Comunicação Científica e Técnica em Odontologia 4

Emanuela Carla dos Santos
(Organizadora)

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APRESENTAÇÃO

A inovação é o combustível do crescimento profissional em todas as áreas, mesmo na mais tradicional até a área mais tecnológica. A Odontologia é a ciência que agrega os princípios técnicos tradicionais, como por exemplo, aqueles postulados por Greene Vardiman Black, às mais avançadas tecnologias, como escâneres intraorais e impressoras 3D capazes de produzirem peças anatomicamente perfeitas, específicas para cada caso.

Pensando na propagação de conhecimento dentro das mais variadas áreas de atuação do Cirurgião Dentista, a Atena Editora disponibiliza mais um compilado de artigos, organizados em dois volumes, com a temática Comunicação Técnica e Científica em Odontologia.

Espero que a leitura do conteúdo deste E-book proporcione ampliação de conhecimentos e que também provoque curiosidade em você, leitor, pois são os novos questionamentos que impulsionam novas descobertas.

Ótima leitura.

Emanuela C. dos Santos

SUMÁRIO

CAPÍTULO 13

SYSTEMATIC REVIEW AND META-ANALYSIS OF CRYOTHERAPY AND HEAT THERAPY IN MORBIDITY AFTER SURGERY

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ABSTRACT: Background: this systematic review and meta-analysis aims to address the issue of PICOS: Is there evidence to indicate the use of cryotherapy and heat therapy after surgical extraction of impacted third molars? **Methods:** electronic searches in the databases were performed according to the PICOS strategy from 01/01/1990 to 12/31/2018, complemented by a manual search. Studies that showed data on the post-operative anti-inflammatory benefits of cryotherapy and heat therapy (regarding extraction of impacted third molars) were included. **Results:** of the 271 citations, 11 articles were selected for evaluation. Ten addressed the effects of cryotherapy, with only one referring to thermotherapy. Of these, five trials were suitable for meta-analysis, all concerning cryotherapy. This analysis indicates, a reduction in postoperative sequelae such as pain, trismus and edema in the groups where cryotherapy was applied, although meta-analysis has only found statistically significant results for the reduction of pain after surgery in the groups which applied ice. **Conclusions:** Additional Randomized Controlled Trials are required and should concentrate on the development of modes, duration and frequency of the application of ice and heat.

KEYWORDS: Cryotherapy. Thermotherapy. Induced hyperthermia. Induced hypothermia. Tooth extraction. Third molars.

INTRODUCTION

Surgery for the extraction of impacted third molars is one of the most common procedures performed by oral maxillofacial surgeons. Although the surgeon's experience is a factor that can influence the severity of postoperative effects, an inflammatory physiological response is practically unavoidable, which severely affects patients' quality of life. The use of cryotherapy and heat therapy is valuable in the prevention and treatment of inflammatory postoperative sequelae, mainly for decreasing pain, however, professionals' scientific bases for prescribing such therapies is still controversial, as they are guided by each surgeon's individual clinical experience(1–3).

Specific knowledge of the indications and contra-indications of these types of therapy requires an understanding of the physiological effects and the physical properties of heat and cold. Cryotherapy and heat therapy, although reducing pain and muscle spasms, have opposing effects on tissue metabolism, blood flow, inflammatory response and connective tissue permeability. Cryotherapy reduces these effects, while heat therapy increases them. Thus, the choice of any type of individual heat therapy depends on many factors, including the size of the area to be treated, ease of application, accessibility, duration of application and depth of penetration (2,3).

The therapeutic efficiency of these types of treatment has not been sufficiently assessed and the results of previous studies lack consistency, varying from the method followed to the agreement or otherwise of the effects encountered post-application (1).

There are, therefore, discrepancies in the literature as to the best protocol to use for these types of therapy, such as intervals of application and rest, and alternation between heat and cold, as well as their impact on reducing the inflammatory effects post- surgery for the extraction of impacted third molars (1).

In light of this, the aim of the systematic review and meta-analysis presented here is to answer if there is scientific evidence to indicate the use of cryotherapy and heat therapy after surgical extraction of impacted third molars, and their impact on postoperative inflammatory sequelae, so that therapeutic protocols can be developed.

MATERIALS AND METHODS

The systematic review and meta-analysis presented here were performed to find Randomized Controlled Trials (RCTs) that use postoperative cryotherapy and heat therapy.

Databases from 1990 to December 2018 were researched, using the following keywords: oral and maxillofacial surgery, cryotherapy, heat therapy, inflammatory complications, cold therapy, anti-inflammatory agents, edema, trismus and pain. Electronic searches were performed using the OvidMEDLINE, SCOPUS (Elsevier), Pubmed, Cochrane Library, Lilacs and Livivo databases, in accordance with the PICOS search strategy and the steps recommended by the PRISMA manual and registered on

the PROSPERO platform under the number: CRD42018091101. Another strategy was the additional consultation of references in selected publications, complemented by a manual search of articles in the main journals in this area. Registers of publications on the Open Grey platform were also examined. The search strategy for the bibliographic databases used different combinations of MeSH terms associated with AND/OR Boolean operators.

RCTs that contained data on the use of postoperative cryotherapy and heat therapy were considered as the inclusion criteria. Studies on animals and in vitro studies were excluded.

All studies were assessed regarding study design, trans-operative data, ethical compliance, monitoring data and reports of surgical results.

Research was carried out in three stages by two independent evaluators (EPML and LFSM) to test sensitivity and specificity.

Data concerning relevant demographics and outcomes were extracted from the articles, including: total number of patients, number of patients receiving cryotherapy and heat therapy treatment, control groups, average age and surgical results from comparison groups (postoperative pain, facial edema, trismus, bleeding, hematoma and quality of life), as well as average follow-up data and a description of each study's data collection process.

Cohen's kappa coefficient for the inclusion of the studies was 98.9% for the titles; reviewer 1 found one additional title and reviewer 2 found two. Agreement between reviewers, after reading the summaries, showed a kappa coefficient of 0.996 (95% confidence interval), an almost perfect agreement that resulted in the choice of 11 articles related to the study's objectives.

For developing meta-analysis calculations, the outcomes of each study were divided into continuous variables (Mean ± SD), using the Mean difference to test the overall effect. Fixed effect (no heterogeneity) and random effect (with heterogeneity) models were chosen using the methods of inverse variance and the two-sided 95% confidence interval. Heterogeneity was measured using Cochran's Q test and Higgins & Thompson's I2 test, considered significant when $p<0.05$ and $I<50\%$(4). RevMan 5 (Review manager version 5.3.5 – Cochrane Collaboration Copyright© 2014) was used. Meta-analysis of the RCT results comprised five studies(5–9)”type”:”article-jo urnal”,”volume”:”136”},”uris”:[“http://www.mendeley.com/documents/?uuid=640a770b-407f-4e71-9674-49fefc7a861d”]},{“id”:”ITEM-2”,”itemData”:{“DOI”:”10.1016/j.ijom.2008.05.011”,”ISBN”:”0901-5027 (Printwith a total of 202 patients who underwent cryotherapy and 198 from the control group.

RESULTS

The complete search strategy is presented in the PRISMA data flow diagram (Figure 1). After the removal of duplicates and having evaluated the titles, 180 abstracts

were selected for analysis, of which 17 were chosen to be read in their entirety. The six studies excluded after a complete reading were due to their being: outside of this review's inclusion criteria (3); studies on animals (1); and not mentioning the application of cryotherapy or heat therapy in isolation after surgical extraction of impacted third molars (2). All 11 of the studies included in the systematic review were RCTs published between 2005 and 2018. No study reported the previous performance of a pilot study. Finally, for the meta-analysis, five articles were found to be appropriate. The summarized demographic data were extracted and are presented in (Table 1).

General description of studies included and study design

The studies assessed were RCTs of patients who underwent cryotherapy and heat therapy. The studies included in this review did not adequately follow the CONSORT checklist for reporting consolidated trials.

The total number of patients selected for the studies ranged from 10 to 139. In total, 706 subjects were assessed, 396 women and 310 men, with ages varying from 17 to 66. The monitoring period went from the preoperative stage to 28 days.

The results shown by the clinical trials often do not include numerical data on the increase and decrease in the variables analyzed, as well as means, standard deviations and percentages.

The way edema and facial trismus were measured varied among the studies. Antibiotic, analgesic and anti-inflammatory protocol also differed among the publications evaluated.

Only the study conducted by Haraji et al. 2016(10)hot water dressing has not to our knowledge been assessed before. Studies of operations for epistaxis or sinus conditions have suggested that irrigation with hot water can reduce bleeding, so we hypothesised that it might be effective in reducing bleeding after extraction too. Ten patients who required bilateral extractions took part in this split-mouth, randomised, single-blind, controlled clinical trial. After extraction, sockets were packed with similar gauze dressings soaked in normal saline 4 ml at room temperature (control, made any reference to the use of heat therapy, through the use of gauze compresses soaked in a saline solution at a temperature of 42°C on the operated region, with continuous application occurring immediately after surgery, for 15 minutes, without any rest breaks.

All studies that made use of cryotherapy assessed pain through a visual analogue scale (VAS), in which 0 represents absence of pain and 10, the worst imaginable pain. Each study presented a previously defined period for the patients to record pain levels. All studies that evaluated pain showed a reduction after the therapy was applied, however, with no statistically significant difference in the groups assessed, with the exception of Laureano Filho et al. 2005(5), Ibikunle; et al. 2016(11)pain, trismus, and quality of life (using Oral Health Impact Profile-14 (OHIP-14, Forouzanfar et al. 2008(6) andJain et al. 2018(9), which showed a significant difference between the treated side and the control side ($p<0.05$), favoring the treated study group (Table 1).

Trismus was assessed by verifying maximum range of jaw motion, recorded between the maxillary and mandibular incisors. Each study presented a specific period for recording the measurements. Among the devices used were: a Vernier caliper (7,8,11,12) a standardized millimeter scale device(13)" and a basic caliper (5,9,14). The studies by Haraji et al. 2016(10)hot water dressing has not to our knowledge been assessed before. Studies of operations for epistaxis or sinus conditions have suggested that irrigation with hot water can reduce bleeding, so we hypothesised that it might be effective in reducing bleeding after extraction too. Ten patients who required bilateral extractions took part in this split-mouth, randomised, single-blind, controlled clinical trial. After extraction, sockets were packed with similar gauze dressings soaked in normal saline 4 ml at room temperature (control, Al-Fahad et al. 2017(15)and Forouzanfar et al. 2008(6)did not evaluate the reduction of trismus after the applied therapy. Ibikunle et al. 2016(11)pain, trismus, and quality of life (using Oral Health Impact Profile-14 (OHIP-14 and Jain et al. 2018(9), showed a statistically significant difference in inter-incisal distance within the group that underwent ice therapy compared to the control group, in the time periods assessed ($P<0.05$). The other studies, although showing greater range of jaw movement after the application of ice therapy, did not show a statistically significant difference (Table 1).

The assessment of edema was recorded via techniques that measure linear distances of the face on a millimeter scale (5,8,11,13), a Vernier caliper (7,12), silk thread (9)and Altimarmak et al. 2018(8)indicate a statistically significant improvement regarding edema in patients that underwent cryotherapy compared to the control group. Van der Westhuijzen et al. 2010(12), Zandi et al. 2015(7) and Altimarmak et al. 2018(8) showed that, even though there was reduction of edema after heat therapy, there was no statistically significant difference when compared to the control group. The studies of Forouzanfar et al. 2008(6); Haraji et al. 2016(10) and Al-Fahad et al. 2017(15)did not evaluate reduction of edema (Table 1).

In the majority of studies in which quality of life after surgery was assessed, patients filled in a questionnaire and reported higher satisfaction after undergoing cryotherapy (6,11,12,14,15). The study by Zandiet al. 2016(7), did not show a statistically significant difference between the groups assessed (satisfaction scores: 7.27 for the ice therapy group and 7.00 for the control group)(5). Ali-Hosein et al. 2008(13); Haraji et al. 2016(10),Altimarmak et al. 2018(8) andJain et al. 2018(9)did not assess the impact of heat therapy on patients' quality of life.

Meta-analysis of RCT results

Meta-analysis of RCT results comprised five studies (5–7,11–14)single-blind, randomized controlled study design was chosen. Participants in group A applied 45 min of repeated compression with ice; those in group B applied 45 min of repeated compression without ice (controlwhich provided a total of 202 patients who underwent cryotherapy and 198 who made up the control group.

Four trials quantitatively assessed pain via a VAS(6–9). Results point to a preference for cryotherapy with a statistically significant difference on days two ($p<0.00001$, $I2= 39\%$) and seven ($p>0.00001$, $I2= 45\%$). Moreover, the studies demonstrated moderate heterogeneity, with the application of the fixed effects model (Figure 2).

Differences between the groups that used ice and those that did not were not statistically significant regarding trismus on the days assessed: day two ($p=0.58$) and day seven ($p=0.08$), however, the control group that did not use ice showed advantages. Specifically for this outcome, numerical data on the group that underwent cryotherapy were larger due to the increase in mouth opening resulting from its application, with the exception of Laureano Filho et al. 2005(5). Therefore, a favorable tendency in the group that did not use ice is to be expected, this being the probable explanation for the outcome. On the days in question, the random effects model was used due to the high level of heterogeneity, (day two $I2= 87$) and day seven $I2=97\%$, $p<0.10$) (Figure 3).

As far as edema is concerned, the differences between the groups that used ice and those that did not, were not statistically significant on the days assessed: day two, $p=0.29$ and day seven, $p=0.18$. However, preference for the group using ice was evidenced. A random effects model was used due to the high level of heterogeneity (day two $I2=99\%$ and day seven $I2=85\%$) (Figure 4).

Data on pain, edema and trismus were not available on days 1, 3 and 5 post-surgery. In addition, data on quality of life, hematoma and bleeding were not sufficient on any of the days on which patient follow-up occurred.

Assessment of the quality of all studies included was conducted with the aid of Cochrane's risk-of-bias tool, which checks for validity evidence concerning interventions and assesses seven conditions: Randomization, Allocation, Blinding of participants, researcher and results, as well as reported results and other sources of bias.

For each entry, the partiality judgments "low risk", "high risk" and "unclear risk" were attributed. The performance of randomization was mentioned in all of the studies, however, for the most part, there was no mention of how it was performed, nor the allocation of patients into the study groups and control groups. In the studies conducted byLaureano Filho et al. 2005(5); Forouzanfar et al. 2008(6);Rana et al. 2011(14); Haraji et al. 2016(10)hot water dressing has not to our knowledge been assessed before. Studies of operations for epistaxis or sinus conditions have suggested that irrigation with hot water can reduce bleeding, so we hypothesised that it might be effective in reducing bleeding after extraction too. Ten patients who required bilateral extractions took part in this split-mouth, randomised, single-blind, controlled clinical trial. After extraction, sockets were packed with similar gauze dressings soaked in normal saline 4 ml at room temperature (controland Altiparmak et al. 2018(8), researcher blinding was mentioned, the last two studies being the only ones to provide adequate information on the blinding of both study groups. The absence of data reported in the studies was observed, except in the case ofForouzanfar et al. 2008(6) e Haraji et al. 2016(10)hot water dressing has not to our knowledge been assessed before.

Studies of operations for epistaxis or sinus conditions have suggested that irrigation with hot water can reduce bleeding, so we hypothesised that it might be effective in reducing bleeding after extraction too. Ten patients who required bilateral extractions took part in this split-mouth, randomised, single-blind, controlled clinical trial. After extraction, sockets were packed with similar gauze dressings soaked in normal saline 4 ml at room temperature (control, theremainingarticlesnotmentioning complete data in respectoftheanalyzedvariables.

The final bias-risk values for the RCTs were unsatisfactory, with 38 conditions of unclear risk of partiality, 28 conditions of high risk and just 11 of low risk of bias. The item most affected was performance bias (blinding of participants and/or researchers), where no author presented low risk of partiality (Figure 5).

DISCUSSION

Cryotherapy and heat therapy may be used at different stages in the management of postoperative morbidity(1,16).

Haraji et al. 2016(10)hot water dressing has not to our knowledge been assessed before. Studies of operations for epistaxis or sinus conditions have suggested that irrigation with hot water can reduce bleeding, so we hypothesised that it might be effective in reducing bleeding after extraction too. Ten patients who required bilateral extractions took part in this split-mouth, randomised, single-blind, controlled clinical trial. After extraction, sockets were packed with similar gauze dressings soaked in normal saline 4 ml at room temperature (controlis the only study in this systematic review to address the use of heat as a complementary therapy after IMTM surgery. Although the application of heat is advocated in late post-surgery, this study carried out immediate application in the trans-operative period, banking on an increase in enzymatic activity with a consequent reduction in coagulation time. To this end, 10 patients received the application via a sterile gauze soaked in 4 ml of saline solution heated to 42ºC, immediately after extraction, for a period of 15 minutes. This article, however, did not evaluate pain, trismus or edema in the groups studied. A significant reduction in postoperative bleeding was observed.

There are no clear guidelines as to the ideal moment and duration when the ice should be applied to attain the clinical objectives of treatment(17). The articles in this review recommend ice therapy immediately after surgery, with revolving applications of 5 to 45 minutes, and rest intervals ranging from 5 to 90 minutes (5–7,11–15). This goes against what was published in the studies byMerrick et al. 2003(17), Bleakley et al. 2004(19)and Kanlayanaphotporn et al. 2005(20), which, although in agreement that ice is effective, suggested that limiting the duration of cold therapy to 10-minute rather than 20-minute intervals could attain the same skin temperature and thereby avoid side effects and potential fresh lesions. Additional support for a 10-minute interval was provided by Meeusen et al. 1986(21). They demonstrated that the permeability of the

lymphatic vessels increased after 10 minutes of cold therapy, and instead of draining the liquid from the damaged tissue back into the cardiovascular system, it may be returned to the area of the area of the lesion and increase the edema.

This difference of opinion may be due to the fact that the studies that were conducted were directed towards the performance of the cryotherapy on soft tissue, unlike those in the studies of this systematic review in which the application of ice was related to postoperative IMTM surgery, the inflammatory sequelae of which are more evident (17,21).

Lokesh et al. 2015(3)suggested that applications above 20 minutes produce a "rebound effect", representing the flow of blood through arteriovenous anastomoses, with a consequent increase in bleeding. The authors note, therefore, that 20 minutes of application with ice in the buccinator region are needed to reduce the blood flow in the oral mucosa, while 10-minute applications showed no significant change. Malone et al. 1992(22)inappropriate use in some individuals can lead to nerve injury resulting in temporary or permanent disability of the athlete. Six cases of cold-induced peripheral nerve injury from 1988 to 1991 at the Sports Medicine Center at Duke University are reported. Although disability can be severe and can render an athlete unable to compete for several months, each of these cases resolved spontaneously. Whereas the application of this modality is typically quite safe and beneficial, clinicians must be aware of the location of major peripheral nerves, the thickness of the overlying subcutaneous fat, the method of application (with inherent or additional compressionadvocated cryotherapy of up to 20 minutes to avoid damaging peripheral nerves.

This notion, however, has been challenged, and studies where cryotherapy is used for 30 minutes did not report any increase in edema (1,5,12,18). However, no RCTs were found with a control group that stopped applying cold versus a test group that continued with the application, to determine if cryotherapy would induce additional edema. Moreover, it should be recognized that there are large variations in individuals' response to cold. There is, therefore, a need to evaluate the gravity and extent of the surgical procedures of an individual patient and, then provide guidance with regard to the intervals of application of the ice.

Merrick et al. 2003(17)and Kanlayanaphotporn et al. 2005(20)argued that the use of the intermittent application of ice, as opposed to continuous use, helps to maintain a lower muscle temperature, without impairing the skin, and allows the surface temperature to return to normal while the deeper muscle temperature remains low. Other researchers have suggested that cooling should be performed continuously after surgery, until such time as the response to the trauma stabilizes, which may occur between 24 and 72 hours (24). Forsgren et al. 1985(18)and Van der Westhuijzen et al. 2010(12)recommended continuous therapy with ice for 2 and 24 horas, though they failed to furnish significant benefits when compared with any cold therapy.

In the present review, the studies byForouzanfar et al. 2008(6)and Van der Westhuijzen et al. 2010(12)used continuous cryotherapy, while those ofLaureano Filho

et al. 2005(5); Ali-Hosein et al. 2008(13); Ibikunle; et al. 2016(11); Zandi et al. 2016(7), Al-Fahad et al. 2017(15)and Altiparmak et al. 2018(8)opted for the application of ice intermittently. Meanwhile, the studies ofRana et al. 2011(14)and Jain et al. 2018(9) performed just one application for 45 minutes. In a comparison of these studies, the intermittent application produced more statistically significant effects than the continuous application, as observed in the studies ofLaureano Filho et al. 2005(5); Ali-Hosein et al. 2008 and Ibikunle et al. 2016(11).

The studies of Van der Westhuijzen et al. 2010(12), Zandi et al. 2016(7)trismus, and oedema after dentoalveolar surgeries. However, information reported in the literature on its effectiveness is insufficient and controversial. This study was performed to evaluate the effect of local cold application in reducing pain, trismus, and swelling after impacted mandibular third molar surgery. Thirty patients (seven males and 23 femalesand Altiparmak et al. 2018(8), included in this review, despite the observation of a reduction in pain, edema and trismus in the groups where cryotherapy was applied, no statistically significant difference was found between the controls, except for the studies conducted by Forouzanfar et al. 2008(6) and Al-Fahad et al. 2017(15), which did not evaluate the parameters for edema and trismus. Forsgren et al. 1985(18)reported that ice, applied continuously for 2 hours subsequent to IMTM surgery, did not demonstrate any benefits with regard to a postoperative reduction in edema, trismus or pain.

In contrast, other studies in this work(6,9,11,12,14,15)single-blind, randomized controlled study design was chosen. Participants in group A applied 45 min of repeated compression with ice; those in group B applied 45 min of repeated compression without ice (controlobserved benefits after the post-surgical application of cryotherapy, particularly with regard to improvements in the patents' quality of life.

Despite the fact that anti-inflammatory drugs have an impact on the reduction of postoperative sequelae, only the studies conducted by Ali-Hosein et al. 2008(13),Van der Westhuijzen et al. 2010(12)andZandi et al. 2016(7) used, as their main exclusion criterion, patients being treated with these agents, in a period of at least 24 hours prior to surgery. Jain et al. 2018(9), for their part, quote a protocol using antibiotics and analgesics after IMTM surgery. Meanwhile, the studies byLaureano Filho et al. 2005(5), Forouzanfar et al. 2008(6), Van der Westhuijzen et al. 2010(12), Rana et al. 2011(14), Zandi et al. 2016(7), Ibikunle; et al. 2016(11) and Altiparmak et al. 2018(8) unanimously mentioned the prescription of anti-inflammatory drugs in post-op. Although this may be a factor which makes it difficult to reach a conclusion about the effect of cold by itself, as the benefits of ice therapy may have been modified as a result of the combination of cryotherapy and anti-inflammatory drugs, among these publications there was an equivalence of data, which permitted a meta-analysis of these studies, with the exception ofVan der Westhuijzen et al. 2010(12)and Ibikunle et al. 2016(11), which made no mention of results with mean and standard deviation values, andRana et al. 2011(14), which did not compare to a control group that did not use ice.

Another point which generates confusion with the presented results is the fact

that, in clinical practice, ice is commonly combined with compression and elevated decubitus, making it difficult to determine the value of the cryotherapy in isolation. The initial consensus seems to be that the addition of ice to the compression is no more effective than compression by itself(15). Taneja et al. 2015(24)found that compression has a significant effect in reducing pain post-IMTM surgery. In the present analysis, Forouzanfar et al. 2008(6)was the only study that applied compression in combination with the application of ice, producing an improvement in the quality of life, though without significant results in terms of the reduction of postoperative pain.

There is no consensus with regard to the best method for applying cryotherapy after oral surgery. Ice cubes in a damp cloth or in the form of a compress, packs of hot/cold gel or a Hilotherm system, could reduce the temperature of the skin and adjacent structures (17). In agreement, Laureano Filho et al. 2005(5); Rana et al. 2011(14); Ibikunle et al. 2016(11)pain, trismus, and quality of life (using Oral Health Impact Profile-14 (OHIP-14; Zandi et al. 2016(7)and Merrick et al. 2003(17)indicated that a block of ice would be better than a gel pack, but the difference in °C was small. Moreover, ice in a damp cloth would be better than ice in a dry cloth because the former helps to reduce the temperature of the tissue(17,19). On the other hand, the studies conducted byAli-Hosein et al. 2008(13); Forouzanfar et al. 2008(6); Van der Westhuijzen et al. 2010(12), Al-Fahad et al. 2017(15), Altiparmak et al. 2018(8)and Jain et al. 2018(9)chose to use hot/cold gel packs for the treatment of postoperative sequelae.

The application of these therapies is subject to a set of problems inherent to the research study, primarily with regard to randomization. For instance, it may be difficult to randomize a subject to a “without ice” group. This is particularly evident in the study byLaba et al. 2010(25),in which 60% of individuals randomized for the group without ice self applied this therapy. Moreover, it can be seen in all of the studies included in this review, that the proper blinding of the study groups subjected to the application of therapies with ice and heat may have been a limitation, since the subjects are an integral part of the therapy, proper blinding being impossible. This creates a performance bias (researcher and patient blinding) in the studies, unless the application takes place simultaneously with the sedation, as found in the study by Rana et al. 2011(14). This aspect, added to the persistent methodological problems, was extremely important where the studies included in this systematic review were submitted to analysis, using Cochrane’s risk-of-bias tool, with a consequent negative impact.

One limiting factor was the restriction with regard to the search by date and the small number of studies included for the numerical analysis of this meta-analysis. The discrepancies in the articles with regard to protocols used in the surgical procedures, the insufficient numerical data and the varied drug prescriptions, were factors that limited the combination of the results of the individual studies. This review indicates, however, a reduction in postoperative sequelae such as pain, trismus and edema in the groups where cryotherapy was applied, although meta-analysis has only found

statistically significant results for the reduction of pain after IMTM surgery in the groups which applied ice.

The heterogeneity between the RCTs was measured using the Higgins & Thompson I2 value, considered significant when p<0.05 and I<50% (Boreinstein et al. 2009)(4). It was quantified as high for trismus and edema outcomes and moderate for the pain outcome. For the latter, it is suggested that meta-analysis has not been significantly affected by the discrepancies in the protocols adopted by the trials. However, analyses of sub-groups, such as results of reports of pain in men and women, outcomes stratified by age and the surgical procedure performed, were not carried out.

The current study corroborates the literature reviews conducted by Bleakley et al. 2004(19), Greenstein 2007(26)andTaneja et al. 2015(24), which argued that the majority of studies found in the literature do not fully consider the physiopathological basis of cryotherapy and, therefore, do not use all of its potential; and that based on the physiological responses to cold application, it is expected that therapy using ice would provide benefits to patients after oral surgery.

Despite the finding that RCTs do not support, or only faintly support the benefits of the use of cryotherapy after oral surgery, and aware of the relevant scientific evidence in the making of decisions that the systematic reviews and meta-analyses impose as a tool for translation into clinical practice, this study aims to contribute, despite the limitations, with pertinent information about the use of these therapies.

Given the lack of consensus among the published studies, and the inadequate proof of the effectiveness of the therapeutic intervention and, evaluating the heterogeneity of the observed results, preliminary recommendations for an ideal protocol are not yet possible. This analysis suggests, therefore, that additional RCTs are required and should concentrate on the development of modes, duration and frequency of the application of ice and heat, in order to provide clinical dental surgeons and oral maxillofacial specialists with clear evidence of its potential effectiveness and versatility in controlling postoperative sequelae, in order to validate, or refute, definitive conclusions in respect of cryotherapy and heat therapy post-surgery of impacted third molar.

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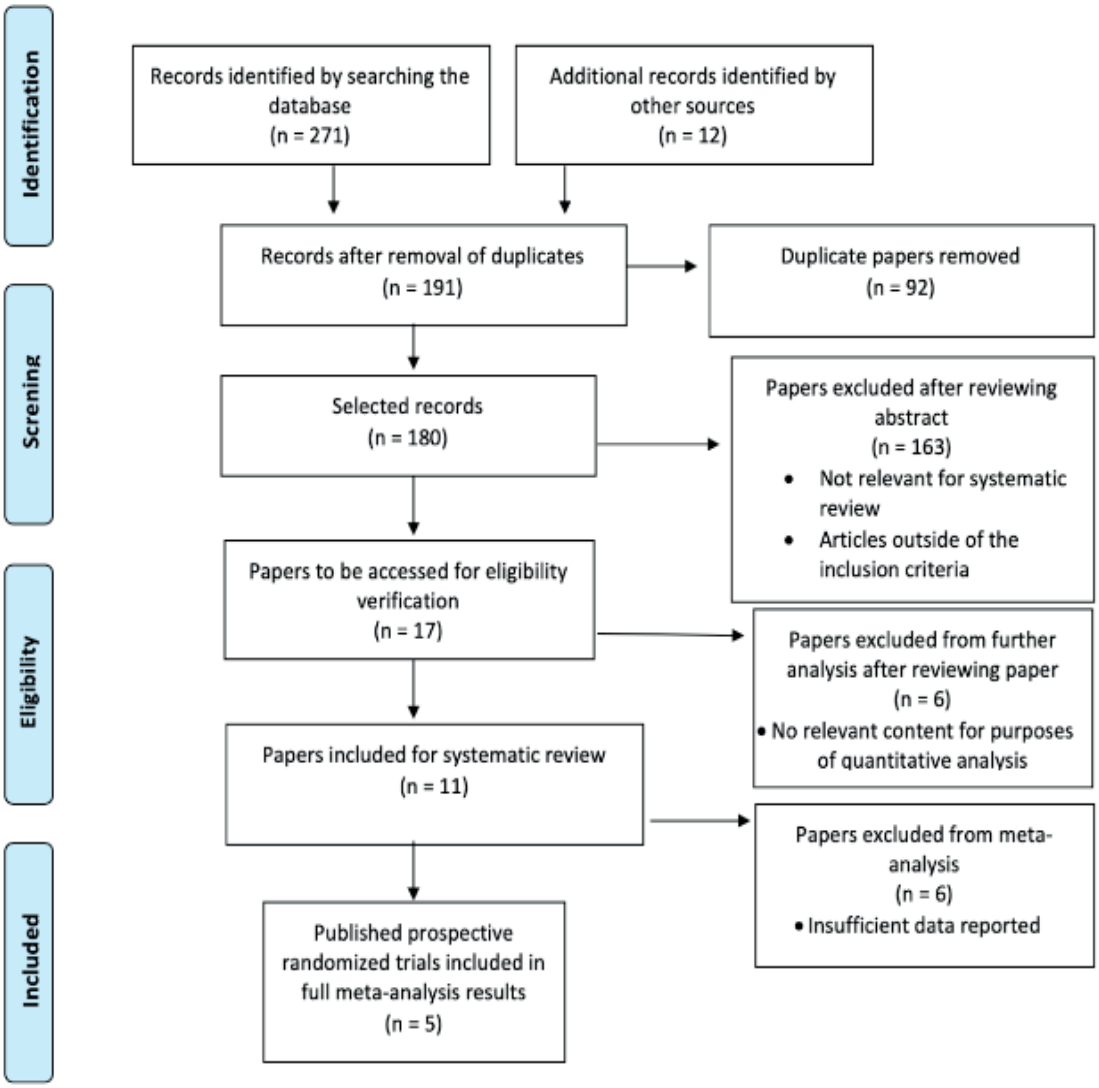

Figure 1: PRISMA Diagram

Study	Number of patients	Mean age (years)	Typeof application	Start of application	Time of application	Mode of application	Duration of application	Rest interval (minutes)
Ibikunle et al. 10	128	33,5	Ice packs wrapped in compress	Immediately after surgery	24 hours	Intermitent	30 minutes	90 minutes
Zandi et al. 15	30	24	Ice packs in plastic bag wrapped in fabric	Immediately after surgery	24 hours	Intermitent	20 minutes	20 minutes
Ali Hossein et al. 16	20	32	Standard ice pack	Immediately after surgery	24 hours	Intermitent	25 minutes	60 minutes

Al-Fahad et al. 18	30	-	Ice Wrap	After surgery or in the morning of the day following surgery	24 hours	Intermitent	20 minutes	40 minutes
Forouzanfar et al. 19	95	26,56	Ice pack (3M Nexcare)	Immediately after surgery	45 minutos	Continuos	45 minutes	No
Van der Westhuijzen et al. 20	60	29	Ice pack (Tecnol)	After 15 minutes of surgery	24 hours	Continuos	24 hours	No
Laureano Filho et al. 21	14	24	Ice packs wrapped in compress	Immediately after surgery	48 hours	Intermitent	30 minutes	90 minutes
Rana et al. 22	30	24,7	Thermoplastic polyurethane mask (Hilotherm)	Immediately after surgery	45 minutes	Continuos	45 minutes	No
Altiparmak et al. 35	18	20,84	Ice Wrap	Immediately after surgery	24 hours	Intermitent	5 minutes	5 minutes
Jain et al. 36	80	31	Ice pack (Polar Ice Pack)	Immediately after surgery	45 minutes	Continuos	45 minutes	No

Table 1: Use ofcryotherapy

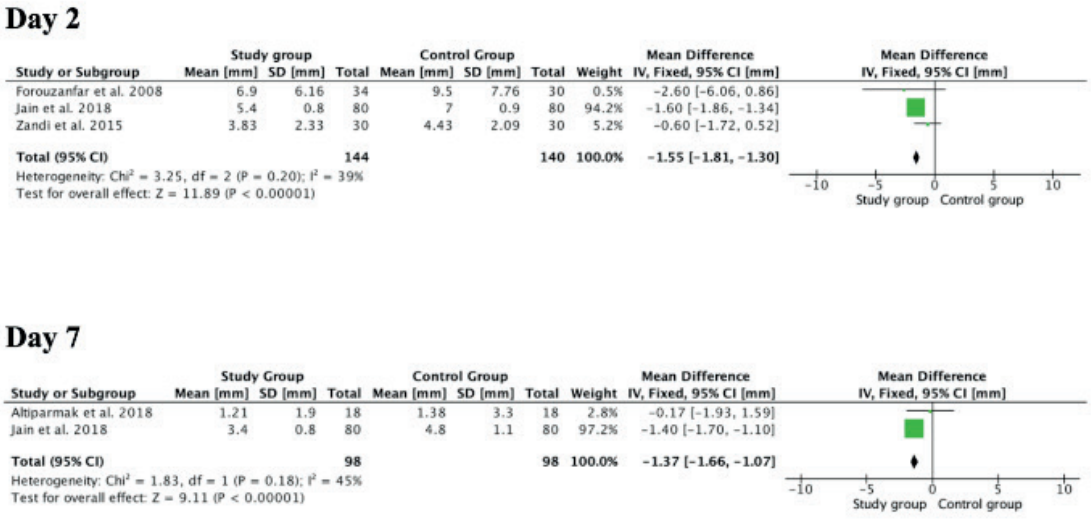

Figure 2: Florest Plot demonstrating a meta-analysis for intensity of pain measured via the VAS, between groups that use and do not use ice, at day 2 and day 7.

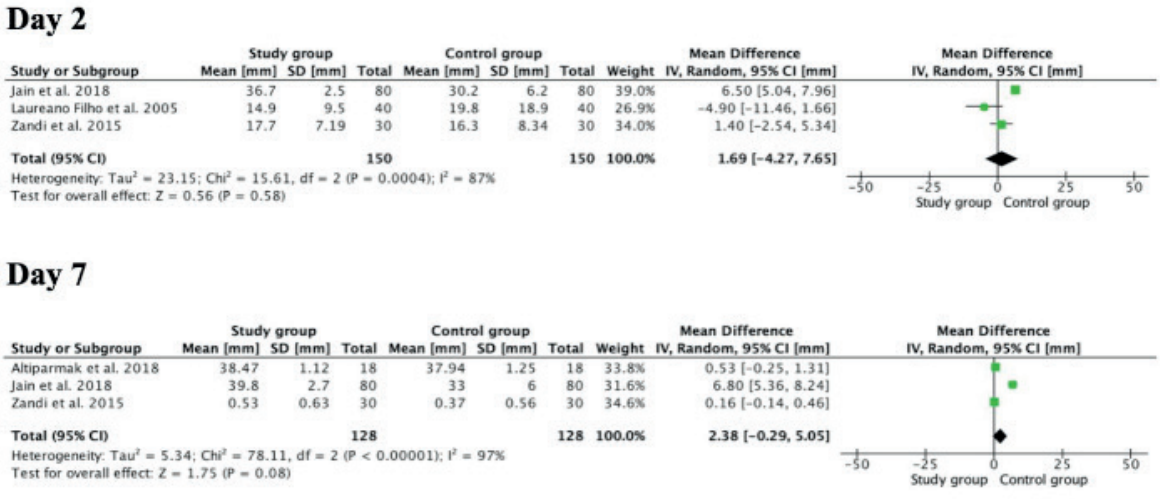

Figure 3: Florest Plot demonstrating a meta-analysis for intensity of trismus, between groups that use and do not use ice, at day 2 and day 7.

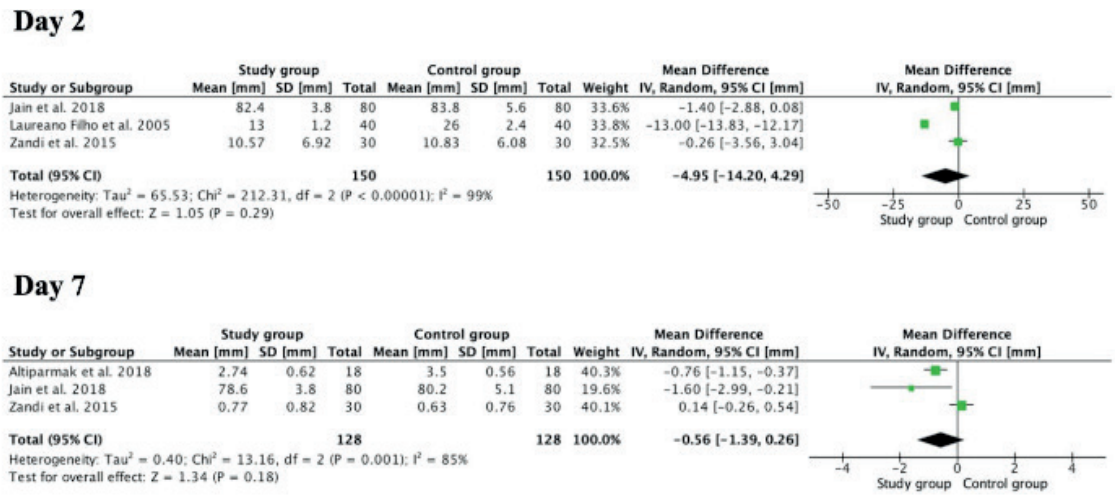

Figure 4: Florest Plot demonstrating a meta-analysis for intensity of edema between groups that use and do not use ice, at day 2 and day 7.

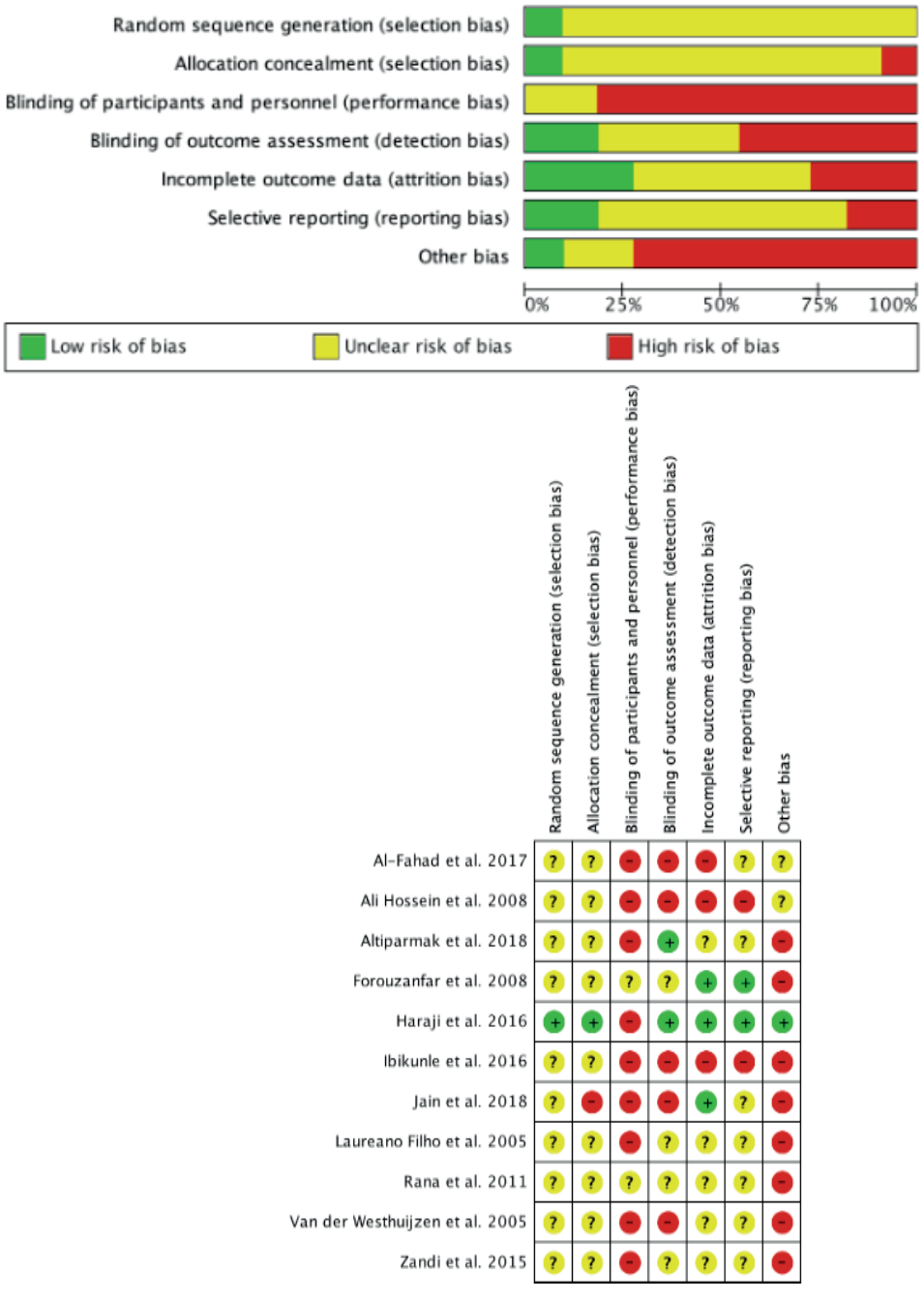

Figure 5: Graph and summary of risk of bias

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