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Efficacy and safety of 4% articaine with epinephrine for the anterior middle superior alveolar nerve block comparing to the computer-controlled and conventional anesthetic delivery: prospective, randomized, cross-over clinical study

Efikasnost i sigurnost 4% artikaina sa epinefrinom za gornji prednji i srednji alveolarni nervni blok primenom kompjuterski kontrolisanog sistema i standardnog pristupa za primenu anestetičkog rastvora: prospektivna, randomizovana, kontrolisana, dvosturko slepa, ukrštena klinička studija

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Abstract

Bacground/Aim. The efficient dental anesthesia, which is related to the clinically adequate depth, duration and the width of anesthetic field, is an important prerequisite for successful dental treatment. The aim of this study was to investigate and compare the pulpal anesthesia and cardiovascular parameters after the anterior middle superior alveolar (AMSA) nerve block with 4% articaine with epinephrine administered by conventional cartridge-syringe and computer-controlled local anesthetic delivery system (CCLADS). **Methods.** This controlled double-blind cross-over randomized clinical study included 38 healthy volunteers. Efficacy of pulpal anesthesia after the AMSA nerve block was evaluated by measuring a success rate, onset and duration of pulpal anesthesia, using an electrical pulp tester. The parameters of cardiovascular function (systolic and diastolic blood pressure, heart rate) were monitored noninvasively. **Results.** Successful pulpal anesthesia of all tested teeth was obtained in 57.9% participants with CCLADS and in 44.7% participants with conventional syringe. The onset time was not significantly different between two investigated groups. The pulpal anesthesia duration was not significantly different neither within nor between investigated groups. The systolic and diastolic blood pressures were significantly decreased in both investigated groups, in comparison with the baseline values. Heart rate significantly decreased within CCLADS from 10th to 30th minute when compared to baseline. **Conclusion.** The efficacy of pulpal anesthesia and safety of cardiovascular profile of 0.6 mL of articaine with epinephrine (1:100.000) delivered with CCLADS were improved in comparison to the conventional syringe delivery. Significant changes of cardiovascular function were not observed.

Key words:
articaine; anesthesia dental; anesthesia, local; therapy, computer assisted; nerve block; injections.

Apstrakt

Uvod/Cilj. Efikasna zubna anestezija u pogledu klinički adekvatne dubine, trajanja i širine anestetičkog polja je važan preduslov za uspešno zubno lečenje. Cilj rada bio je ispitivanje i upoređivanje parametra anestezije zubne pulpe i kardiovaskularnih parametra posle gornje prednje i srednje alveolarne (AMSA) sprovodne anestezije postignute 4% artikainom sa epinefrinom, primenom standardne karpul-brizgalice i kompjuterski kontrolisanog sistema za primenu anestetičkog rastvora (CCLADS). **Metode.** U ovom randomizovanom, prospektivnom, kontrolisanom, dvostruko slepom ukrštenom kliničkom istraživanju učestvovalo je 38 ispitanika. Kvalitet anestezije zubne pulpe posle AMSA anestezije praćen je na osnovu uspešnosti, latentnog perioda i trajanja anestezije zubne pulpe, primenom električnog pulp-testera. Parametri kardiovaskularne funkcije (sistolni i dijastolni krvni pritisak, srčana frekvencija) praćeni su neinvazivno, primenom aparata za monitoring. **Rezultati.** Uspešna anestezija zubne pulpe svih ispitivanih zuba bila je

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prisutna kod 57,9% ispitanika posle kod CCLADS i kod 44,7% ispitanika posle primene standardne karpul-brizgalice. Latentni period i trajanje anestezije zubne pulpe nisu se značajno razlikovali između ispitivanih grupa. Sistolni i dijastolni pritisak bili su značajno sniženi u praćenim vremenskim intervalima u odnosu na početne vrednosti. Srčana frekvencija je bila značajno snižena kod CCLADS grupe od 10 do 30 minuta u odnosu na početne vrednosti. **Zaključak.** Kontrolisanom kompjuterizovanom primenom (CCLADS) 0,6 mL 4% artikaina sa epinefrinom (1:100,000) za AMSA sprovodnu anesteziju, postignut je bolji kvalitet anestezije zubne pulpe u odnosu na primenu artikaina sa epinefrinom standardnom karpul brizgalicom. Nisu uočene bitne promene funkcija kardiovaskularnog sistema.

Ključne reči:
artikain; anestezija, stomatološka; anestezija, lokalna; lečenje, kompjuterom vođeno; blokada živca; injekcije.

Introduction

The efficient dental anesthesia, which is related to the clinically adequate depth, duration and the width of anesthetic field, is an important prerequisite for successful dental treatment. Most commonly, the pulp of the maxillary teeth, surrounding bone and soft tissue are anesthetized by buccal supraperiosteal infiltration of local anesthetic in the projection of the tooth apex [1]. Recently, the anterior middle superior alveolar (AMSA) nerve block has been introduced as a technique which provides pulpal anesthesia of multiple maxillary teeth with single site injection, without collateral anesthesia of lip, face and muscles of facial expression [2]. The local anesthetic solution for the AMSA nerve block is deposited palatal, at the point which bisects the maxillary premolars, and midway between the mid-palatal raphe and premolar free gingival margin crest. The target area is the anatomical region where the anterior superior alveolar (ASA) and the medial superior alveolar (MSA) nerves' branches converge and form the dental neural plexus. Therefore, an anesthetic effect of a single AMSA block injection extends to the pulpal tissue of maxillary teeth from the central incisor through the second premolar, innervated by the ASA and MSA nerves, with additional anesthesia of soft palatal tissue in the same region.

Generally, the palatal injections with a conventional syringe have the potential to be unpleasant and painful. The new approach in the dental anesthesia techniques develops systems of controlled anesthetic delivery is aimed to reduce not only a patient's discomfort during palatal soft tissue anesthesia, but also to increase quality of bone and dental pulp anesthesia. Some of the published studies using this computer-controlled local anesthetic delivery system (CCLADS) for the AMSA nerve block, showed that continuous and controlled dosage of 2% lidocaine with epinephrine may achieve profound pulpal anesthesia from central incisor through second premolar, what was not seen after conventional delivery [2–4]. Although obtained clinical results were more favorable with the CCLADS than with conventional delivery, the modest to low success rate, slow onset and rapid anesthesia duration declining observed after 2% lidocaine with epinephrine may decrease the clinical utilization of AMSA nerve block due to the anatomical properties of palatal injection site, as well as pharmacological properties of lidocaine with epinephrine solution [5, 6].

Since the AMSA nerve block is obtained following diffusion of local anesthetic solution through the palatal bone before reaching the dental nerve plexus, the characteristics of local anesthetic could influence the parameters of local anesthesia. Articaine is an amide local anesthetic with the unique properties due to the characteristics of thiophene ring in its structure, which ensures that a diffusing property of articaine through soft and hard tissues is more pronounced than of other amide local anesthetics [7]. There is evidence that palatal soft tissue anesthesia occasionally may be obtained by articaine diffusion after maxillary infiltration without an additional palatal injection [8–10].

To our knowledge, there are no data concerning the efficacy and safety of AMSA nerve block obtained with 4% articaine with epinephrine. Therefore, the aim of this study was to investigate and compare the parameters of pulpal anesthesia and cardiovascular functions after the AMSA nerve block with 4% articaine with epinephrine administered by a conventional syringe and the CCLADS.

Methods

This prospective, double-blind cross-over randomized study included the healthy volunteers [American Socity of Anesthesiologists (ASA) I] who were admitted for the regular dental examination at the Clinic of Oral Surgery, School of Dental Medicine, University of Belgrade, Serbia. After approval of the Ethics committee of the School of Dental Medicine (36/5-2015), the study was performed in accordance with ethical standards laid down in 1964 Declaration of Helsinki and its later amendments. The United States National Institutes of Health Clinical Trial registration was performed (ClinicalTrials.gov: NCT02440347). All participants signed the informed consent after they were informed in details, verbally and in written form, about the study procedures and possible side effects.

Participants' eligibility

Inclusion criteria were as follows: full maxillary dental arch with all maxillary teeth free of caries and restorations, without history of trauma, sensitivity or orthodontic treatment, with a visible pulpal chamber on intraoral radiogram, responsive to electrical stimulation by the pulp tester and clinically and radiographically healthy periodontium. The allergy to local anesthetics, presence of orofacial pain, and/or use of any medicine within the previous 48 hours, pregnancy, lactation, drug and/or alcohol abuse, tobacco smoking and inhibition to give informed consent were exclusion criteria.

Study procedure

The patients served as their own control in cross-over design. The AMSA injection on one side of the maxillary arch was administered using CCLADS (Anaeject®, Septodont, France) while conventional cartridge-syringe was used for the opposite side. The AMSA injection site was located at a point that bisects the maxillary first and second premolars, and midway between the crest of the free gingival margin and mid-palatine suture. The needle was orientated at a 45 degree angle with the bevel facing palatal tissue. All dental anesthesia glass cartridges were marked at the level of 0.6 mL of anesthetic solution. The 0.6 mL of 4% articaine with epinephrine 1:100 000 was administered in two minutes period, both with CCLADS, or conventional cartridge-syringe. CCLADS enabled a slow and constant administration of anesthetic, approximately 0.005 mL per second. The sound mode during the administration of local anesthetic with CCLADS was switched off, in order to disable the patient to distinguish the method of administration. The patients were instructed to rest prior to the injection in supine position for 15 minutes in an isolated dental office. In addition, the patients were blindfolded with a commonly used sleeping mask so they would not distinguish which anesthetic delivery system was used. The same operator administered anesthesia of both sides and was excluded from measuring data and statistical analysis. The order of anesthesia techniques was blinded and randomly selected from a sealed envelope for each patient, with a washout period of 2 weeks between the appointments.

Parameters of pulpal anesthesia

The pulpal anesthesia parameters were tested in the following teeth: upper central and lateral incisor, canine, first premolar and second premolar with contralateral canine as a control tooth.

The anesthetic success, onset and duration were registered with the electrical pulp tester (EPT) (Vitality Scanner, Sybron Endo Model 2006®, Orange, CA, USA). The primary outcome was a success of pulpal anesthesia. The anesthesia was considered successful when 2 consecutive no response at maximum (80) readings stimulation were obtained. Before the anesthesia was given, the experimental teeth and contralateral control canine were tested by means of Vitality Scanner to record the baseline vitality. The fluoride gel (Fluorogal Forte®, Galenika, Belgrade, Serbia) was used as an electrolyte between the tooth and pulp tester probe. The tip of pulp tester probe was placed in the middle third of the buccal side of tested teeth. The pulp response was tested immediately after the end of anesthetic application, from the central incisor through second premolar order, making the repeated measurements for each tooth 4 minutes apart.

The secondary outcomes were onset and duration of pulpal anesthesia. Onset time for anesthesia was defined as the time from completion of the anesthetic injection to the time when profound anesthesia was achieved EPT ≥ 80. The duration of pulpal anesthesia was a period between the first and the last 80 readings on EPT, what was considered to be profound anesthesia.

Parameters of cardiovascular function

The cardiovascular parameters, such as the systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were recorded by the electrocardiogram monitor (Datex-Engstrom AS/3, Helsinki, Finland) 6 times: 5 minutes prior anesthesia, during anesthetic injection, and 5, 10, 15 and 30 minutes after administering anesthesia. Also, the participants were monitored for the potential changes in a cardiac rhythm and the possible signs of myocardial ischemia.

Statistical analysis

The data concerning the demographic characteristics of participants were compared by the χ^2-test. A success of pulpal anesthesia was evaluated by the descriptive statistical methods with the χ^2-test and Fisher's test for within group analysis and the McNemar test for between groups comparisons. The obtained differences in the onset and duration of pulpal anesthesia between the groups were tested for a significance by the Wilcoxon Sign Rank test, while the Kruskall-Wallis test was used for within group analysis, followed by the Mann-Whitney *U* test. The parameters of cardiovascular function (SBP, DBP and HR) were analyzed by the two-way repeated measures ANOVA with the group and time as the main factors. The changes of cardiovascular parameters over time within investigated groups (baseline vs. observed time intervals), were compared by means of one-way repeated measures ANOVA with the Bonferroni *post hoc*. Between group comparisons in the cardiovascular function at the observed time intervals were performed by the paired samples *t*-test. The statistical analysis was carried out using the SPSS 20.0 (Inc., Chicago, IL, USA) with the level of significance set at 0.05. It was necessary to include at least 34 participants to obtain 20% difference in the pulpal anesthesia duration between the techniques with 80% statistical power at a two-tailed level of significance 0.05 using the Mann Whitney *U* test.

Results

Demographic data and participants flow

The participants flow is presented in Figure 1. Sixty-seven participants were assessed for eligibility, and 40 of them were recruited to participate in this study. All participants received both treatments, but two of them had unsuccessful anesthesia with both delivery systems and were excluded from the further analysis. The final number of analyzed participants with successful pulpal anesthesia of at least one tested tooth was 38, 20 females and 18 males, aging between 19 and 31 years (25.27 ± 2.46) with the mean body mass of 67.30 ± 15.03 kg/m^2.

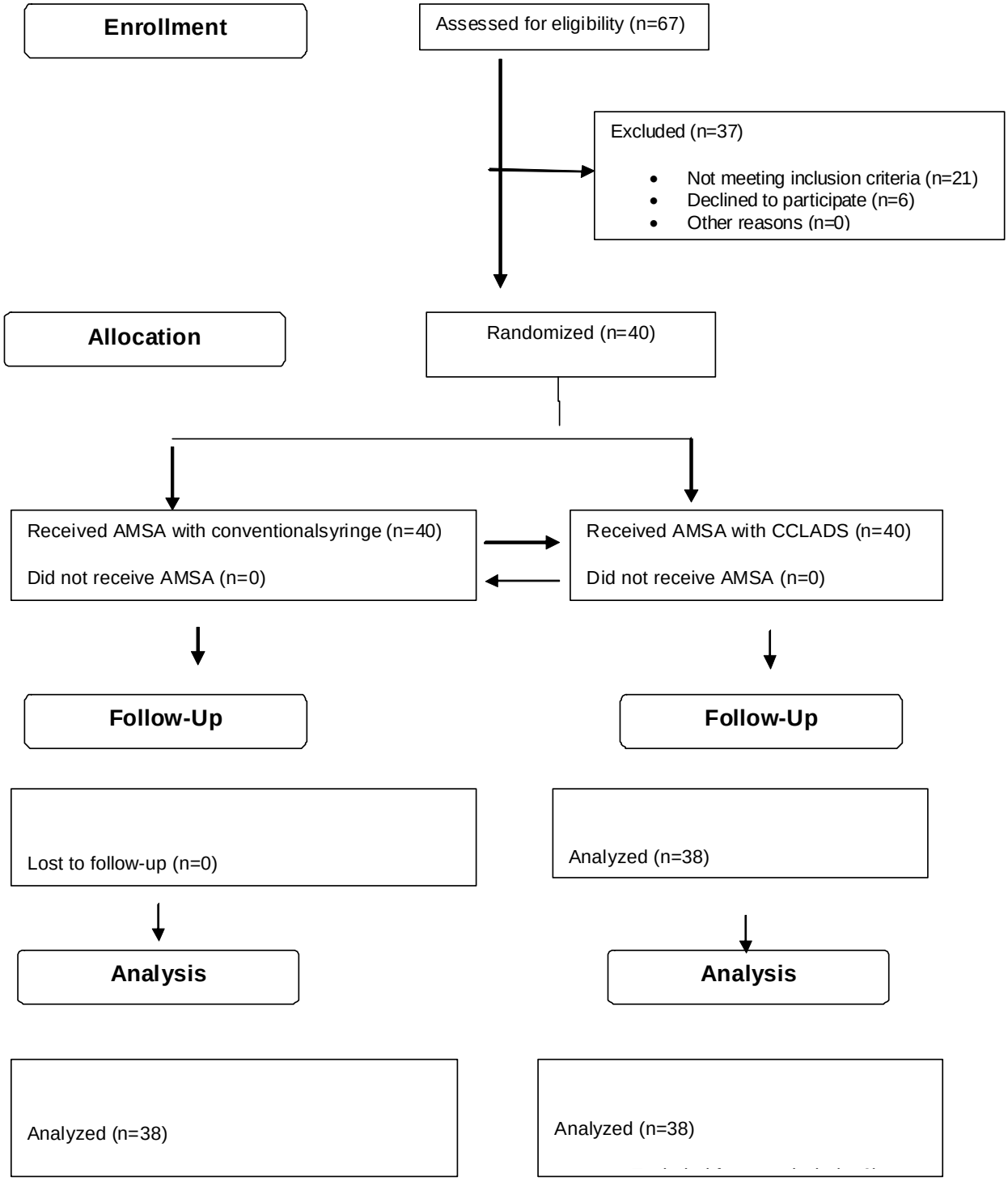

Fig. 1 – Flow diagram of randomization to either conventional injection, or computer-controlled local anesthetic delivery system (CCLADS) for the anterior and middle superior alveolar (AMSA) nerve block (CONSORT Statement 2010 Flow Diagram from Schulz KF, Altman DG, Moher D, for the CONSORT Group (2010) CONSORT 2010 statement: Updated guidelines for parallel group randomized trials. J Pharmacol Pharmacother. doi: 10.4103/0976-500X.72352).

Parameters of pulpal anesthesia

Successful pulpal anesthesia of all tested teeth was achieved in 22 (57.9%) participants of the CCLADS group and in 17 (44.7%) participants of the conventional syringe group. A success rate with CCLADS was 68.4% for the central incisor, 100% for the lateral incisor and canine, 76.3% for the first premolar and 86.8% for the second premolar; with the conventional syringe, a successful anesthesia was achieved in 71% for the central incisor, 94.7% for the lateral

incisor, 81.6% for the canine, 71% for the first premolar and 68.4% for the second premolar. Within group analysis of pulpal anesthesia a success rate in the CCLADS group revealed: a significantly higher success for the lateral incisor in comparison with the central incisor ($p < 0.001$) as well as for the lateral incisor in comparison with the first premolar ($p = 0.012$), and also for the canine in comparison with the central incisor ($p < 0.001$), and for the canine compared to the first premolar ($p = 0.012$). In the conventional injection group, pulpal anesthesia was significantly more successful for the lateral incisor compared to the central incisor ($p = 0.012$), for the lateral incisor compared to the first premolar ($p = 0.012$), as well as for the lateral incisor compared to the second premolar ($p = 0.006$). Between groups comparison showed that for the canine and second premolar a significantly higher success rate of pulpal anesthesia was observed after CCLADS vs. conventional injection (Table 1).

The onset and duration of pulpal anesthesia with conventional syringe and CCLADS are presented in Table 2. The onset time was not significantly different between these 2 investigated anesthetic techniques. Within group comparison revealed that there were no significant differences in the onset time among the teeth after the CCLADS injection. However, the onset of anesthesia was significantly longer in the conventional injection group for the central incisor in comparison with the lateral incisor ($p = 0.024$), for the central incisor compared to the first premolar ($p = 0.037$), and also when the central incisor was compared to the second premolar ($p = 0.022$), as well as for the canine in comparison with the first premolar ($p = 0.044$). The significant differences in the pulpal anesthesia duration were not observed neither within nor between the investigated groups (Table 2).

Table 1

Success of pulpal anesthesia after anterior middle superior alveolar (AMSA) injection of 4% articaine with conventional syringe and the computer-controlled local anesthetic delivery system (CCLADS)

Tooth	Delivery system		
	Conventional syringe (n/N)	CCLADS (n/N)	p^a
Central incisor	27/38	26/38	ns
Lateral incisor	36/38*	38/38*	ns
Canine	31/38	38/38*	0.016
First premolar	27/38	29/38	ns
Second premolar	26/38	33/38*	0.016
p^b	0.020	< 0.001	

N – number of participants; n – number of successfully anesthetized teeth.
[a] – between groups comparison (McNemar test); [b] – within group comparisons (χ^2-test, Fisher's test *post hoc*); *$p < 0.05$: conventional injection for the lateral incisor vs. the central incisor ($p = 0.012$), the lateral incisor vs. the first premolar ($p = 0.012$), the lateral incisor vs. the second premolar ($p = 0.006$); the CCLADS injection for the lateral incisor vs. the central incisor ($p < 0.001$), the lateral incisor vs. the first premolar ($p = 0.012$), the canine vs. the central incisor ($p < 0.001$), the canine vs. the first premolar ($p = 0.012$).

Table 2

Onset and duration of successful pulpal anesthesia after the anterior middle superior alveolar (AMSA) injection of 4% articaine with a conventional syringe and the computer-controlled local anesthetic delivery system (CCLADS)

Tooth	Onset			Duration		
	Conventional (n)	CCLADS (n)	p^a	Conventional (n)	CCLADS (n)	p^a
Central incisor	10.61 ± 5.31* (27)	(26)	0.692	24.62 ± 18.92 (27)	28.31±15.79 (26)	0.411
Lateral incisor	8.01 ± 4.17 (36)	8.00 ± 4.68 (38)	0.959	33.14 ± 19.95 (36)	28.11 ± 17.51 (38)	0.168
Canine	9.45 ± 4.58* (31)	8.68 ± 5.03 (38)	0.149	32.19 ± 17.04 (31)	29.58 ± 19.38 (38)	0.710
First premolar	7.07 ± 5.45 (27)	7.74 ± 6.59 (29)	0.646	32.55 ± 14.30 (27)	26.34 ± 9.26 (29)	0.057
Second premolar	7.08 ± 5.05 (26)	6.84 ± 5.02 (33)	0.896	31.62 ± 16.11 (26)	29.46 ± 17.94 (33)	0.407
p^b	0.042	0.172		0.251	0.821	

Values given in minutes as mean ± standard deviation (SD); n – number of successfully anesthetized teeth.
[a]between groups comparison (Wilcoxon Sign Rank test); [b] within group comparison (Kruskal-Wallis test, Mann-Whitney *U* test *post hoc*); *$p < 0.05$: conventional injection for the central incisor vs. the lateral incisor ($p = 0.024$), the central incisor vs. the first premolar ($p = 0.037$), the central incisor vs. the second premolar ($p = 0.022$); the canine vs. the first premolar ($p = 0.044$).

Parameters of cardiovascular function

The two-way repeated measures ANOVA revealed a significant effect of time factor for SBP ($p < 0.001$), DBP ($p < 0.001$) and HR ($p = 0.008$), with the significant interaction of main factors only for SBP ($p = 0.010$) (data not presented).

The repeated measures one-way ANOVA with the Bonferroni *post hoc* test in the CCLADS group showed a significant decrease in SBP 5 minutes ($p < 0.001$), 10 minutes ($p = 0.009$) and 15 minutes ($p = 0.008$) after an injection in comparison with the baseline values; after conventional injection, SBP was significantly lower after 10 minutes ($p = 0.001$), 15 minutes ($p = 0.001$) and 30 minutes ($p = 0.029$) when compared to the baseline values. Significantly lower SBP was observed at 5th minute ($p = 0.006$) after conventional vs. CCLADS injection (Figure 2).

The statistical analysis revealed that there was a significant decrease in DBP over time in the CCLADS group at 5th minute ($p = 0.037$) and 10th minute ($p = 0.036$) when compared to the baseline values, while after conventional injection, a significant decrease in DBP was observed after 10 minutes ($p = 0.001$) and 15 minutes ($p = 0.006$) in comparison with the baseline values (Figure 3).

The significant changes in HR were observed only in the CCLADS group during the observation time, with the significantly decreased values at 10th ($p = 0.008$), 15th ($p = 0.008$) and 30th minute ($p = 0.003$) when compared to the baseline (Figure 4).

The changes in the cardiac rhythm and signs of myocardial ischemia were not observed on electrocardiogram during the observation period.

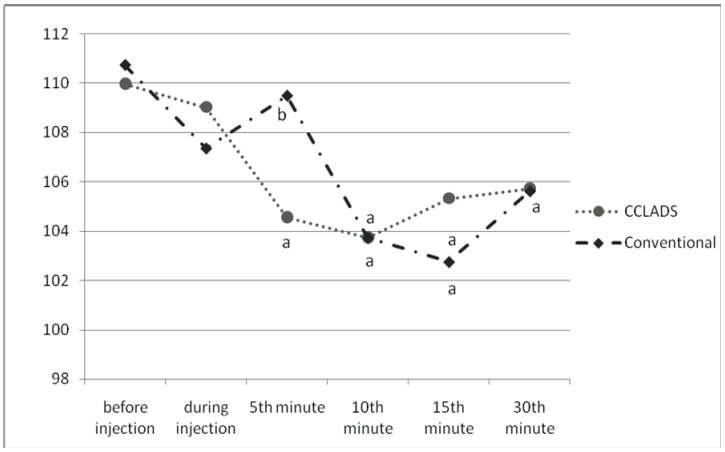

Fig. 2 – Changes in systolic blood pressure.

[a] within group comparison, One-way repeated measures ANOVA (baseline vs. observed time interval, Bonferroni *post hoc* test); for CCLADS 5th min ($p < 0.001$), 10th min ($p = 0.009$), 15th min ($p = 0.008$); for conventional injection 10th min ($p = 0.001$), 15th min ($p < 0.001$), 30th min ($p = 0.029$).
[b] between groups comparison, Paired samples *t*-test, 5th min ($p = 0.006$).
CCLADS – computer controlled local anesthetic delivery system.

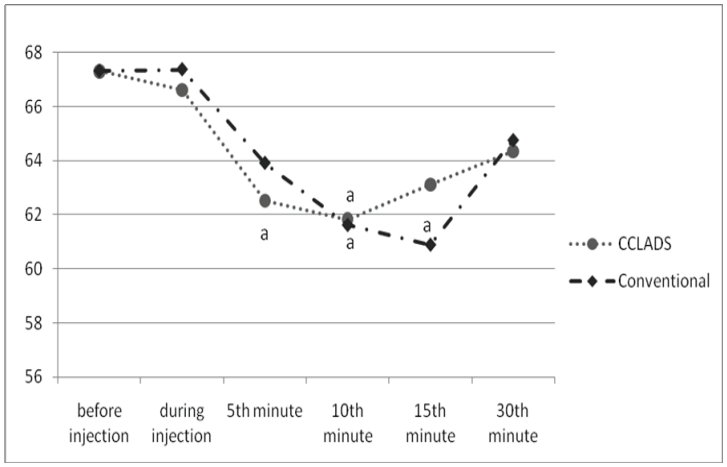

Fig. – 3 Changes in diastolic blood pressure.

[a] within group comparison; One-way repeated measures ANOVA (baseline vs. observed time interval, Bonferroni *post hoc* test); for CCLADS 5th min ($p = 0.037$), 10th min ($p = 0.036$); for conventional injection 10th min ($p = 0.001$), 15th min ($p = 0.006$).
CCLADS – computer controlled local anesthetic delivery system.

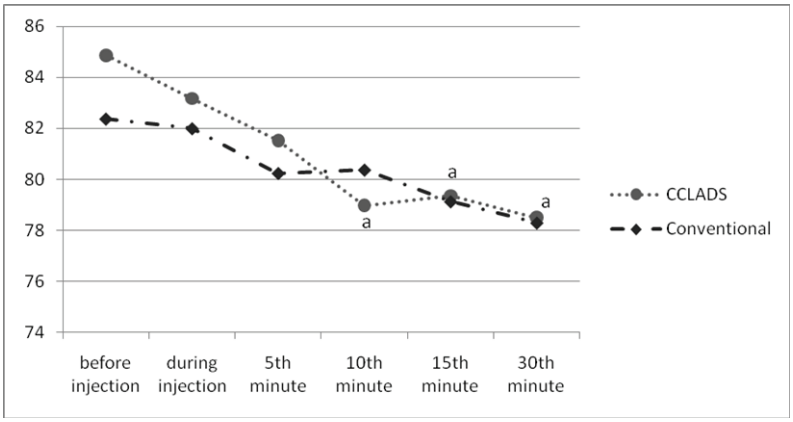

Fig. 4 – Changes in heart rate.

[a] within group comparison, One-way repeated measures ANOVA (baseline vs. observed time interval, Bonferroni *post hoc* test); for the CCLADS 10th min ($p = 0.008$), 15th min ($p = 0.003$), 30th min ($p = 0.003$).
CCLADS – computer controlled local anesthetic delivery system.

Discussion

This prospective, controlled double-blind, cross-over randomized clinical study in the healthy volunteers evaluated and compared the anesthetic and cardiovascular effects of 0.6 mL 4% articaine with epinephrine (1:100.000) used for the AMSA nerve block delivered by the computer-controlled delivery system and conventional syringe.

The overall success rate of pulpal anesthesia, as a primary outcome of the study, with CCLADS ranged from 68.4% to 100%, while with conventional syringe, it was between 68.4% and 94.7%. Pulpal anesthesia in the present study was considered successful if two, or more consecutive 80 readings were obtained by the electrical pulp test without the participant's response. Regarding the fact that the parameters of pulpal anesthesia after the AMSA nerve block obtained with articaine with epinephrine were not investigated, the available evidence concern the use of 2% lidocaine with epinephrine as a "gold standard". Namely, in the study of Fukayama et al. [3], the lower success rates were observed (between 42% and 72%), based on one registered 80 reading without a participant's response during the electrical stimulation, after the AMSA nerve block obtained with 1.8 mL of 2% lidocaine with epinephrine 1 : 80.000 delivered by the computer controlled system WAND. Similarly low success rates, evaluated according to two consecutive 80 readings without a participant's response to the electric pulp test, were also reported in a comparative study by Lee et al. [5] during the 60-minute observation period, after 1.4 mL of 2% lidocaine with 1 : 100.000 epinephrine delivered for the AMSA nerve block, either by computer controlled system (success rate between 35% and 58%), or using conventional syringe (success rate between 20% and 42%). On the other hand, Corbett et al. [6] reported a higher anesthetic success of pulpal anesthesia (between 42% and 85%) during the 47-minute observation period, regarding minimum two consecutive 80 readings without a response to the electrical stimuli, when 1 mL of 2% lidocaine with epinephrine 1 : 80.000 was delivered with the WAND system for the AMSA nerve block in comparison with the infraorbital nerve block. Considering factors that influence a success rate of pulpal anesthesia, as an important parameter of anesthesia quality, several of them, such as the anesthetic pharmacological profile, regional anatomical specificity and local anesthesia technique, could contribute to a higher success rate of local intraoral anesthesia. Since no difference was observed between delivery systems (CCLADS and conventional cartridge-syringe), our results could be explained rather by pharmacological properties of local anesthetic applied than the anesthetic technique used. Articaine is an amide local anesthetic with the characteristic molecular structure that includes the presence of tiophene ring. The presence of tiophene ring increases the anesthetic liposolubility, and it is suggested that articaine diffuses more readily through the soft and bone tissue than other local anesthetics. Increased lipid solubility of articaine (partition coefficient 17) in comparison with lidocaine (partition coefficient 4) permits the more active anesthetic molecules to effectively penetrate the lipid nerve membrane, what is reflected in the increased anesthetic potency of articaine. Concerning that, it is clear that articaine provides higher rates of pulpal anesthesia success than lidocaine when used for infiltration and block anesthesia during the routine dental treatments [11].

Further analysis of success rate in the present study compared the efficacy of CCLADS and conventional syringe delivery in obtaining successful pulpal anesthesia of specific teeth. Our results showed that pulpal anesthesia of canine and second premolar was significantly more successful after CCLADS injection in comparison with conventional injection. A significantly higher success rate of pulpal anesthesia using CCLADS compared to conventional injection was also observed in a comparative study by Lee et al. [5], but for all tested teeth from the lateral incisor to the second premolar after the AMSA nerve block achieved with 1.4 mL of 2% lidocaine with epinephrine 1 : 100.000. A lower success rate obtained with conventional injection could be due to the difference in the pressure gradient and flow rate between computer controlled and conventional delivery, since, using computer controlled delivery system, both factors were more precisely controlled and constant, providing the better conditions for anesthetic solution diffusion through the alveolar

and palatal bone. Furthermore, within the groups, the most successful pulpal anesthesia was observed for the lateral incisor and canine, while the lowest success rate was observed for the central incisor and first premolar regardless the delivery system used. The obtained results could be explained by the anatomical variability in innervation of the anesthetized area, since it is possible that the buccal root of the first premolar may be innervated by the accessory branches of posterior superior alveolar nerve [12]. Also, the buccal position of the root defines the greater distance and diffusion path of anesthetic solution which is deposited palatal. Similarly, the distance of central incisor's root from the deposition site could affect diffusion of anesthetic solution, leading to a comparatively lower pulpal anesthesia success rate.

The onset of pulpal anesthesia was similar between the investigated groups in our study. The results of previous studies, after the AMSA nerve block performed with 2% lidocaine with epinephrine, showed that the onset time ranged between 5 and 11 minutes with CCLADS delivery system, and between 6 and 12 minutes with conventional injection delivery [4, 6]. Similar results were obtained in our study. Similarly to the previously mentioned studies, the longer onset time was observed for the central incisor and canine, using both delivery systems. It is possible that this delay in the onset was due to a greater diffusion distance of anesthetic solution through the alveolar and palatal bone [6].

Only two studies reported that the duration of pulpal anesthesia after the AMSA nerve block was achieved with 2% lidocaine with epinephrine. In a study by Fukayama et al. [3], the authors reported the duration of pulpal anesthesia up to 40 minutes, including all tested teeth from the central incisor to the first molar, after the AMSA nerve block obtained with 2% lidocaine with epinephrine 1:80.000 using CCLADS delivery system. Similarly, Velasco and Soto [4] observed the duration of pulpal anesthesia of tested teeth between 23 and 40 minutes when 2% lidocaine with epinephrine 1:100.000 was applied with the conventional cartridge-syringe [4]. However, in the mentioned studies, the statistical analysis of pulpal anesthesia duration was not performed due to a low number of participants with a successful pulpal anesthesia. In the present controlled clinical study, with confirmed statistical power, duration of pulpal anesthesia comparing two delivery systems was similar and ranged from 24 to 32 minutes for conventional syringe delivery, and between 26 to 29 minutes for CCLADS. Regarding the pharmacological profile of articaine, the degree of articaine protein binding (95%), which is higher than that of lidocaine (65%), is expected to ensure the more firm attachment of articaine molecules to the protein receptors sites, responsible for a longer duration of clinical activity. However, further comparative study of articaine and lidocaine might confirm anesthetic superiority concerning anesthesia duration after articaine delivery for the AMSA nerve block.

It still remains unclear whether the AMSA nerve block truly acts as a nerve block, since anesthetic solution is not deposited directly in the vicinity of any main nerve trunk. Furthermore, a success as well as duration of pulpal anesthesia varied with the distance and bone thickness between the tooth apex and deposition site, which favors more tissue infiltration as a type of anesthesia, over the nerve block conduction [6]. Taking all together, there could be a possibility that the AMSA nerve block acts as an intraosseous injection, which directly reflects to a significance of articaine + epinephrine safety profile. This route of administration, due to the deposition of local anesthetic in the highly vascularized bone area, allows the rapid resorption of both, local anesthetic and vasoconstrictor. Therefore, the safety profile of AMSA nerve block in the present study was evaluated by the cardiovascular parameters monitoring. The systolic blood pressure was a significantly decreased within CCLADS group from 5th to 15th minutes in comparison with the baseline values, and in the conventional group, from 10th to 30th minute when compared to the baseline. At the 5th minute, the systolic blood pressure significantly increased after the conventional injection in comparison with CCLADS. The decreased systolic blood pressure within both groups in our study implies a good safety of AMSA technique with regard to cardiovascular stability, which is supported also by the decreased values of diastolic blood pressure from 5th to 10th minute for the CCLADS injection and from 10th to 15th minute for conventional injection, in comparison with the baseline values. A heart rate was significantly decreased only in the CCLADS group from 10th to 30th minutes, which suggests the more preferable cardiovascular profile after CCLADS injection, since the heart rate is a cardiovascular parameter that is the most sensitive to the exogenous epinephrine effects [13].

Conclusion

In conditions of the present double-blind randomized controlled cross-over clinical study, the efficacy of pulpal anesthesia, especially for the lateral incisor and canine as well as safety of cardiovascular profile of 0.6 mL of articaine with epinephrine (1:100.000) delivered using CCLADS overcome conventional syringe delivery.

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