amides constitutes a major contribution to the high level of safety attained in modern local anaesthesia. Among the acid amides, articaine takes a special position, because instead of having a benzene ring, it possesses a heterocyclic thiophene ring and an additional ester group [18].

With its mean span of 20 min, the elimination half-life of articaine is significantly shorter than that of the other amide-based local anaesthetics [7]. In addition, its clinical use is characterised by good tissue penetration [19]. Articaine also provides the most favourable relationship between efficacy and toxicity [21], and therefore, affords the possibility of applying higher-dosed injection solutions (4%) as compared with other local amide anaesthetics, supposedly resulting in a higher anaesthetic efficacy [19].

In dentistry, articaine is usually applied in a 4% solution (without or with epinephrine 1:100,000 or 1:200,000). In Germany, a 2% injection solution with an epinephrine addition of 1:200,000 has recently become available for dental use. Discussion on whether preference should be given to the 2% solution or the 4% solution is controversial. Whilst some authors favour the 2% solution because of its lower toxicity [13, 16, 27, 28], others tend to doubt its anaesthetic effect and recommend the high-dosed solution [2, 11]. For this reason, a randomised double-blind study investigated whether a reduction of anaesthetic potency is to be expected in tooth extractions in the upper and lower jaws when cutting the concentration of the active to half the usual dose in an articaine solution with epinephrine added at 1:200,000.

Materials and methods

The efficacy and tolerability of articaine 4% with epinephrine 1:200,000 and articaine 2% with epinephrine 1:200,000 in dental local anaesthesia were to be evaluated in a randomised double-blind study. The investigation was approved by the ethics committee of the Medical Faculty of Dresden, University of Technology (Nr. EK070296). The study included a total of 155 participants, i.e. 87 male and 68 female patients aged 19 to 63 years (mean age 52.0± 16.5 years) where extraction of a tooth was indicated in

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either the upper or the lower jaw. Inclusion criteria comprised: patient at least 18 years old, no epinephrine or articaine intolerance, no pre-medication and no signs of acute inflammation. Local infiltration anaesthesia was the anaesthetic method used throughout (i.e. mandibular nerve block was abandoned) by a vestibular (1.8 ml) and a palatal/lingual injection (0.2 ml). The injections and the extractions were performed by certified dentists of the Department of Oral and Maxillofacial Surgery of the University of Technology. The following agents were applied for anaesthetisation: Ultracain D-S (articaine 4% plus epinephrine 1:200,000) 80 mg (2.0 ml) and Ultracain 2%-Suprarenin (articaine 2% plus epinephrine 1:200,000) 40 mg (2.0 ml). Blood pressure and pulse rate were taken before each injection (reading 1), before starting the intervention, i.e. 5 min after the injection (reading 2), and at 10-min intervals (readings 3 and 4) using an automated sphygmomanometer (Boso, Bosch+Sohn GmbH und Co, Germany). Evaluation of the local anaesthetic effect relied on the subjective assessment given by the patients upon completion of the intervention with the help of a visual analogue scale (VAS). Ratings were as follows: complete anaesthesia (intervention absolutely painless), satisfactory anaesthesia (mild but tolerable pain) or unsatisfactory anaesthetic effect (second injection required).

In addition, patients were asked to assess the injection pain, again using the VAS. Moreover, existing ischaemia in the field of intervention and duration of soft tissue anaesthesia (time from the injection to complete resolution of the anaesthetic effect) were recorded. Furthermore, the patients were asked to give a subjective assessment of their post-operative wound pain by grading the pain experienced as "minor", "moderate" or "severe" pain. For wound assessment, attending dentists were to grade the extent of

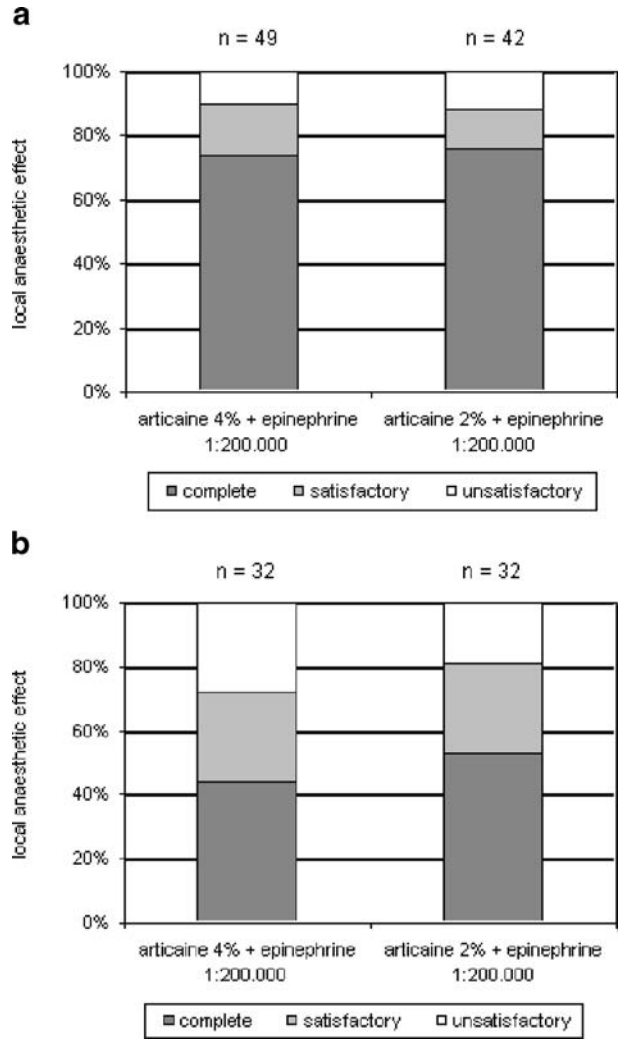

Fig. 1 Local anaesthetic effects of articaine 4% and articaine 2% (epinephrine 1: 200,000) in infiltration anaesthesia in the upper jaw (**a**) and of the lower jaw (**b**)

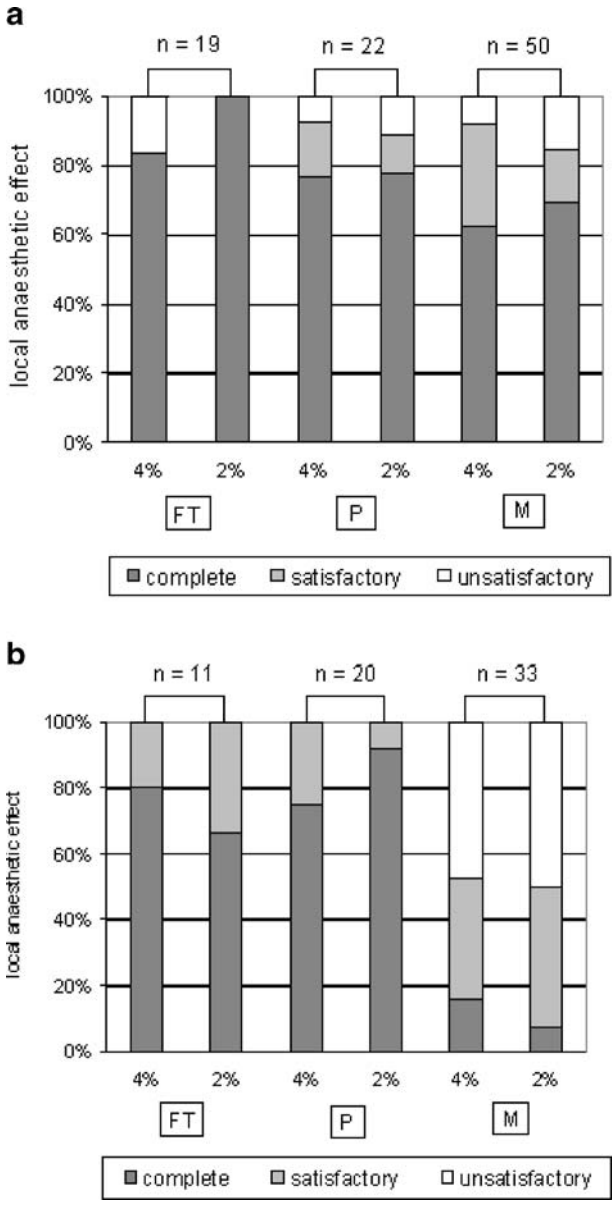

Fig. 2 Local anaesthetic effects of articaine 4% and articaine 2% (epinephrine 1:200,000) in infiltration anaesthesia in the upper (**a**) and in the lower (**b**) front teeth (FT), premolar (PM) and molar regions (M)

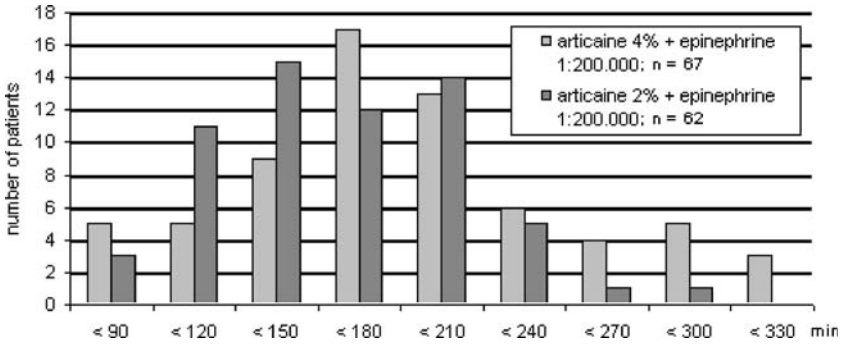

Fig. 3 Distribution of the duration of soft tissue anaesthesia

post-operative swellings as "minor", "moderate" or "severe". Moreover, all wound-healing problems (like wound/suture dehiscence, alveolitis) were recorded. The computer programme SPSS-Data Entry II was used for statistical processing of the data obtained. Analyses included Pearson's chi-square test (comparison of two frequencies) and the *t* test (comparison of means). The significance level for these procedures was 5% (α=0.05).

Results

The local anaesthetic effect provided by articaine 4% applied in the upper jaw was found to be complete in 36 patients (74%), satisfactory in eight patients (16%) and unsatisfactory in five patients (10%). Anaesthesia produced by the 2% solution was considered complete in 32 patients (32%), satisfactory in five patients (12%) and unsatisfactory in five (12%) of the patients (Fig. 1a). The analysis of the anaesthetic quality in the lower jaw showed that articaine 4% produced complete anaesthesia in 14 cases (44%), satisfactory anaesthesia in nine cases (28%), and an unsatisfactory effect in another nine cases (28%). After injection of articaine 2%, complete anaesthesia was attained in 17 cases (53%), anaesthesia was satisfactory in nine cases (28%) and unsatisfactory in six cases (19%) (Fig. 1b). In the two groups the difference between the two local anaesthetics was not significant (p=0.740 and p=0.948) (chi-square test). In the upper jaw, evaluation of the individual tooth groups revealed a slope in anaesthetic effect from the front teeth to the molar region. Whilst an average of 92% of the patients described complete anaesthesia in the region of the front teeth, the intervention was rated completely painless by 77 and 65% for the pre-molar region and the molar region, respectively (Fig. 2a). With no failure rates, the two test solutions attained best results in the extraction of lower front teeth and pre-molars, where interventions were painless in 83 and 77%. As could be expected, anaesthetic quality was poorest for extractions of mandibular molars. A mere 11% of the patients described the anaesthetic effect as complete (Fig. 2b). Approximately, every second patient (49%) needed a second injection (mandibular block). Anaesthesia attained after these second injections was found to be complete in five cases and satisfactory in four cases for articaine 4%, whilst it was complete in two patients and satisfactory in

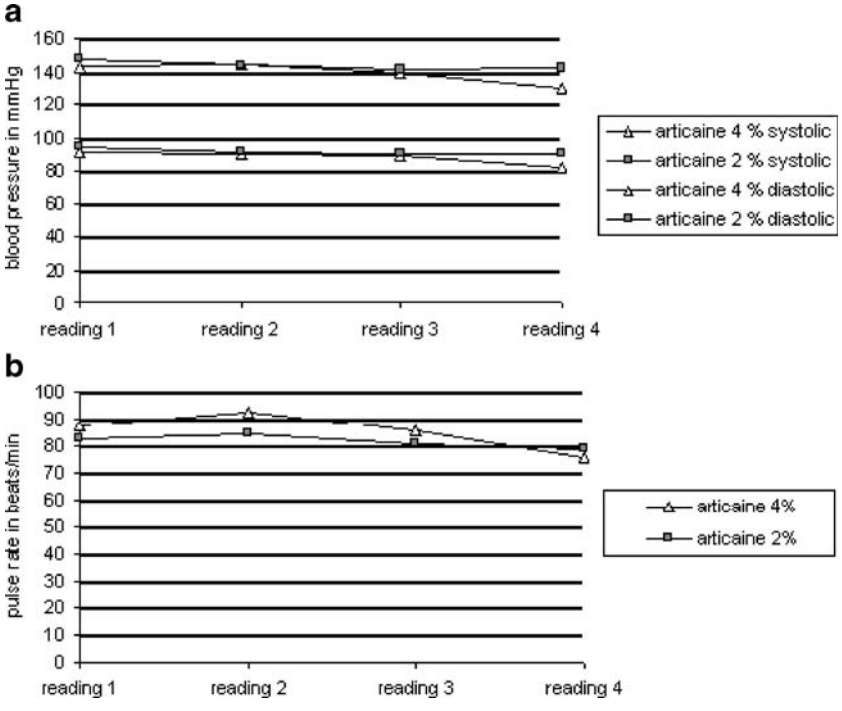

Fig. 4 Mean values of systolic and diastolic blood pressure (**a**) and pulse rate (**b**) after injection of articaine 4% and articaine 2% (epinephrine 1:200,000) (articaine 4%, n=67; articaine 2%, n=62)

five patients under articaine 2%. It follows, therefore, that the failure rate in the lower jaw was twice as high as in the upper jaw. Statistical analysis of the VAS ratings for local anaesthetic efficacy again showed no superiority of the 4% articaine solution (chi-square test). Mean values of articaine 4% and articaine 2% were 0.6 for the two concentrations in the upper jaw and 1.3 and 1.5 in the lower jaw. VAS differences between the mandibular molar regions (VAS score 2.7) and the front tooth and pre-molar regions (VAS range 0.4 to 0.6) were statistically significant (chi-square test).

The values determined with the help of the VAS for the assessment of injection pain were 1.0 for articaine 4% and 0.8 for articaine 2%, with the difference not being statistically significant (chi-square test).

After administration of the 2% articaine solution study participants reported an average soft tissue anaesthesia of 145 min, equalling a statistically significant difference of 29 min less than the 4% articaine solution (*t* test) (Fig. 3).

Whilst a comparison of the two formulations for ischaemia yielded no statistically significant divergence, the higher-dosed solution tended to perform better in this respect. Mild (43.6%) to moderate (51.7%) haemorrhages were found to be most frequent. Massive haemorrhage occurred in only 4.7%.

Blood pressure fluctuations were recorded in the two groups to a similar extent (Fig. 4a). Differences were not statistically significant (*t* test). Both systolic and diastolic pressure proved to be highest before injection in all cases (reading 1). Pressure values decreased during treatment and, by the end of treatment, had already returned to below baseline values (readings 3 and 4).

After the administration of either injection solution, the time profiles for pulse rate also reflected only minor fluctuations in the readings (Fig. 4b). As could be expected maximum rates were registered upon administration of the test solutions, i.e. shortly before the intervention (reading 2). The differences between the two test solutions were not significant (*t* test), and measurements tended to converge towards each other as treatment proceeded.

The distribution of side effects for the two solutions is summarised in Table 1.

A 6.9% rate of incidence (nine patients) was determined for adverse effects after the administration of the two local anaesthetics. The most common side effects were non-specific and concerned perspiration and dizziness.

During the intervention, i.e. after the beginning of surgery, the rate of complications was 9% (11 patients).

Table 1 Frequency distribution of complications following the administration (FA) of articaine and occuring during the intervention (DI) under articaine (epinephrine 1:200,000) (*n*=130)

Formulation	Side effect	Number (FA)	Number (DI)
Articaine 4%	Perspiration	3	5
Articaine 2%	Perspiration	4	3
Articaine 2 and 4%	Dizzines	2	2
	Nausea	0	1

Table 2 Extent of the post-operative swelling, post-operative wound pain and post-operative complications during the healing phase (*n*=127)

		Articaine 4%	Articaine 2%
Post-operative wound pain	No pain	36	38
	Minor pain	21	21
	Severe pain	8	3
Post-operative swelling	Minor	42	48
	Moderate	19	12
	Severe	4	1
Post-operative bleeding		16	9
Wound healing disorders		9	5

Again, only mild adverse effects were observed under the two formulations (perspiration, dizziness, nausea).

One hundred twenty-seven patients presented for evaluation at the follow-up visit 1 week after surgery. Whilst assessments of post-operative complications established a tendency for better outcomes under the 2% test solution in terms of post-operative bleeding or wound healing problems, these differences were not significant (Table 2).

Discussion

The present study evaluated the local anaesthetising effect and time of efficacy of a 4% articaine solution (Ultracain D-S) vs a 2% articaine solution (Ultracain 2%-Suprarenin), with the two solutions containing epinephrine 1:200,000, in tooth extractions under local infiltration anaesthesia. Direct comparison of the local anaesthetic effect did not establish a superior efficacy for the articaine solution with the 4% concentration of the active. Our findings corroborate those of Fritzsche [5] as well as Fritzsche and Päβler [4], who also conducted a clinical double-blind study evaluating articaine 4% (epinephrine 1:200,000) and articaine 2% (epinephrine 1:200,000) in the extraction of lower molars, but chose nerve block anaesthesia. Their comparison revealed no superiority of articaine 4% for onset of effect and depth of anaesthesia. The same results were obtained by Winther and Nathalang [27] and by Knoll-Köhler [14], who did not determine any difference in the anaesthetic action profiles of a 2 and 4% solution of articaine or a 74-mM (=2.4% solution) and a 148-mM (=4%) solution of articaine with an epinephrine addition of 1:200,000 and 1:100,000, respectively. Winther and Nathalang [27] solely determined differences in the duration of anaesthesia. Corresponding results were again obtained in a subsequent study by Winther and Patirupanasura [28]. The reports of some other authors [3, 17, 22, 23] that tested the suitability of articaine solutions of different concentrations contradict our results in that they established the safety of articaine 2% (although without the addition of epinephrine) to be clearly inferior to that of the 4% articaine solution with epinephrine 1:200,000. The fact that in these studies adrenaline-

containing 4% test solutions were compared with 2% articaine solutions without the addition of a vasoconstrictor may explain the pronounced differences in efficacy found by the authors. The co-administration of a vasoconstrictive agent increases the anaesthetic rate of success, because more molecules reach the site of action over a prolonged period of time [12].

The failure rate of 11% (ten patients) in maxillary anaesthesia was slightly higher than we had expected. In the literature [11, 17, 20, 26, 28], a failure incidence in the range of 0–7.7% is reported for the administration of the 4% articaine solution with epinephrine 1:200,000 in terminal infiltration anaesthesia of the upper jaw. The poorer result in this study may be a function of the relatively high rate of maxillary complications, which ultimately led to exceeding the therapeutic time window and, thus, to secondary injections, which produced a noticeable impact on the failure rate. In four cases, for instance, a subsequent injection was necessary because of surgical removal and in two cases because the maxillary sinus had to be opened. Patients with signs of acute inflammation had been excluded from the study to avoid corruption of the results.

The secondary injection rate of 23.5% established in the lower jaw was about twice as high as in the upper jaw. Whilst no secondary injections were necessary in any case in the front teeth and pre-molar regions, almost every second extraction of a lower molar required a secondary injection in the form of mandibular nerve block. Haas et al. [6] obtained similar results after buccal infiltration anaesthesia of articaine 4% with epinephrine 1:200,000 for extractions. Their success rate was 63% (pulpal anaesthesia) and 50% (lingual soft tissue anaesthesia) for the extraction of lower second molars. In the lateral dental region of the lower jaw, the excessively thick and compact cortical substance may be considered a limiting factor for satisfactory anaesthesia.

Whilst some authors recommend against stand-alone local infiltration anaesthesia at the lower pre-molars [2, 21], the studies covered by our literature research [20, 22, 24] were able to establish clearly positive results and, thus, confirmed our own investigations. Päβler and von Wickede [20] tested the success rate of a 4% articaine solution with a vasoconstrictor of 1:200,000 in lower front teeth and pre-molars after only a vestibular injection and were not able to demonstrate failure in either group of teeth.

In our study, the most obvious difference between the two solutions concerned the duration of anaesthesia in soft tissue. The overall mean duration of anaesthesia was 174 min after the administration of the 4% articaine solution. The soft tissue anaesthesia provided by the 2% articaine solution was shorter by 29 min, with the difference being significant vs the 4% solution. Because the anaesthetic effect in soft tissue is sustained beyond that of pulpal anaesthesia, it is not a suitable basis for the calculation of the therapeutic time window provided. According to Lemay et al. [15], the latter has a share of 90% in the overall duration of anaesthesia, depending on the dose and method of anaesthesia applied. Szabo and Divinyi [25] determined a mean duration of soft tissue anaesthesia of approximately 150 min. Moreover, nerve block anaesthesia provides prolonged anaesthetisation as against terminal infiltration anaesthesia [10].

Children and elderly patients particularly benefit from shortened soft tissue anaesthesia, in that it can reduce the likelihood of autogenous traumatisation. Clinical studies by Jakobs and co-workers [8, 9] were not able to demonstrate differences in the efficacy of the 2 and 4% solution in children. It is especially in this group of patients that the low-dosed anaesthetic should be preferred over the 4% solution due to the increased risk of absolute overdosing. Further shortening of soft tissue anaesthetisation can be attained by abandoning mandibular block in the lower front teeth and pre-molar regions. An additional pro is that accompanying effects (numbness of the lip, tongue and the muscles of facial expression), which patients often find disagreeable, are avoided. Moreover, the increased rate of complications (intravasal injection, paresis of the facial muscles, nerve lesions, paraesthesias) associated with nerve block can be minimised.

Conclusion

Lowering the concentration of the active from 4 to 2% did not affect the safety of the onset of action, the local anaesthetic effect or tolerability. This proves articaine 2% with adrenaline 1:200,000 to be essentially suitable for dental local anaesthesia. In the front teeth and pre-molar regions of the lower jaw nerve block, anaesthesia may be circumvented by applying terminal infiltration anaesthesia using the two injection solutions. However, abandoning mandibular anaesthesia is not possible in extractions of the lower molars.

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