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ARTICLE

EFFECT OF IBUPROFEN AND LOW-INTENSITY PULSED ULTRASOUND ON THE REDUCTION OF PAIN AFTER INITIAL ARCHWIRE PLACEMENT: A DOUBLE-BLIND RANDOMIZED CLINICAL TRIAL.

Efecto del ibuprofeno y el ultrasonido pulsado de baja intensidad en la reducción del dolor después de la colocación inicial del arco de ortodoncia: un ensayo clínico aleatorizado doble ciego.

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ABSTRACT:

Objective: This study aimed to compare the effect of ibuprofen and low-intensity pulsed ultrasound (LIPUS) on the reduction of pain after the placement of initial archwire in orthodontic patients.

Material and Methods: This double-blind clinical trial study was carried out on 60 female candidates for fixed orthodontic treatment referring to the Orthodontic Department of School of Dentistry in Mashhad University of Medical Sciences, Mashhad, Iran, during 2015-2016. The subjects were divided into four groups of ibuprofen, LIPUS, placebo, and mock LIPUS. A questionnaire and a rectangular and flexible cubic silicone were given to each patient to record the severity of pain based on the visual analog scale at specified time points (*i.e.*, 2 h, 6 h, at bedtime, 2nd, 3rd, and 7th days after archwire placement) when biting the silicone block with the anterior and posterior teeth and without biting at all. Repeated measures analysis of variance was used in order to compare the pain severity at different time points.

Results: The comparison of pain severity at various time points showed that the highest and lowest mean scores of pain were reported at bedtime and seven days after the intervention ($p<0.001$). In each of the three conditions (*i.e.*, biting the silicone block with the anterior and posterior teeth and without biting the teeth) at six time points (*i.e.*, 2 h, 6 h, at bedtime, 2nd, 3rd, and 7th days following archwire placement), no significant difference was observed in the severity of pain ($p>0.05$).

Conclusion: In conclusion, LIPUS (with a frequency of 1 MHz and an intensity of 100 mW) and ibuprofen have no significant effects on reduction of the pain severity at different time points and various conditions in orthodontic patients.

KEYWORDS:

dentistry; orthodontics; archwire; ibuprofen;ultrasonic therapy; pain.

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RESUMEN:

Objetivo: Este estudio tuvo como objetivo comparar el efecto del ibuprofeno y el ultrasonido pulsado de baja intensidad (LIPUS) en la reducción del dolor después de la colocación del arco inicial en pacientes de ortodoncia.

Material y Métodos: Este estudio de ensayo clínico doble ciego se llevó a cabo en 60 candidatas a tratamiento de ortodoncia fija referidas al Departamento de Ortodoncia de la Facultad de Odontología de la Universidad de Ciencias Médicas de Mashhad, Mashhad, Irán, durante 2015-2016. Los sujetos se dividieron en cuatro grupos: ibuprofeno, LIPUS, placebo y LIPUS simulado. Se entregó un cuestionario y un bloque de silicona cúbica rectangular y flexible a cada paciente para registrar la intensidad del dolor según la escala analógica visual en puntos de tiempo específicos (es decir, 2 h, 6 h, hora de acostarse, 2do, 3er y 7mo día después de la colocación del arco) al morder el bloque de silicona con los dientes anteriores y posteriores, y sin morder en absoluto. Se utilizó el análisis de varianza de medidas repetidas para comparar la intensidad del dolor en diferentes momentos.

Resultados: La comparación de la intensidad del dolor en varios puntos de tiempo mostró que las puntuaciones medias de dolor más altas y más bajas se informaron a la hora de acostarse y siete días después de la intervención (p<0,001). En cada una de las tres condiciones (es decir, al morder el bloque de silicona con los dientes anteriores y posteriores, y sin morder) en seis momentos (2 h, 6 h, antes de acostarse 2do, 3er y 7mo día después de la colocación del arco), no se observó diferencia significativa en la severidad del dolor (p>0.05).

Conclusión: En conclusión, LIPUS (con una frecuencia de 1 MHz y una intensidad de 100 mW) y el ibuprofeno no tienen efectos significativos en la reducción de la severidad del dolor en diferentes puntos de tiempo y diversas condiciones en pacientes de ortodoncia.

PALABRAS CLAVE:

odontología; ortodoncia; alambres para ortodoncia; ibuprofeno; terapia por ultrasonido; dolor.

INTRODUCTION.

Like any medical treatment, orthodontic treatment may have side effects such pain, root resorption, periodontal disease, temporomandibular dysfunction, caries, speech problems and enamel damage.[1-5] Pain is a common experience in orthodontic patients and is considered the most important factor deterring patient referral for further treatment.[6] Orthodontic pain arises from ischemia, inflammation, and edema in the compressed periodontal ligament.[7]

Some mediators, such as histamine, prostaglandin, serotonin, enkephalin, glutamate, and gamma aminobutyric acid, are secreted in the compressed periodontal ligament leading to the stimulation of the nerve endings of the pain receptors, thereby causing pain.[6]

The orthodontic pain is an inflammatory pain followed by the cascade of inflammatory responses, such as vascular changes and secretion of neurogenic and proinflammatory mediators.[8]

Orthodontic pain usually begins at 2 h after the initial archwire placement and reaches its maximum at bedtime and lasts about 5 to 7 days.[6] The pain due to orthodontic problems has a significant effect on patient satisfaction and daily activities.

Most patients receiving orthodontic treatment have moderate or severe difficulty in chewing and biting hard foods. In addition, about 50% of the subjects undergoing orthodontic treatment faced complications in their daily activities on the first and second days after the initial archwire placement.[9] Additionally higher dental sensitivity has been recorded at the end of orthodontic treatment after debonding[10] or during the execution of particular treatments.[11]

In general, methods of pain management in orthodontics include two main categories of pharmacological methods, namely nonsteroidal anti-inflammatory drugs (NSAIDs), and nonpharmacological approaches.

Analgesics, such as ibuprofen, are often used for the management of orthodontic pain preemptively or after the treatment.

Ibuprofen is a nonselective cyclooxygenase inhibitor, which is derived from propionic acid, and its anti-inflammatory mechanism is blocking the synthesis of prostaglandin, especially prostaglandin E2 in the periodontal ligament.[12] However, despite effectiveness in the reduction of pain, ibuprofen may lead to some adverse reactions .[13]

Cold pack and ultrasound are some nonpharmacological approaches for the alleviation of postsurgical pain.[14] Recently, the use of physical interventions to control pain has been promoted. These noninvasive and easy procedures approaches, including mechanical stimuli, electromagnetic fields, and low-level laser, are suggested for pain control in patients undergoing orthodontic treatment .[15-17]

The use of ultrasound is one of the main approaches to reduce bone healing duration and other complications of orthognathic surgery. Based on the results of some studies, the use of low-level lasers decreases pain and swelling after orthognathic treatment.[16,18] Low-intensity pulsed ultrasound (LIPUS) with an intensity of 0.01-3 mW/cm^2 and a frequency of 1.5-4 MHz is a proper approach for controlling the complications of orthognathic surgery and improving fresh fractures, which is approved by the Food and Drug Administration.[19,20]

Due to the side effects of drug therapy as well as the need for the evaluation of a new approach for pain control in patients undergoing orthodontic treatment, the current study aimed to compare the effects of ibuprofen and LIPUS on the reduction of pain after the placement of initial archwire in orthodontic patients.

MATERIALS AND METHODS.

This double-blind clinical trial study was carried out on 60 female patients candidates for fixed orthodontic treatment referring to the Orthodontic Department of School of Dentistry in Mashhad University of Medical Sciences, Mashhad, Iran during 2018-2019.

Participation characteristic

The subjects within the age range of 10-32 years with moderate dental crowding and candidates for orthodontic treatment were entered in the present study. Moreover, the patients with systemic disease and those who used analgesics were excluded from this study.

Instrument

An ultrasound COMBINED (200 µl, Bracco, Milan, Italy(device with a standard head of 5 cm^2 was used for the irradiation of low-intensity ultrasound waves for 5 min with a frequency of 1 MHz and an intensity of 100 mW (EME Co., Italy).

The irradiation was performed by rotational movements on the skin of the face. Ultrasound gel (Bazaar Darman Co., Iran) was applied on the head of the ultrasound device. In this study, the stainless steel brackets (Discovery; Dentaurum, Ispringen, Germany) and archwires (G&H Wire Company, Franklin, IN, USA) were used.

Study Design

This study was performed on 60 women within the age range of 10-32 years candidate for orthodontic treatment (Figure 1). Exclusion criteria was any systemic disease or use of any medications one week before the intervention.

With respect to the Patel *et al.*,[21] study, with an alpha error of 0.05 and a test power of 90%, sample size was calculated as 15 patients per group. The 60 participants were randomized into the four groups (ibuprofen, LIPUS, placebo, and mock LIPUS) using a random number table.

In the first group, after archwire placement, performed in one session, the patients received a 400 mg dose of ibuprofen (Raha Pharmaceutical Company, Esfahan, Iran). In the second group, LIPUS waves were irritated for 5 min with the ultrasound COMBINED after the archwire placement among the patients with the help of the device. The ultrasound COMBINED received LIPUS waves for 5 min with a frequency of 1 MHz and an intensity of 100 mW around the mouth (Figure 2A).

The third group received a placebo containing lactose, and the turned-off EMA device was used for

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the patients in the fourth group.

A placebo was given to the subjects in the third group in coded capsules with the same coating (made by the Department of Pharmacokinetics, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran) (Figure 2B). If any patients experienced intolerable pain she was excluded from study and treated with analgesics.

In the first session, a packet containing five capsules with the same coating was given to the patients in the ibuprofen and placebo groups, and the subjects were asked to simultaneously take one of the capsules. The participants in the fourth group underwent turned-off LIPUS therapy.

Moreover, a questionnaire and rectangular and flexible cubic silicone (Figure 2C) (made by Faculty of Engineering, Ferdowsi University, Mashhad, Iran) were given to each patient to record the severity of pain based on the visual analog scale (VAS) at the specified time points (*i.e.*, 2 h, 6 h, bedtime, 2nd, 3rd, and 7th days after the archwire placement) when biting the silicone block with the anterior and posterior teeth and without biting at all.

The questionnaire was in the form of a three-page booklet, including the horizontal VAS from 0 to 10. The patients were instructed to check the scale at each time interval to represent the perceived severity of pain during each of the three conditions (*i.e.*, biting posterior teeth together, fitting anterior teeth together, and without fitting teeth together.

The incidence and severity of pain were recorded by the patient at 2 h, 6 h, bedtime, 2nd, 3rd, and 7th days after the archwire placement. All the patients were followed for one week.

Harms

In this study, no serious harm was observed.

Statistical Analysis

In the present study, SPSS software (version 11.5, Chicago, IL, USA) was used to analyze the data. The normality of the data was assessed using the Shapiro-Wilk test. Quantitative variables were described through mean and standard deviation, and qualitative variables were explained by frequency and percentage.

Repeated-measures analysis of variance (ANOVA) was used in order to compare the pain severity at different time points.

Post-hoc Tukey test was applied for data analysis between the groups. A *p*-value of less than 0.05 was considered statistically significant.

Ethical considerations

The protocol of the present study was approved by the Research Ethics Committee of Mashhad University of Medical Sciences (IRCT20190825044606N1). Before the initiation of the study, the objectives of the study were explained to patients and their parents.

In addition, informed consent was obtained from all the study participants. The patients were also assured that their information would remain confidential and they could withdraw from the study at any time

RESULTS.

A total of 60 women with a mean age of 18.37±5.37 years (range: 10-32 years) after the initial archwire placement were entered in this study. The groups were matched in terms of age (p=0.47). Table 1 tabulates the comparison of pain severity among the groups at the specified time points and different conditions. None of our participants experienced intolerable pain during the study.

Based on the obtained results of the present study, no significant difference was observed among the four groups regarding pain severity when biting by the anterior or posterior teeth 2 h, 6 h, 2nd, 3rd, and 7th days after the intervention (p>0.05). The comparison of pain severity when biting with the anterior teeth showed that there was a significant difference at different time points among the LIPUS (χ^2=42; p<0.001), mock LIPUS (χ^2=29.2; p<0.001), ibuprofen (χ^2=28.92; p<0.001), and placebo (χ^2= 21.28; p=0.001) groups. In all the groups, the highest and lowest mean scores of pain when biting with the anterior teeth belonged to bedtime and a week after the intervention.

Moreover, the comparison of pain severity when biting with the posterior teeth demonstrated that

there was a significant difference at different time points among the LIPUS (χ^2=42.22; p<0.001), mock LIPUS (χ^2=23.2; p<0.001), ibuprofen (χ^2=22.77; p<0.001), and placebo (χ^2=27.76; p=0.001) groups. Moreover, the highest and lowest mean scores of pain when biting with the posterior teeth were reported for bedtime and a week after the intervention in all the groups.

In addition, a significant difference was observed at different time points among the LIPUS (χ^2=42.22; p<0.001), mock LIPUS (χ^2=23.29; p<0.001), ibuprofen (χ^2=22.77; p<0.001), and placebo (χ^2=16.6; p=0.005) groups when the teeth were not bitten at all. In all the groups, the highest and lowest mean scores of pain when the teeth were not bitten at all was reported for bedtime and a week after the intervention.

Table 2 shows the pairwise comparison of pain severity among all the groups at specified time points and different conditions.

Figure 1. CONSORT flow diagram of the study.

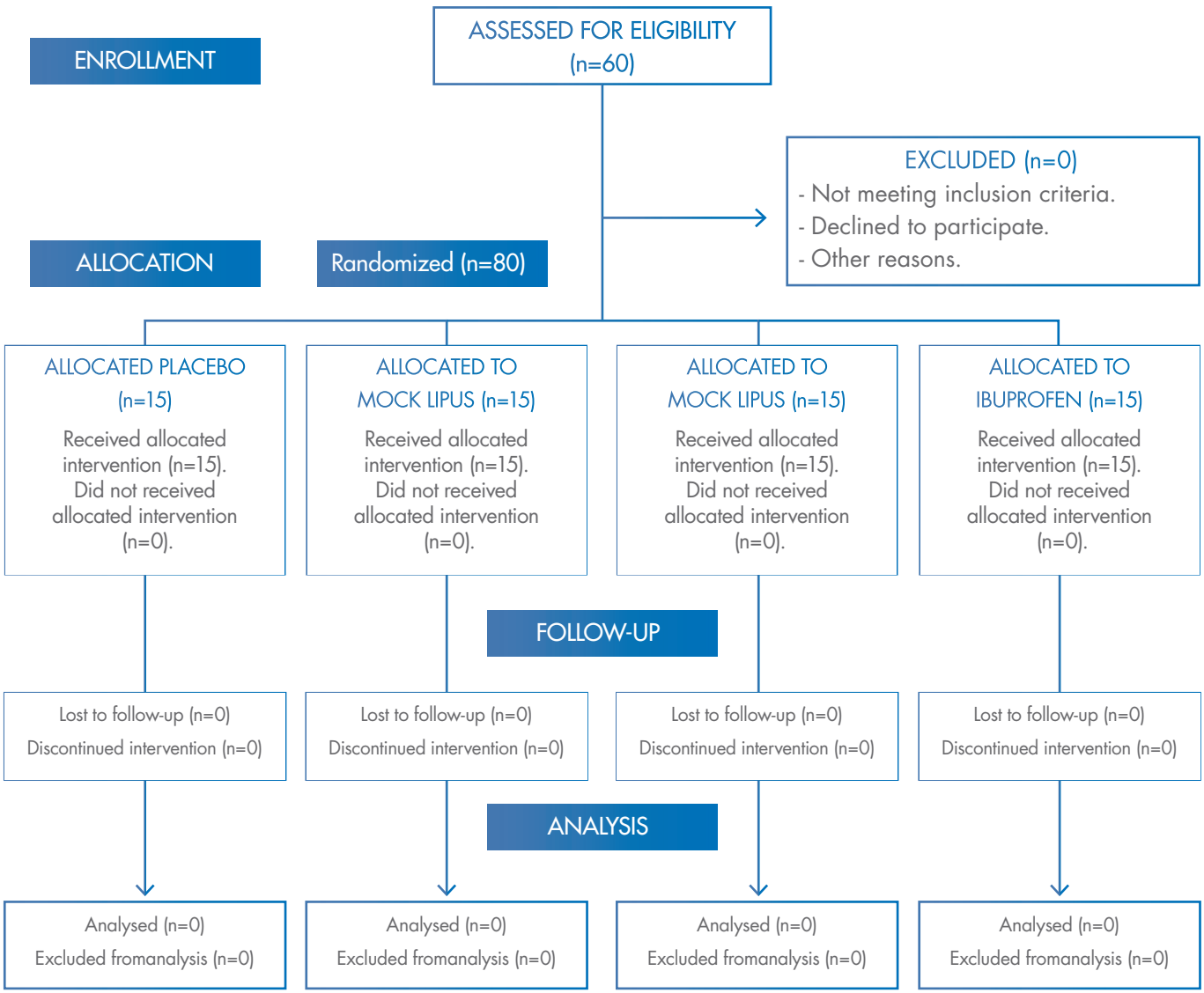

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Figure 2. Materials and technique used in the study.

2A. Ibuprofen and placebo in undistinguishable capsules. **2B.** LIPUS irradiation after initial archwire placement. **2C.** The rectangular and flexible block of silicone used for biting on during this study.

Table 1. Comparison of pain severity among groups at specified time points and under different conditions.

DIFFERENT CONDITIONS	DIFFERENT TIME POINTS	LIPUS		MOCK LIPUS		IBUPROFEN		PLACEBO		X^2	*p*-value
		MEAN	S.D	MEAN	S.D	MEAN	S.D	MEAN	S.D		
Biting with anterior teeth	2 h	3.07	2.55	3.33	3.02	3.6	3.46	2.6	2.95	0.77	0.85
	6 h	5.2	2.24	4.27	2.81	5.67	3.31	5.53	3	2.97	0.39
	Bedtime	6.2	2.04	5.07	3.24	6.67	2.66	5.87	3.14	2.44	0.48
	Second day	4.47	2.07	4.07	2.6	5.13	3.04	5.6	3.56	1.88	0.59
	Third day	3.6	1.92	3.13	2.29	4.33	2.85	4.07	3.41	1.96	0.58
	One week	1.4	1.5	1.47	1.88	2.67	2.64	2.27	2.52	2.72	0.43
Biting with posterior teeth	2 h	2.27	1.62	3.07	2.91	2.73	2.84	1.6	1.92	2.5	0.47
	6 h	4.4	2.47	3.93	2.79	4.6	2.82	3.87	2.45	0.85	0.83
	Bedtime	5.4	2.29	4.27	3.26	4.6	2.9	4.73	2.55	0.9	0.82
	Second day	3.47	2.67	3.13	2.39	4.13	2.85	4.2	2.81	1.65	0.64
	Third day	2.93	2.52	2.6	2.82	3.2	3.1	3.47	3.11	0.63	0.88
	One week	1.13	1.51	1	1.73	1.73	2.71	1.4	2.13	0.79	0.85
Without biting	2 h	1.33	1.5	1.8	2.14	1.47	2.26	1.27	1.94	1.41	0.702
	6 h	3.33	2.69	3.2	2.51	3.47	3	3.2	2.62	0.05	0.99
	Bedtime	4	3	4.13	2.53	3.93	2.55	3.6	2.92	0.4	0.94
	Second day	2.6	2.59	2.67	2.58	1.6	1.64	3.07	3.56	1.68	0.64
	Third day	1.93	2.28	1.73	2.43	1.07	1.49	2.6	3.29	1.86	0.601
	One week	0.53	0.92	0.8	1.7	0.73	1.22	1.07	2.15	0.34	0.95

LIPUS: Low-intensity pulsed ultrasound. **S.D:** Standard Deviation.

Table 2. Comparison of pain severity among groups at specified time points and under different conditions.

Different time points		BITING WITH ANTERIOR TEETH				BITING WITH POSTERIOR TEETH				WITHOUT BITING			
		LIPUS	Mock LIPUS	Ibuprofen	Placebo	LIPUS	Mock LIPUS	Ibuprofen	Placebo	LIPUS	Mock LIPUS	Ibuprofen	Placebo
2 h	6 h	0.126	1	0.47	0.25	0.060	1	0.68	0.25	1.00	0.856	0.060	0.856
	Bedtime	0.002*	0.95	0.109	0.14	0.007*	1	1	0.07	0.19	0.05	0.01*	0.109
	Second day	1	1	1	0.37	1	1	1	0.37	1	1	1	1
	Third day	1	1	1	1	1	1	1	1	1	1	1	1
	One week	1	0.109	1	1	1	0.32	1.00	1.00	1	1	1	1
6 h	Bedtime	1	1	1	1	1	1	1	1	1	1	1	1
	Second day	1	1	1	1	1	1	1	1	1	1	0.606	1
	Third day	0.76	1	0.53	1	0.03*	1	0.85	1	1	0.372	0.027*	1
	One week	<0.001*	0.001*	0.002*	0.04*	<0.001*	0.003*	0.003*	0.01*	0.037*	0.005*	0.005*	0.477
Bedtime	Second day	0.37	1	1	1	0.76	1	1	1	1.00	1.00	0.146	1
	Third day	0.02*	0.32	0.12	0.85	0.004*	1	1	1	0.19	0.016*	0.004*	1
	One week	<0.001*	<0.001*	<0.001*	0.02*	<0.001*	0.003*	0.008*	0.004*	0.001*	<0.001*	0.001*	0.003*
Second day	Third day	1	1	1	1	1	1	1	1	1	0.764	1	1
	One week	0.01*	0.002*	0.07	0.07	0.01*	0.02*	0.03*	0.07	0.16	0.01*	1	0.606
Third day	One week	0.22	0.37	1	1	1	0.28	1.00	0.25	1	1	1	0.68

LIPUS: Low-intensity pulsed ultrasound. **S.D:** Standard Deviation.

DISCUSSION.

In summary, the results of the present study showed no difference among the ibuprofen, LIPUS, placebo, and mock LIPUS groups in terms of pain severity after the archwire placement at different time points. The highest and lowest mean scores of pain were related to bedtime and a week after the archwire placement. The pain score decreased a week after the treatment indicating that the pain after the archwire placement improves without any treatment.

Many studies indicate that pretreatment with analgesics is effective in the reduction of post treatment pain.[21-24] Several studies have been performed on the effect of various analgesics, such as NSAIDs, in decreasing pain after orthodontic treatment. It is possible that the use of NSAIDs to manage orthodontic pain interferes with tooth movement by the inhibition of cyclo-oxygenase activity, thereby producing prostaglandin, as proven in some animal studies.[25,26] Moreover, NSAIDs are problematic when they are chronically used.

In some studies, higher effectiveness of ibuprofen (as a NSAID) is proven in comparison to other agents, such as acetaminophen.[21-24] A study carried out by Law et al. demonstrated the preemptive effects of ibuprofen on the reduction of pain upon chewing at 2 h after the archwire placement in comparison to postoperative ibuprofen or placebo.[27]

However, the obtained results of the current study rejected the therapeutic effect of ibuprofen on the pain severity due to archwire placement. Similar to the results of the present study, Salmassian *et al.*[28] observed no difference in analgesic effect in initial orthodontic treatment between the three groups of ibuprofen, acetaminophen, and placebo.

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Moreover, non preference was noticed in pre-emptive ibuprofen (400 mg) and acetaminophen (650 mg) therapy, compared to that reported for placebo in another study by Kawamoto *et al.*[29]

On the other hand, some studies showed that the analgesic effect of ibuprofen on orthopedic postoperative pain is lower than other analgesics. Kohli *et al.*[30] have examined the preoperative use of analgesics, such as ibuprofen and naproxen. Similar to the findings of the present study, patients were asked to determine the degree of their experienced discomfort at specified time intervals and various conditions (*i.e.*, biting, chewing, and fitting the anterior and posterior teeth). They showed that using a 20 mg dose of piroxicam is more effective in comparison to the administration of a 400 mg dose of ibuprofen or a placebo..

In a clinical trial carried out by Ireland et al., the use of chewing gum for the relief of orthodontic pain was compared to ibuprofen indicating no important difference between the two groups. They showed that the use of sugar-free chewing gum may decrease ibuprofen administration.[31] In addition, the analgesic effect of chewing gum may have a subjective impact. In the current study, no difference was observed between the administration of placebo and ibuprofen in terms of pain severity.

In another study conducted by Polat *et al.*,[22] the analgesic effect of the three groups of ibuprofen (400 mg), placebo, and naproxen sodium (550 mg) was investigated 1 h before the initial archwire placement in four different conditions, including biting, chewing, and placing the anterior and posterior teeth on each other.

They measured the severity of pain in the posterior teeth at 2 h, 6 h, bedtime, 2nd, 3rd, and 7th days after the placement of the archwire demonstrating that naproxen is more effective in the pain severity in comparison to ibuprofen and placebo, especially at 2 h, 6 h, and bedtime. Similarly, in the present study, the severity of pain was higher 6 h later and at bedtime in all the groups.

The NSAIDs are commonly used after orthognathic surgery; nevertheless, the use of these drugs has many side effects, such as allergic reactions, skin rashes, neutropenia, and bleeding.[14] To date, many studies have been carried out to determine the efficacy of non pharmaceutical approaches in the reduction of orthodontic pain.[14,32-34]

Recently it has been demonstrated that the use of probiotics[35] and natural compounds[36] can modify clinical and microbiological oral parameters. These compounds could have an effect also in combination with NSAIDs for pain control. All these variables should be considered in future clinical trials. The use of LIPUS waves is introduced as a method without side effects after orthognathic surgery. A study conducted by Tehranchi *et al.*,[14] determined the effect of LIPUS therapy on bone regeneration and pain relief after orthognathic surgery.

However, in the current study, no difference was reported among LIPUS in on-position and off-position, ibuprofen, and placebo in terms of pain relief. The aforementioned findings were confirmed by another study by Dominguez *et al.*,[37] Moreover, Alan *et al.*,[38] observed no difference between LIPUS and control groups in terms of inflammation, pain, and trismus except for pain on the seventh day. There was no difference between LIPUS on-position and off-position regarding pain severity even on the seventh day.

Although many studies have been performed to evaluate the potential effects of LIPUS therapy on hard and soft tissues,[33] no study has confirmed the effect of low-intensity and low-power ultrasound waves on the reduction of pain after placement of initial archwire in orthodontic patients.

Similar studies have examined the effect of low-power lasers on the reduction of pain. Based on the evidence, it was shown that low-power lasers can decrease inflammatory processes and inflammatory responses in clinical conditions. Based on a study, the effectiveness of a low-power laser was similar to ketorolac.[17] Although a low-power laser seems to be effective in increasing orthodontic movements of teeth and reducing pain, further studies are required to achieve the best treatment protocol for the prevention of energy consumption.[39]

Differences in the effect of ultrasound and ibuprofen on pain relief in various studies could be due to individual differences, demographic factors, environmental effects, socio-psychological factors, and placebo effect. Since pain is a subjective experience, it is strongly dependent on individual differences. The communication between a patient and physician, both verbally and nonverbally, without the use of any separate treatment, can cause a placebo effect.[38] The placebo effect is now recognized as a powerful and determining factor in resolving the problem and creating health in relation to various diseases.[40]

The placebo mechanism acts via the stimulation and release of endogenous opioids, such as enkephalins and endorphins, into the brain leading to pain control.[41] Moreover, the placebo effect acts through nonopioid mediators. For example, a type of antagonistic mechanism, a nonopioid mediator called cholecystokinin, leads to increasing the placebo effect through the reinforcement of the placebo-activated opioid system. In fact, placebo analgesic responses in the brain are the results of a balance between endogenous opioids and endogenous cholecystokinin.[41]

It should be mentioned that the major disadvantages of LIPUS are its higher cost and chair time. Other methods including topical use of anesthetic gels, chewing gums or bite wafers, and transcutaneous electrical nerve stimulation has been studied in the literature.[6,42-45]

Advantages and limitations

The assessment of homogeneous patients and use of two control groups are considered the main strengths of the present study. The retrospective nature of the study, small sample size, and presence of one gender were also the main limitations of the current study.

Therefore, it is suggested to carry out further studies with a larger sample size to determine the validation of the present findings. Moreover, it is recommended to perform further studies on the therapeutic effects of low-intensity ultrasound, especially on the reduction of pain and inflammation after orthodontic treatment

CONCLUSION.

In conclusion, LIPUS (with a frequency of 1 MHz and an intensity of 100 mW) and ibuprofen have no significant effects on reduction of the pain severity at different time points and various conditions in orthodontic patients.

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Conflict of interests:

All the authors declare not presenting any conflict of interest.

Ethics approval:

The protocol of the present study was approved by the Research Ethics Committee of Mashhad University of Medical Sciences (IRCT20190825044606N1).

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