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The Effect of Needle-free Injection System on Dental Injection Pain in Children: A Cross-over, Randomized Clinical Trial

2.

3. Materials and Methods

3.1 Study design

The present cross-over randomised clinical trial follows the Consolidated Standards of Reporting Trials (CONSORT) [Kaynak] guidelines and was performed at Marmara University, Shool of Dentistry, Department of Pediatric Dentistry clinics (Türkiye). The trial complies with the requirements set forth by the World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE).

3.2 Study population

The study population consisted of 28 children, aged 6 to 12 years of both genders who met the criteria were recruited for the study. The inclusion criteria were; children with good general health without any history of allergic reactions as determined by a written history; not currently taking any analgesics or sedative medication that would alter their pain perception; children demonstrated either 'positive' or 'definitely positive' behaviour according to the Frankl Behavior Scale (FBS); requiring treatment on their maxillary primary molars bilaterally with similar operative difficulties. The exclusion criteria were the existence of medical or developmental situations, history of chronic disease, 'negative' or 'definitely negative' behavior rating according to the Frankl Behavior Scale (FBS), and the presence of inflammation at the injection site.

3.3 Procedure

The study was conducted by two expert pediatric dentists. One of them gave all explanation, spoke with the children and carried out the anesthesia procedure and did the treatment procedure (FE) and the other (SP) was observing and assessing the children's pain perception.

In this study's cross-over design, children received both types of injections before filling/pulpotomy treatment on their maxillary primary molars in two separate appointments with a minimum interval of at least 1 week between procedures, on a side of the dental arch with the use of a needle free injection and on the other side with the traditional syringe. Type and sequence of administration to each individual were randomly assigned (using a coin). All dental equipment were introduced using 'tell-show-do technique. A total of 56 procedures were performed and divided into 2 groups according to the anesthesia technique. Non of the children have undergone any previous dental local anesthetic experience, in order to be not influenced by a positive or negative memory.

3.3.1 Injection with the needle-free (NF) system

The device used for needle free system was **Comfort-in™ (**Mika Medical **Global Co, Busan, Korea**) anesthesia device (Figure 1). The **Comfort-in™ system**, has a micro-hole injection needle (0.15 mm) that injects the anesthetic solution under the mucosa. The pressure can be controlled according to the dose of the drug to be used, thereby reduced the pain that may occur with the needle in the injection. Before the injection procedure, the children were demonstrated the popping sound produced by device to prevent reflex reactions, and they informed that they would feel as if their gum were punched. The NF injection device was prepared according to the manufacturer's instructions, placed in full contact with the buccal mucosa and a pre-withdrawn dose of 0.1 ml was applied to the buccal region for topical purposes by the pushing the top of the device. After 10-15 seconds, the same procedure was repeated with withdrawn dose of 0.3 ml. After 5 min the treatment commenced, and the children were instructed to raise their hand if they experienced pain during the procedure. Each time the child indicated pain, in accordance with the same protocol an additional 0.3 ml of anesthetic solution was administered, until the sufficient anesthetic effect was obtained and the final amount of anesthetic solution

were recorded. Precautions were taken to prevent tissue ballooning. After the treatment, duration of the analgesia effect (min) were also recorded. The presence of post-operative pain in patients was assessed via a phone call 1 day after the procedure.

3.3.2 Injection with the traditional method (TM)

The TM was used with traditional syringe on the opposite side of the dental arch. The injection site was dried with a cotton-tip applicator, and topical anesthetic spray (Lidocaine 10%, Vemcain, Turkey) was applied to the injection area with cotton-tip for 1-2 min. The traditional injection was performed with a 26-gauge, 40-mm, disposable syringe with a needle (Genject, Turkey). The depth of penetration was only a few millimeters and 0.3ml of anesthetic solution was deposited. After 5 min the treatment commenced, and the children were instructed to raise their hand if they experienced pain during the procedure. Each time the child indicated pain, in accordance with the same protocol an additional 0.3 ml of anesthetic solution was administered, until the sufficient anesthetic effect was obtained and the final amount of anesthetic solution were recorded. Precautions were taken to prevent tissue ballooning. After the treatment, duration of the analgesia effect (min) were also recorded. The presence of post-operative pain in patients was assessed via a phone call 1 day after the procedure.

Both NF and TM anesthesia techniques were performed with 4% articaine hydrochloride with 1/100,00 epinephrine (Ultracaine D-S forte, Hoechst Canada Inc., Montreal Queebec, Canada) as an anesthetic agent.

3.3.3 Subjective assessment

Pain levels were subjectively evaluated using the Wong-Baker Faces Pain Rating Scale (WB PRS) (Wong DL, 1988), which measures the unpleasantness or affective dimension of a child's pain experience. The PRS consists of a set of cartoon faces with varying facial expressions ranging from a smile/laughter to tears, and each child is asked to select the facial expression that best represents his/her experience of discomfort. Each face has a numerical value ranging from 0 (smiling face, 'no hurt') to 5 (crying/screaming face, 'hurts worst'). This scale was explained to the children carefully in advance. Immediately after the each injection, the children were asked to rate the level of pain perceived during the administration, using the PRS.

3.3.4 Objective assessment

Pain level also objectively evaluated by the operator using the Face, Legs, Activity, Cry, Consolability (FLACC) Scale. (Merkel SI, 1997) This scale includes the following points: face, leg, activity, cry and consolability. Each one of these five categories records either 0, 1, or 2 which result in either a minimum degree of 0 or a maximum degree of 10. According to this scale: 0 = quiet and relaxed (no pain), 1–3 = mild discomfort or pain, 4–6 = moderate pain, and 7–10 = severe pain.

3.4 Data collection

A structured form was designed to collect information regarding

(1) patient's age;
(2) gender;
(3) type of teeth injected
(4) type of dental treatment (filling or pulpotomy);
(5) total amount of local anesthetics (LAs) used (ml)
(6) duration of the analgesia effect (min)
(7) post-op pain (after one day)
(8) score on WB PRS after injection
(9) score on FLACC during injection.

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Statistical Analysis

Post hoc power analysis was conducted for the study and the results of the comparison between the injection systems and Wong Baker scores were evaluated. According to this, with a total data set of 28 individuals, consisting of two independent groups and two dependent measurements, the power of the study was found to be 0.94 according to the G*Power 3.9.1.4 program, based on the partial eta squared (η^2) value of 0.108 obtained with a 0.05 error margin from the repeated measures ANOVA. The data were statistically analyzed using SPSS software (version 15.0, SPSS). Paired t-tests or Wilcoxon nonparametric tests were used to compare data within groups over two time periods, according to check the distribution whether normally distributed or not. The Chi-square test (X^2-test) was also used to compare discrete random variables. Spearman's Rho correlation coefficient was used to find any relationship between two continuous variables. A p-value ≤ 0.05 was considered statistically significant.

4. Results

Total of 28 children, consisting of 18 girls (64.3%) and 10 boys (35.7%) aged 6–12 years were involved in this study. Mean age was 8.07 years with a standard deviation of 1.41 years. At the end of this study, a total of 56 injections were obtained for 28 children as NF injection (n = 28) and TM injection (n = 28).

In the study, when the distributions of the parameters (gender, type of dental treatment, type of teeth, and post-operative pain) were evaluated according to the type of injection technique, it was found that there was no statistically significant difference between the groups. (Table 1)

Table 1. Distribution of injection techniques based on evaluation parameters

Variables		Needle Free (NF) n	Traditional Method (TM) n	Total	*p*
Gender	Girl	18	18	36	1,000
	Boy	10	10	20	
Type of dental treatment	Filling	22	14	36	0,051
	Pulpotomy	6	14	20	
Type of teeth injected	1st primary molar	12	7	19	0,259
	2nd primary molar	16	21	37	
Post-op pain (after one day)	Pain	5	7	12	0,746
	No pain	23	21	44	

**The Chi-square test (X^2-test) was also used to compare discrete random variables.*

Accordingly Table 2, in the group that received Needle-Free anesthesia in the first session and Traditional Method in the second session, the Wong-Baker scores were 4.44±3.28 and 1.55±0.88, respectively. On the other hand, in the group that received Traditional Method anesthesia in the first session, the WB score was 1.68±1.91, while in the Needle-Free anesthesia group, the WB score was 2.52±2.56. In both cases, regardless of the method of anesthesia applied first, no statistically significant difference was found in the two groups. In the FLACC scores, for the Traditional Method - Needle Free group significant change was observed (p = 0.025) while for the Needle Free- Traditional Method group no statistically significant difference was observed (p=0.141). There were significant differences in the Amount of Anesthetic Solution (ml) and Duration of the Analgesia Effect (min) between the first and second visits for both injection methods, respectively as p=0.003 for NF-TM and p<0.0001 for

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TM-NF groups. The amount of anesthetic solution used for the 1st visit NF injection was 0,91±0,48 ml and 0,65±0,30 ml was for the 2 nd visit NF injection. These amounts were statistically lower than TM injection in both visits. In the first visit, the mean duration of the analgesia effect in the NF group was 85.00±39.05 min, whereas in the second visit, the mean duration for NF injection was found to be 90.26±43.25 min. In the TM group, the mean anesthesia duration for the first and second visits was 140.00±59.97 min and 130.00±50.74 min, respectively. Regardless of the visit in which it was first applied, the duration of the analgesia effect in the NF group was found to be statistically significantly shorter than in the TM group (p<0,001).

Table 2: Comparison of the 1st visit and 2nd visit measurements for continuous random variables in Needle Free-Traditional Method and Traditional Method - Needle Free

	1st visit	2nd visit	*p*
Wong Baker (WB) Scores			
Needle Free-Traditional Method	4,44±3,28	1,55±0,88	0,056
Traditional Method - Needle Free	1,68±1,91	2,52±2,56	0,119
FLAAC			
Needle Free-Traditional Method	0,78±1,09	0,11±0,33	0,141
Traditional Method - Needle Free	0,21±0,41	0,68±0,67	**0,025**
Amount of Anesthetic Solution (ml)			
Needle Free-Traditional Method	0,91±0,48	1.62±0,38	**0,003**
Traditional Method - Needle Free	1,37±0,42	0,65±0,30	**<0,0001**
Duration of the Analgesia Effect (min)			
Needle Free-Traditional Method	85,00±39.05	130,00±50,74	**0,001**
Traditional Method - Needle Free	140,00±59,97	90,26±43,25	**<0,001**

**paired t-test was used*
**Needle Free-Traditional Method group: 1st visit Needle Free and 2nd visit Traditional Method was used of injection.*
**Traditional Method - Needle Free group: 1st visit Traditional Method and 2nd visit Needle Free was used of injection*

Table 3: Wong-Baker and FLACC Scores in Needle Free-Traditional Method and Traditional Method - Needle Free groups based on gender

	Gender	Needle Free-Traditional Method Group		*p*	Gender	Traditional Method-Needle Free Group		*p*
		1st visit Needle Free	2nd visit Traditional Method			1st visit Traditional Method	2nd visit Needle Free	
Wong Baker	**Girl N=6**	4.1, (1.5-8.5)	2, (0-2)	*0,141*	**Girl N=12**	2, (0.5-2)	1, (0-3.5)	*0,558*
	Boy N=3	4.1, (2-4)	2, (2-2)	*0,18*	**Boy N=7**	0, (0-4)	2, (2-4)	*0,059*
FLACC	**Girl N=6**	0, (0-1.5)	0, (0-0.25)	*0,414*	**Girl N=12**	0, (0-0)	0.5, (0-1)	*0,053*
	Boy N=3	1, (0-1)	0, (0-0)	*0,180*	**Boy N=7**	0, (0-1)	1, (0-1)	*0,317*

**Wilcoxon nonparametric test was used*
**Needle Free-Traditional Method group: 1st visit Needle Free and 2nd visit Traditional Method was used for injection.*
**Traditional Method - Needle Free group: 1st visit Traditional Method and 2nd visit Needle Free was used for injection*
** The values are presented as Median, (Inter Quartile Range)*

In our study, which used a crossover design, we evaluated the effect of gender differences on Wong-Baker and FLACC scores for needle-free and traditional method injections administered

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in different sequences over two sessions. The analysis showed no statistically significant differences between the groups (Table 3). Similarly, present study evaluated the impact of the type and sequence of restorations (filling-filling, filling-pulpotomy, pulpotomy -filling) on Wong-Baker and FLACC scores for needle-free and traditional method injections administered in different sequences over two sessions. Results demonstrated that there were no statistically significant differences between the groups (Table 4).

Table 4: Wong-Baker and FLACC Scores in Needle Free-Traditional Method and Traditional Method - Needle Free groups based on type of dental treatment

	Type of Dental Treatment	Needle Free-Traditional Method Group		*p*	Type of Dental Treatment	Traditional Method-Needle Free Group		*p*
		1st visit Needle Free	2nd visit Traditional Method			1st visit Traditional Method	2nd visit Needle Free	
Wong Baker	**Filling-Filling N=4**	7, (3-9.5)	2, (0.5-2)	*0,109*	**Filling-Filling N=8**	2, (0.5-2)	2, (0.5-5.5)	*0,167*
	Filling-Pulpotomy N=3	4, (2-4)	2, (0-2)	*0,180*	**Filling-Pulpotomy N=2**	0, (0-0)	1, (0-1)	*0,317*
	Pulpotomy-Filling N=2	1, (0-1)	2, (2-2)	*0,317*	**Pulpotomy-Filling N=9**	2, (0-3)	2, (0-4)	*0,655*
FLACC	**Filling-Filling N=4**	0.5, (0-2.5)	0, (0-0)	*0,180*	**Filling-Filling N=8**	0, (0-0)	1, (0-1)	*0,096*
	Filling-Pulpotomy-N=3	1, (0-1)	0, (0-0)	*0,180*	**Filling-Pulpotomy-N=2**	0, (0-0)	0.5, (0-0.5)	*0,317*
	Pulpotomy-Filling N=2	0, (0-0)	0.5, (0-0.5)	*0,317*	**Pulpotomy-Filling N=9**	0, (0-1)	1, (0-1)	*0,257*

**Wilcoxon nonparametric test was used*
**Needle Free-Traditional Method group: 1st visit Needle Free and 2nd visit Traditional Method was used for injection.*
**Traditional Method - Needle Free group: 1st visit Traditional Method and 2nd visit Needle Free was used for injection*
** The values are presented as Median, (Inter Quartile Range)*
**filling-filling group: 1st visit filling and 2nd visit filling restoration have been done*
**filling-pulpotomy group: 1st visit filling and 2nd visit pulpotomy restoration have been done*
**pulpotomy-filling group: 1st visit pulpotomy and 2nd visit filling restoration have been done*

Table 5. Amount of Anesthetic Solution (ml) in Needle Free-Traditional Method and Traditional Method - Needle Free groups based on type of dental treatment

	Type of Dental Treatment	Needle Free-Traditional Method Group		*p*	Type of Dental Treatment	Traditional Method-Needle Free Group		*p*
		1st visit Needle Free	2nd visit Traditional Method			1st visit Traditional Method	2nd visit Needle Free	
Amount of Anesthetic Solution (ml)	**Filling-Filling N=4**	0,65, (0.325-1.125)	1.3, (1.05-1.85)	*0,068*	**Filling-Filling N=8**	1.1, (1-1.85)	0.55, (0.325-0.9)	***0,012***
	Filling-Pulpotomy-N=3	0.9, (0.3-0.9)	2, (1.5-2)	*0,180*	**Filling-Pulpotomy-N=2**	1.4, (1.3-1.4)	1, (1-1)	*0,180*
	Pulpotomy-Filling N=2	1.35, (1.2-1.35)	1.75, (1.5-1.75)	*0,180*	**Pulpotomy-Filling N=9**	1.5, (1.1-1.85)	0.6, (0.3-0.9)	***0,008***

**Wilcoxon nonparametric test was used*
**Needle Free-Traditional Method group: 1st visit Needle Free and 2nd visit Traditional Method was used for injection.*
**Traditional Method - Needle Free group: 1st visit Traditional Method and 2nd visit Needle Free was used for injection*
** The values are presented as Median, (Inter Quartile Range)*
**filling-filling group: 1st visit filling and 2nd visit filling restoration have been done*
**filling-pulpotomy group: 1st visit filling and 2nd visit pulpotomy restoration have been done*
**pulpotomy-filling group: 1st visit pulpotomy and 2nd visit filling restoration have been done*

Table 5 showed the evaluation whether the type and sequence of different restorations administered in different sequences over two sessions with needle-free and traditional method

injections resulted in any differences in the amount of anesthetic solution used. The results indicated a significant difference in the amount of anesthetic solution used in the group that received TM injection in the first session and NF injection in the second session, the group that received filling in both the first and second sessions, and the group that received pulpotomy in the first session and filling in the second session. A significantly lower amount of anesthetic solution was used in the NF injection in both groups (Table 5).

According to Spearman's Rho correlation coefficient test, no correlation was found between age and Wong Baker, FLACC scores, and the amount of anesthetic solution administered respectively (p=0,830, p=0,436, p=0,976). Similarly, no correlation was found between Wong Baker scores and the amount of anesthetic solution administered (p=0,537) and Wong Baker scores and the duration of the analgesia effect (p=0,468). However, a negative correlation was found between the FLACC score and the amount of anesthetic solution (p=0,033). Moreover a positive correlation was found between the FLACC score and Wong Baker scores as well as between the amount of dose administered and duration of analgesia effect respectively (p=0,000, p=0,009).

Informed Consent Form (English)

VOLUNTARY CONSENT FORM
I have read the text above, which shows the information that should be given to the volunteer before the study. I have been given written and verbal explanations about these. Under these conditions, I agree to participate in this clinical trial voluntarily and without any pressure or coercion.

Volunteer
Name-surname
Address (telephone no., fax no., if available, ...):

Signature:

For those under custody or guardianship, the name and surname of the parent or guardian:
address (telephone no., fax no., if any,...):

Signature:

Name-surname and signature of the researcher who made the explanations:

Organization official who witnessed the consent process from the beginning to the end

name-surname: position:

Signature:

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Declaration of the Participant/Patient

I was informed by Dr. Figen Eren Giray that medical research would be conducted at Marmara University Faculty of Dentistry, Department of Pedodontics and I was given the above information about this research. After this information, I was invited as a "participant" (subject) in such research. If I participate in this research, I believe that the confidentiality of my personal information, which should remain between me and the physician, will be treated with great care and respect during this research. I have been given sufficient confidence that my personal information will be carefully protected during the use of the research results for educational and scientific purposes.

I can withdraw from the research without giving any reason during the conduct of the project. However, I am aware that it would be appropriate to inform the researchers in advance that I will withdraw from the research in order not to leave them in a difficult situation. I am also aware that I can be removed from the research by the researcher in order to avoid any damage to my medical condition. I do not assume any financial responsibility for the expenses to be incurred for the research. I will not be paid. I have been given the necessary assurance that any medical intervention will be provided in the event of any health problem that may arise, whether directly or indirectly, as a result of the research. I know that I will not be under any financial burden regarding these medical interventions. If I encounter a health problem during the research; I know that I can call Dr. Figen Eren Giray at the Department of Pedodontics, Faculty of Dentistry, MÜ. Faculty of Dentistry and at 02164211621/1542 I do not have to participate in the research and I cannot participate. I have not encountered any coercive behavior about my participation in the research. I also know that it will not bring any harm.

I have understood all the explanations given to me in detail. After a period of reflection on my own, I have made the decision to take part in this research project as a "participant". I accept the invitation to do so with great satisfaction and voluntarily. I will be given a copy of this signed form. If I refuse to take part, I understand that this will not affect my medical care and my relationship with the physician.

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GÖNÜLLÜ BİLGİLENDİRME FORMU

Objective: To evaluate the anesthetic effect of a needle-free injection system in children using different methods in clinical to be evaluated as

The method to be used in the study:
The success of treatment in pediatric dentistry depends on the child's lack of pain and cooperation. Fear of pain is an important barrier to dental treatment and this may negatively affect general health. The first method used for this purpose is to numb the tooth with local anesthesia (LA) before treatment.

In this procedure, your child's teeth will be numbed so that the necessary dental treatment can be carried out painlessly. For this purpose, the teeth will be numbed before the treatment of two baby teeth using two different methods. In one of the sessions, a routine injection will be used.
In the other, the tooth to be treated will be numbed using a needle-free injection system. Whether the teeth are numb before the treatment will be checked by lightly pricking the probe into the gum, if the numbness is not complete, additional numbing will be done with injection application and dental treatment will continue after the numbness is completely achieved. There may be a slight bleeding in the gum during the pricking of the probe. If pain is felt again despite additional numbing during dental treatment, your child will be asked to raise his/her hand and numbing will be done again with injection.
To assess the fear and anxiety your child feels during both LA methods, a picture with facial expressions will be shown and he/she will be asked to show how he/she feels by choosing one of the facial expressions. Before and during the procedure, a pulse oximeter device that can measure pulse and oxygen saturation (SpO2) values will be attached to the finger and the values will be recorded.

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Side effects and negative effects that may occur as a result of participating in the study:

Your child may experience anxiety, pain and bleeding gums during numbing of the tooth before the treatment, the gums may bleed when the probe is gently inserted into the gums during numbness control, and sores on the cheek, lips or tongue may occur as a result of your child scratching, biting or chewing the numb area after numbing.

Depending on the medication used during anesthesia, systemic reactions such as syncope, allergic reaction
complications may occur.

With needle injection, complications such as needle breakage, infection or emphysema (swelling) can occur.

In the needle-free injection system, there may be a bitter taste if the solution is sprayed into the mouth, and slight bleeding of the mucosa may occur if it is administered in a different angle.

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Privacy:

The names of the individuals participating in the research will be kept confidential and will not be disclosed without their consent.