



Research Paper

Comparative Analgesia Between Acupuncture and Dipyrone in Odontalgia



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Abstract

The aim of this study was to assess whether the effectiveness of acupuncture is similar to the use of analgesics in the management of toothache. The research included 56 volunteers who were divided into 4 groups: Real Acupuncture group, Placebo Acupuncture group, Real Dipyrone group, and Placebo Dipyrone group. The interventions of the study were performed before the dental care. Inclusion criteria were toothache of pulpal origin with pain scale (Visual Analogue Scale) above 4, absence of medication for the pain, and aged over 18 years. The Real Acupuncture volunteers received a session of acupuncture using piercing needles, while volunteers from the Placebo Acupuncture group received an acupuncture session using non-piercing sham needles. Volunteers from the Real Dipyrone group received a dipyrone tablet and the Placebo Acupuncture group received a tablet with no active ingredient. Before any therapeutic intervention, we collected samples from the volunteers' saliva to analyze the salivary cortisol, the volunteers rated the intensity of their pain using VAS, and we measured their energy level by the Ryodoraku method. After 20 minutes of treatment, all the volunteers' analysis parameters were collected again. The Real Acupuncture group presented a greater reduction of VAS than the reduction obtained by the Real Dipyrone group ($p < 0.05$). There was no statistically significant difference between the groups for the salivary cortisol and energy level variables. It can be concluded that acupuncture was more effective in reducing odontalgia than the dipyrone and that it can be an alternative for odontalgia management.

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1. Introduction

Acute toothache (pulpitis) is the most frequent cause for searching emergency dental services [1,2]. The pain caused by irreversible pulpitis only has final resolution if clinical measures are taken, such as by pulpectomy, carried out by a dental surgeon.

The use of analgesic and antiinflammatory medications in the management of this pain before and after dental treatment is common [3]. The analgesic dipyrone is the pharmacotherapy of choice of a large part of dental surgeons and patients because of its low cost and ease of access and also it promotes good results [4,5,6]. Dipyrone is very effective in cases of pain due to the blocking of entry of calcium inside free nerve endings, stabilizing the membrane of nociceptors and reducing the state of hyperalgesia [7,8].

Despite its widespread use, dipyrone may cause adverse effects [9] that can affect the well-being of the patient, thus requiring the use of a therapeutic option that presents minor adverse reactions but with the same ability to reduce pain.

Acupuncture has been a nonpharmacological treatment option widely used to relieve various dental symptoms [10,11], including acute pulpitis [12]. Zotelli et al [13] conducted an intervention with acupuncture in patients who were waiting for dental care and complained of toothache and observed that 76.8% of the cause of the pain was pulpitis.

Because pain is a sensory and emotional experience difficult to be quantified [14], we proposed in this study to assess the concentration of the hormone cortisol in the saliva [15,16,17] and the circulating energy through the Ryodoraku method as variables to evaluate the effect of acupuncture [18], as well as the visual analog scale (VAS).

Therefore, the aim of this study was to assess whether the effectiveness of acupuncture is similar to that of the use of analgesics in the management of pain caused by irreversible pulpitis in patients who sought emergency dental services.

2. Methods

2.1. Study design

This is a double-blind randomized clinical trial. The study protocol was approved by the Research Ethics Committee of the Piracicaba School of Dentistry (CEP CAAE 78633317.1.0000.5418) and registered in the Brazilian Registry of Clinical Trials (REBEC) under number RBR-8sxw2r.

2.2. Participants

The volunteers were captured at the emergency dental services of the Piracicaba School of Dentistry (FOP/Unicamp) and of the Piracicaba Center of Dental Specialties (CEO) between 6:30 a.m. and 9 a.m. for 10 months. During the study, a total of 442 volunteers were analyzed.

Volunteers older than 18 years, with irreversible pulpitis diagnosed by a dentist, pain reported as moderate or severe (more than 4 in VAS), and who took no pain medication in the last 12 h were selected to participate in the study. Exclusion criteria applied were as follows: patients experiencing dental pain from other sources, taking pain medication, being pregnant, being allergic to dipyrone, and younger than 18 years.

The research team was composed of 1 acupuncturist (performed by the first author herself) and 4 dental surgeons responsible for confirming the diagnosis of irreversible pulpitis.

2.3. Interventions

The volunteers were randomized to 4 study groups (Fig. 1):

Real acupuncture group (n = 14): patients were submitted to a session of acupuncture, following a protocol of dental analgesia with acupuncture in accordance with the protocol by Grillo et al. [12], using the acupoints LI4 (Hegu), ST44 (Neiting), and CV23 (Lianquan), as well as the Yintang point.

Placebo acupuncture group (n = 14): patients were submitted to a session of acupuncture using nonpiercing sham needles in the same points of the protocol from the real acupuncture group.

Real dipyrone group (n = 14): patients received 1 tablet of 500 mg dipyrone. The tablets used in the real dipyrone group were acquired in a community pharmacy (batch: LOC2882, best before: 06/2019; EMS S/A, Hortolândia, Sao Paulo, Brazil). After intake of the tablet, the patient was kept at rest for 20 min.

Placebo dipyrone group (n = 14): patients received 1 tablet with no active ingredient. The tablets used in the placebo dipyrone group were made exclusively for the study in a specialized compounding pharmacy (Phitopharma Farmácia de Manipulação, Americana, Sao Paulo, Brazil), presenting the same organoleptic characteristics (color, odor, and flavor) of the tablets used in the real dipyrone group. After intake of the tablet, the patient was kept at rest for 20 min.

The volunteers of real dipyrone and placebo dipyrone groups received envelope containing information about the group that they belonged to and were delivered to the dentist of the emergency service to make medication that was needed after the intervention.

All patients, regardless of the allocation group, were cared for at the emergency dental service for proper dental intervention. The interventions of the study were performed before the dental care.

The real acupuncture was performed using piercing needles made of stainless steel of size 30 mm × 0.25 mm (Qizhou brand; Wujiang City Shenli Medical & Health Material Co. Ltd, Wujiang, Suzhou, Jiangsu, China). The placebo acupuncture was performed using sham Streitberger needles (nonpiercing) made of stainless steel of size 30 mm × 0.30 mm (Asia-Med Brand, Asia-med GmbH & Co. KG, Pullach, Germany). The sham needle is retractable, and thus, it does not pierce the skin; however, it touches the skin, causing the same feeling compared with that

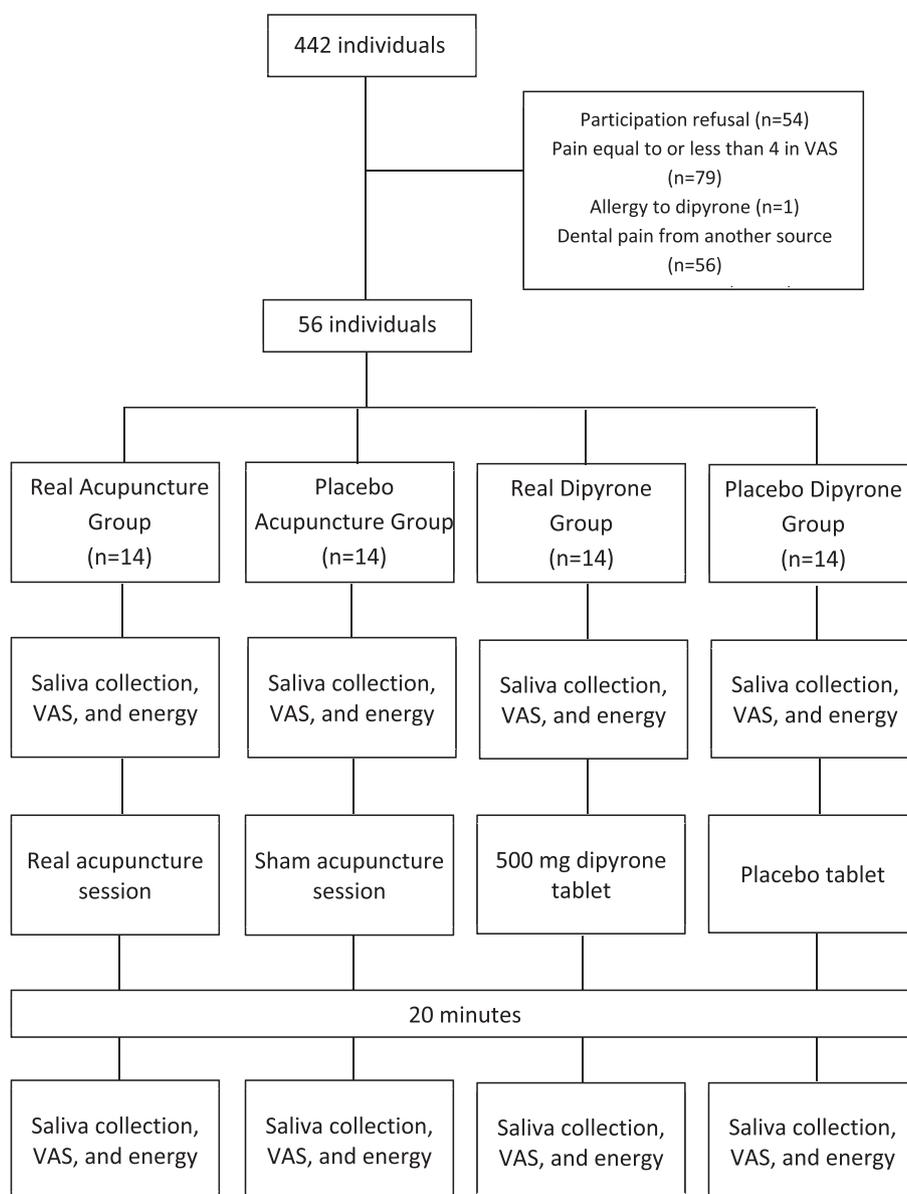


Figure 1 Criteria for sample definition. The profiles of the participants of the sample are shown in [Table 1](#).

obtained when a real needle is pierced in the patient. To fixate the sham needle, a circular device was used (resin ring, 1-cm diameter) set in the patient's skin with a 0.12-cm-wide hypoallergenic tape (Nexcare; 3M, Sumaré, São Paulo, Brazil). This device was also used for the real acupuncture group.

The application of acupuncture, in both groups, followed the following steps ([Appendix 2](#)):

1. Needle insertion at the LI4 point until reaching the DeQi
2. Wait for 5 min and record the value of the VAS
3. If VAS = 0, the session was finished/if VAS > 0, insertion at the ST44 point until reaching the DeQi
4. Wait for 5 min and record the value of the VAS
5. If VAS = 0, the session was finished/if VAS > 0, insertion at the CV23 and Yintang points until reaching the DeQi
6. Wait for 5 min and record the value of the VAS
7. Finish the session.

2.4. Independent variables

In addition to the variables of interest described in the following (VAS, cortisol, and energy), we collected demographic data including age (asked to the volunteer and registered in numbers) and sex (female or male). The volunteer's experience with acupuncture was asked using the following question: "Have you ever done acupuncture?" with possible answers "Yes" or "No." We asked volunteers which treatment group they thought they were taking part of with the following question: "Do you believe you participated in the real or placebo group?" with possible answers "Real" or "Placebo." The term "placebo" was explained and adjusted to the participants, when necessary, so that understanding was clear. The expectation of the patient before treatment was also verified with the following question: "Do you think acupuncture/dipyron may improve the toothache problem you are feeling right

Table 1 Number of participants, means, and standard deviation of the VAS, salivary cortisol and initial energy, mean age, sex distribution, prior experience with acupuncture, and perception of participation in the groups.

| Variables | Real acupuncture n = 14 | Placebo acupuncture n = 14 | Real dipyrone n = 14 | Placebo dipyrone n = 14 | Total |
|---|-------------------------------|--------------------------------|--------------------------------|--------------------------------|------------|
| Initial VAS* ($\bar{X} \pm SD$) | 7.49 ^A \pm 1.75 | 6.46 ^A \pm 1.93 | 6.94 ^A \pm 2.09 | 7.37 ^A \pm 1.94 | 7.06 |
| Initial salivary cortisol* (\bar{X} in $\mu\text{g/dL} \pm$) | 0.28 ^A \pm 0.25 | 0.38 ^A \pm 0.25 | 0.35 ^A \pm 0.27 | 0.30 ^A \pm 0.18 | 0.33 |
| Initial energy* ($\bar{X} \pm SD$) | 10.71 ^A \pm 4.27 | 15.64 ^A \pm 7.45 | 12.71 ^A \pm 6.07 | 11.71 ^A \pm 3.86 | 12.69 |
| Age* ($\bar{X} \pm SD$) | 38.14 ^A \pm 9.87 | 32.21 ^A \pm 11.71 | 34.29 ^A \pm 12.37 | 35.93 ^A \pm 10.79 | 35.14 |
| Sex [†] | | | | | |
| n (%) | | | | | |
| Female | 8 (57.14) ^a | 5 (35.71) ^a | 6 (42.86) ^a | 8 (57.14) ^a | 27 (48.21) |
| Male | 6 (42.86) ^a | 9 (64.29) ^a | 8 (57.14) ^a | 6 (42.86) ^a | 29 (51.79) |
| Experience with acupuncture [†] | | | | | |
| n (%) | | | | | |
| No | 12 (85,71) ^{A,a} | 11 (78,57) ^{A,a} | 13 (92.86) ^{A,a} | 13 (92.86) ^{A,a} | 49 (87.50) |
| Yes | 2 (14,29) ^{A,b} | 3 (21,43) ^{A,b} | 1 (7.14) ^{A,b} | 1 (7.14) ^{A,b} | 7 (12.50) |
| Expectation [†] | | | | | |
| n (%) | | | | | |
| Without | 6 (42,86) ^a | 3 (21,43) ^a | 7 (50,00) ^a | 6 (42,84) ^a | 22 (39,29) |
| With | 8 (57,14) ^a | 11 (78,57) ^b | 7 (50,00) ^a | 8 (57,14) ^a | 34 (60,71) |

SD = standard deviation; VAS = visual analog scale; \bar{X} = mean.

Different capital letters on the same line mean statistically different results. Different lowercase letters on the same column mean statistically different results.

* test ANOVA.

[†] test of proportion.

now?" with the following possible answers: "No," "I do not think so," "Maybe," "I think so," or "Yes." For this present study, we considered as positive expectation those who replied "Yes" and "I think so."

2.5. Outcomes

2.5.1. Visual analog scale

The measurement of pain reported by the patient was performed using the VAS, which is represented by a 10-cm-long continuous horizontal line, with each end of the scale related to pain intensity [19]. The VAS was measured before and after the proposed therapeutic intervention and presented in numerical form for statistical analysis.

2.5.2. Energy analysis

The Ryodoraku method consists in measuring an individual's circulating energy by using the Ryodoraku device (batch 00218, RDK/NKL; Produtos Eletrônicos Ltda. Brusque/SC, Brazil) in the acupuncture points defined by Nakatani and Yamashita [20], which present lower electrical resistance and greater electric current intensity, which can be measured using the Ryodoraku device in 12 specific points of the body with answer showed in microamperes (mA). The device used to carry out this measurement is a portable unit, which connects to a computer via USB and has two electrodes, one of them being a return stick, which the patient holds with the hand, and the other, a probe with a hole in its end that allows placement of a cotton swab that must be moistened in water before touching the patient's skin. There are 24 measuring points referring to the respective meridians, 12 located on the wrists of the right and left hands ((LU9-Taiyuan, PC7-Daling, HT7-Shemen, SI5-Yanggu, TE4-Yangchi, LI5-Yangxi) and 12 located on the left and right feet (SP3-Taibai, F3-

Taichong, KI3-Taixi, BL64-Jinggu, GB40-Qiuxu, ST42-Chongyang) [21,22]. The measured values are represented in a graph, in which each column is related to the energy measured in that meridian, which was obtained through its representative point of the energy measure. In this study, the energy levels were measured before and after the proposed therapeutic interventions to understand the patients' energy profile as well as possible changes caused by the treatments, comparing the values of the means in microamperes.

2.5.3. Analysis of the salivary cortisol hormone

The analysis of salivary cortisol was used as an objective parameter related to the patient's pain. Saliva collection occurred before and after the proposed therapeutic intervention according to which group the patient was allocated to. The saliva was collected in the Salivette, plastic tubes suitable for this procedure, consisting of a cylindrical container plastic with a cotton tube. The cotton tube was inserted in the patient's mouth by the researcher, holding it for 1 min. The patient was instructed to move the cotton through the oral cavity with the aid of the tongue, to collect saliva from all the salivary glands. The researcher then removed the cotton soaked in saliva from the patient's mouth and placed it inside the Salivette. The Salivette was immediately placed under refrigeration and taken to storage.

Saliva samples were stored and analyzed in the laboratory of Pediatric Dentistry, Piracicaba School of Dentistry (FOP/Unicamp).

To remove the saliva from the Salivette, the tubes were kept at room temperature for 15 to 30 min and centrifuged for 15 min at 3000 rpm. The samples were transferred to tubes duly identified and kept frozen at -30°C until the time of dosage.

The dosage of salivary cortisol concentration was carried out by the immunoassay [enzyme-linked immunosorbent assay (ELISA)], using the Salivary Cortisol kit (Salimetrics, State College, PA, USA). The laboratory analysis occurred as indicated by the manufacturer's instructions. The samples were evaluated using a reader microplate for absorbance at 450 nm, and the cortisol levels were determined in accordance with the standard curves provided by the manufacturer.

2.6. Sample size

The sample size was defined by the following parameters: a significance level of 5%, 95% test power, and the proportion of pain reduction verified individually for each test group (acupuncture and dipyrone). The pain reduction proportion parameter used for the group treated with dipyrone was 50% [23], and for those treated with acupuncture, a reduction of 99% was expected [12]. The sample calculation demonstrated the need for 14 participants in each group.

2.7. Randomization and allocation

For randomization of the volunteers in the research groups, 56 opaque envelopes were made, being encoded from 1 to 28 in red, referring to the real acupuncture and placebo acupuncture groups, and those encoded from 29 to 56 in blue referring to the real dipyrone and placebo dipyrone groups. The envelopes were previously encoded by a person external to the study and sealed. Each patient chose an envelope and, based on the number drawn, was allocated in the study group. The meaning of the codes in the envelopes used in the randomization was stored in a sealed envelope, being revealed only after the end of data collection and analysis.

2.8. Blinding

The study was double-blind because the researcher and the volunteers were unaware of to which group they belonged.

2.9. Statistical methods

The effectiveness of acupuncture compared with dipyrone was assessed by the outcomes of the salivary cortisol

analysis, energy analysis, and VAS. The data obtained were analyzed statistically in the BioEstat program (version 5.3; Instituto de Desenvolvimento Sustentável Mamirauá, Tefé, Amazonas, Brazil), using *t* test for evaluation of demographic data, paired *t* test for evaluation of intragroup parameters, and analysis of variance (ANOVA) test for comparison of the parameters among the groups, adopting $p \leq 0.05$. In case of difference between groups, Tukey test $p \leq 0.05$ was used.

3. Results

We invited 442 individuals present in emergency dental services of FOP and CEO at the time of the research, between 6:30 a.m. and 9:00 a.m. ($n = 442$), in the established collection period, between February and November 2018, and who met the inclusion criteria.

After analysis of the inclusion and exclusion criteria of the study, the sample amounted to 56 people. Among those excluded, 7 individuals presented pain less than 4 in the VAS, 79 were medicated for pain, 1 was allergic to dipyrone, 56 were evaluated by the dentist but their pain had another source (DTM, pericoronite, periodontitis, residual root fracture), 54 refused to participate in the research, and 196 patients were present in the waiting room but were not assessed (Fig. 1).

The study groups were similar concerning the variables of interest (VAS, cortisol, and energy) at the beginning of the study ($p \leq 0.05$). The mean age of study participants was 35.14 years, and the frequency of men (51.79%) and women (48.21%) was also equally distributed. Of the 56 participants in the study, only 7 (12.50%) had already had some prior experience with acupuncture.

Some volunteers reported believing to be in a group different from the initially allocated one. This occurred both in the acupuncture group and in the dipyrone group.

The means and standard deviation of the VAS, cortisol concentration, and energy evaluated before and after interventions in each study group are presented in Table 2.

There was a decrease in pain in all groups. For cortisol, this decrease occurred only in the real dipyrone group. For energy, the decrease occurred in the placebo acupuncture group (Table 2).

The analysis of the differences of the means of pain, cortisol, and energy of the study presented a statistically significant difference among the groups only to VAS values (Table 3). The ANOVA test for the comparison of the VAS between the study groups resulted in $p < 0.0001$, and

Table 2 Means and standard deviation of the VAS, salivary cortisol, and energy before and after interventions according to the study group.

| | VAS $\bar{X} \pm SD$ (p) | Concentration of cortisol $\bar{X} \pm SD$ in $\mu\text{g/dL}$ (p) | Energy $\bar{X} \pm SD$ in mA (p) |
|---------------------|---------------------------|---|-----------------------------------|
| Real acupuncture | 6.71 \pm 2.11 (<0.0001) | 0.02 \pm 0.10 (<0.493) | 1.07 \pm 2.40 (<0.119) |
| Placebo acupuncture | 4.25 \pm 1.47 (<0.0001) | 0.04 \pm 0.16 (<0.338) | 2.43 \pm 2.82 (<0.007) |
| Real dipyrone | 3.00 \pm 1.78 (<0.0001) | 0.09 \pm 0.14 (<0.041) | 1.64 \pm 3.71 (<0.122) |
| Placebo dipyrone | 2.14 \pm 2.19 (<0.0001) | 0.001 \pm 0.11 (<0.966) | 1.07 \pm 3.43 (<0.263) |

SD = standard deviation; \bar{X} = mean.
Paired *t* test was used.

Table 3 Difference of the initial and final VAS mean and standard deviation values according to the study groups.

| Comparison | Difference of the VAS means and standard deviations | p |
|--|---|-------|
| Real acupuncture x placebo acupuncture | 2.457 ± 4.814 | <0.01 |
| Real acupuncture x real dipyrone | 3.707 ± 7.264 | <0.01 |
| Real acupuncture x placebo dipyrone | 4.571 ± 8.957 | <0.01 |
| Placebo acupuncture x real dipyrone | 1.250 ± 2.449 | ns |
| Placebo acupuncture x placebo dipyrone | 2.114 ± 4.145 | <0.01 |
| Real dipyrone x placebo dipyrone | 0.864 ± 1.693 | ns |

*Tukey test/*p* ≤ 0.05.

therefore, the Tukey test was performed, the results of which are listed in Table 3.

The decrease in pain in the real acupuncture group was statistically higher than the reduction promoted in the other groups. The reduction of pain in the real acupuncture group was greater than that promoted in the placebo acupuncture group. Pain reduction was similar between the groups real dipyrone and placebo dipyrone, as well as when compared with the placebo acupuncture group.

The decrease of the mean of salivary cortisol concentration before and after interventions was significant only in the real dipyrone group (Table 2). However, comparing the groups, this difference was not evidenced in the VAS (Table 3).

The decrease of energy before and after interventions was significant only in the placebo acupuncture group (Table 2). However, comparing the groups, this difference was not evidenced in the VAS (Table 3).

The VAS values after inserting each acupuncture point can be found in Figs. 2 and 3.

The reduction of VAS occurred in the insertion of the first acupuncture point (LI4-Hegu) in most patients of both

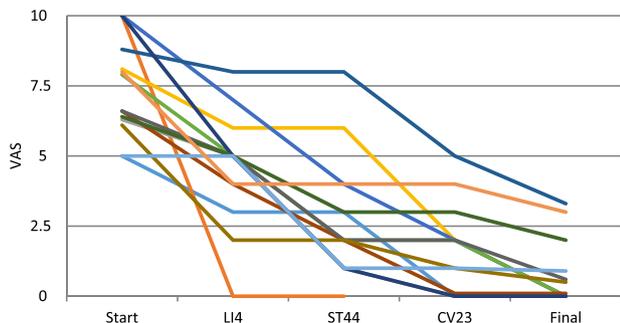


Figure 2 VAS measured before, at each acupuncture point, and after the acupuncture session for each volunteer in the real acupuncture group. Acupuncture points: LI = large intestine; ST = stomach; CV = conception vessel; VAS = visual analog scale.

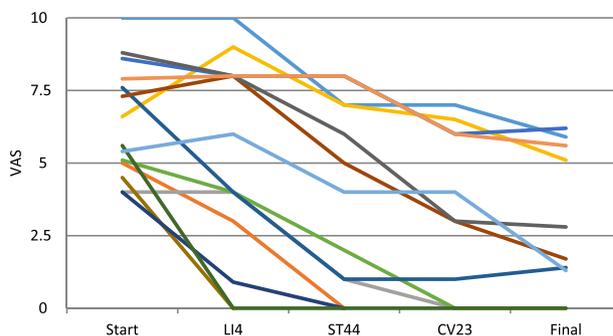


Figure 3 VAS measured before, at each acupuncture point, and after the acupuncture session for each volunteer in the placebo acupuncture group. Acupuncture points: LI = large intestine; ST = stomach; CV = conception vessel; VAS = visual analog scale.

groups. There was a sharper decrease in the real acupuncture group (Fig. 2) than in the placebo acupuncture group (Fig. 3), with 3 volunteers reporting absence of pain only with this point (LI4-Hegu)—2 from the placebo acupuncture group and 1 from the real acupuncture group.

When asked in which groups the patients thought they were allocated (Real or Placebo), more than half (n = 8) from the real dipyrone group believed to belong to the placebo group. This also occurred in the placebo acupuncture group, i.e., the majority (n = 10) believed to be in the real acupuncture group.

To analyze the difference of the initial and final VAS according to belief of the patients, the ANOVA test was performed, resulting in *p* < 0.0001, and following the Tukey test, the data are shown in Table 4.

The analysis of the differences of VAS means showed a statistically significant difference between the real acupuncture and real dipyrone groups, which believed to be allocated in the real group.

The analysis of expectation regarding treatment is shown in Table 5. To analyze the difference of the initial and final VAS according to expectation of the patients, the ANOVA test was performed, resulting in *p* < 0.0007, and following the Tukey test, the data are shown in Table 5.

In the comparison within each study group, VAS reduction was similar, regardless of the expectations. In the

Table 4 Difference of the initial and final VAS means and standard deviation of patients according to their belief.

| | Real n/ $\bar{X} \pm SD$ | Placebo n/ $\bar{X} \pm SD$ |
|---------------------|-------------------------------|-------------------------------|
| Real acupuncture | 11/7.26 ^{A,a} ± 2.02 | 3/4.67 ^{A,a} ± 0.74 |
| Real dipyrone | 6/3.88 ^{A,b} ± 1.85 | 8/2.34 ^{A,a} ± 1.50 |
| Placebo acupuncture | 10/4.92 ^{A,a} ± 0.99 | 4/2.57 ^{A,a} ± 1.10 |
| Placebo dipyrone | 4/2.85 ^{A,a} ± 1.47 | 10/1.85 ^{A,a} ± 2.43 |

Tukey test was used.

\bar{X} = mean; SD = standard deviation.

Equal capital letters on the same line mean statistically similar results. Equal lowercase letters on the same column mean statistically similar results.

Table 5 Difference of the initial and final VAS means and standard deviation distributed according to expectation.

| | With expectation n/ $\bar{X} \pm SD$ | Without expectation n/ $\bar{X} \pm SD$ |
|------------------------|---|--|
| Real acupuncture | 8/6.50 ^{A,a} \pm 1.99 | 6/6.98 ^{A,a} \pm 2.41 |
| Real dipyrone | 7/3.50 ^{A,b} \pm 1.43 | 7/2.49 ^{A,b} \pm 2.05 |
| Placebo acupuncture | 11/4.12 ^{A,a} \pm 1.57 | 3/4.73 ^{A,a} \pm 1.10 |
| Placebo dipyrone | 8/2.12 ^{A,a} \pm 1.41 | 6/2.15 ^{A,a} \pm 3.13 |

Tukey test was used.

\bar{X} = mean; SD = standard deviation.

Equal capital letters on the same line mean statistically similar results. Equal lowercase letters on the same column mean statistically similar results.

comparison among groups, there was greater pain reduction in the real acupuncture group compared with the real dipyrone group.

4. Discussion

This study demonstrated that acupuncture was more effective than the analgesic dipyrone, resulting in a greater reduction of pain caused by toothache in patients who sought emergency dental service due to irreversible pulpitis.

Acupuncture is a nondrug technique that is not widely used as main or complementary treatment for physical and psychological symptoms. Studies used acupuncture for reducing insomnia [23], relief of pain of cancer origin [24], blood pressure control [25], lumbago [26], and headache [27], for example.

Acupuncture is gaining great importance in the dental area for relief of orofacial pain [10,11], facial paralysis [28], and nausea caused by dental procedures [29]. A study analyzed 2,168 adults living in a poor and culturally diverse area of London and has shown a high prevalence of orofacial pain (30.2%), with toothache being responsible for 20.4% [30]. Therefore, methods for the management of orofacial pain should be investigated. It is important to note that, with the use of a single acupuncture point (LI4-Hegu), there was total remission of pain in 3 patients and reduction of pain in the remaining ones, even in the placebo group, confirming the importance of the actions described in this point, known as acupuncture's "analgesic point." The use of other points (ST44-Neiting and CV23-Lianquan) refer to an earlier study on their effectiveness in the control of odontalgia [12].

Currently, many studies are being carried out, comparing the effects of acupuncture with Western medication in various areas of health, such as a clinical trial with 56 patients with rheumatoid arthritis, which was conducted to compare the effects caused by acupuncture (observation group) and by the drugs ibuprofen, methotrexate, and folic acid combined (control group). The authors concluded that acupuncture improves symptoms of rheumatoid arthritis, as well as the physiological patterns related to blood stasis [31].

The use of the analgesic dipyrone for pain of dental origin is well reported in the literature [32]. Dipyrone is one of the most prescribed active principles to control odontalgia because it promotes quick pain reduction due to its differentiated action mechanism [33]. In this study, it was possible to verify pain reduction using dipyrone; however, this reduction was smaller than the one caused by acupuncture.

A comparison of the analgesic effects of acupuncture and of the drug ibuprofen concerning irreversible pulpitis was carried out, in which the 157 participants were allocated into 3 different groups: real acupuncture, placebo acupuncture, and ibuprofen. To analyze the pain, the VAS was used before the interventions and 15, 30, 45, and 60 min after and again 12, 24, and 48 h after the procedure. The authors concluded that the real acupuncture group showed higher toothache reduction than the placebo acupuncture and ibuprofen groups [34]. In this study, we found the same answer regarding the drug dipyrone, with greater reduction in the VAS in the real acupuncture group than in the real dipyrone group, as described in the literature when other drugs for pain control were used.

The mechanism of action by which acupuncture and dipyrone cause pain reduction are different. Similar to any medicinal drug administered orally, dipyrone is metabolized by liver enzymes and is biotransformed into a molecule capable of having a pharmacological effect and thus reducing the painful stimulus when on the therapeutic target [35]. Acupuncture promotes the release of hormones and neurotransmitters at the needle insertion site, as well as promoting effects on the central and peripheral nervous systems, thus causing pain reduction [36]. The results of this study demonstrated reduction of pain by both therapies, the reduction of pain with the use of acupuncture being greater.

The use of a placebo group in clinical trials serves as negative control of the treatment group in which any substance or technique is being tested, to eliminate or reduce uncertainty. The placebo effect involves several psychological aspects, such as the expectation of treatment [37] and the reinterpretation of stimuli with emotional impact [38], and may contribute to the creation of a biological system and physiological reactions that may have huge importance during a treatment [39].

The presence of a placebo group to compare the effects caused by acupuncture is widely used in the literature. In this study, the placebo dipyrone reduced pain as much as real dipyrone, and this reaction might be associated with the placebo effect. A study evaluated the effects of administration of placebo caffeine in dopaminergic neurotransmission using computed tomography scans and has shown that placebo caffeine induced changes similar to the effects of real caffeine [40]. Another example of a placebo effect of acupuncture in dentistry relates to a research that studied the antiemetic effect of the PC6 (Neiguan) point during jaw molding procedures. It was evaluated during a randomized clinical trial, using a group of real acupuncture and a placebo group (sham acupuncture). The authors concluded that the PC6 (Neiguan) point was effective in controlling nausea during the molding and that the reduction caused was statistically similar in both groups [29]. A

patient from this study reported total remission of nausea, even though he was allocated to the placebo group [41].

The stimulus generated by the touch of the adhesive and resin ring used to position the sham needle may have caused an effect of acupressure on patients from the placebo acupuncture group, generating positive results. A randomized clinical trial compared the antiemetic effect of acupressure on the PC6 and of antiemetics drugs in surgical postoperative patients and concluded that both are effective, concluding that acupuncture is a good non-pharmacological alternative [42]. The effect of acupressure was also verified in cardiac patients, reducing the symptoms of depression, improving quality of life, and decreasing sensitivity to pain [43].

The analysis performed within the study groups showed that the expectation and belief of allocation did not interfere with VAS reduction in this study. The comparison made between the study groups echoed the results previously obtained with the VAS (the real acupuncture group caused greater pain reduction than the real dipyrone group), with no interference of expectation in the comparison between the real groups. For the placebo groups, the absence of statistical difference may be related to the reduced sample number for verification of this relation.

A systematic review showed a significant association between patients' expectations and the results of treatment with acupuncture and also that the placebo effect is part of the treatment's result [44]. The expectation of 282 parents was evaluated before and after their children's surgeries regarding acupuncture being effective to relieve vomit and related it with some predictors, such as the parents' anxiety levels. The authors concluded that the parents' expectation tends to change before and after surgery (being more pronounced in more anxious parents), becoming more positive over time, which positively affected the results of the treatment with acupuncture [45]. The study by Kaasinen et al. [40] administered placebo caffeine to 8 individuals, but instructing that there was a 50% chance of them receiving real caffeine. The study demonstrated dopaminergic responses via computed tomography scans similar to those caused by caffeine, concluding that the volunteers' expectation influenced positively on the results.

Believing to be in the real or placebo group appears to not have interfered in the results because in the comparison within each study group, the reduction remained the same, and the comparison between groups confirmed the greater pain reduction in the real acupuncture group. However, it is interesting that this outcome was not reproduced in those who believed to be in the placebo group, thus indicating a possible interference in the reduction of the results in those who, despite being in the real group, believed to be in the placebo. However, it should be highlighted that the reduced comparison numbers may not have had statistical power to demonstrate this reduction.

Fleckenstein et al. [46] suggest that attention and care during treatments, whether real or sham, can induce physiological effects and psychological response, corroborating with the results found in this study, because both groups were admitted in the same way.

Salivary cortisol levels grow significantly during a stress situation, be it physical or psychological. However, these levels tend to fall and reestablish homeostatic balance after 15-20 min of cessation of the stress stimulation source [47]. As found in the literature, in this study, there was no statistically different reduction of salivary cortisol concentration before and after the interventions proposed for the study groups. A clinical study carried out with women who underwent in vitro embryo transfer showed that acupuncture did not alter serum cortisol levels when compared with a placebo group [48]. Acupuncture also did not alter the levels of cortisol in dysphonic speaker patients compared with a placebo sham acupuncture group [49]. Taking into consideration that cortisol levels tend to rise in the morning [47] and even more in a situation of stress/pain, the nonincrease of cortisol found in this study may suggest that the treatments had some effect. However, in the real dipyrone group, there was a statistically significant reduction in the levels of salivary cortisol, as reported in studies conducted in animals [50,51]. However, when comparing the study groups, it lost statistical significance.

A limitation of the study may have been the fact that the volunteers were not distributed homogeneously regarding belief of to which group they belonged, especially those who believed to be in the placebo group. This unequal distribution observation also happened concerning previous experience with acupuncture. Another limitation is related to the time that the patient could stay in the study as they were waiting for dental care and, therefore, the study could not extend beyond 20 min the time to verify the outcome variables (VAS, cortisol, and energy) after application of the methods.

The use of acupuncture as a substitute for drugs, which can cause side effects, and/or as an adjunct of the conventional treatment provides decrease not only of pain but also of anxiety, making dental care more comfortable and providing pain relief and decreased anxiety, thus broadening therapeutic resources and possibilities.

This study demonstrated that acupuncture was effective in reducing the pain of patients suffering from odontalgia and this reduction was greater than that promoted by the analgesic dipyrone. This study found that acupuncture can be an alternative for the management of acute pain in patients with odontalgia.

Disclosure statement

The authors declare that there are no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jams.2019.07.005>.

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