Title

EFFECTS OF THE ADDITION OF TRANSCUTANEOUS ELECTRICAL STIMULATION TO NON-PHARMACOLOGICAL MEASURES IN LABOUR PAIN: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL

Abstract

Background: Labor, although natural and physiological, is a period that can be marked by stress, pain, anxiety, suffering, fear, anguish for a woman. Thus, non-pharmacological measures to reduce pain during labor are important to allow a better experience without the use of drugs. A non-pharmacological method that has been investigated is the use of Transcutaneous Electrical Stimulation (TENS). Thus, the aim of this study is to assess the effects of non-pharmacological pain relief measures added or not the application of TENS on pain, satisfaction with the childbirth of labor duration and conditions of birth of newborns. **Methods:** This is a randomized controlled clinical trial, with a non-probabilistic sample for convenience, composed of women during the first active phase of labor, admitted to a public institution. The volunteers will be divided into 3 groups: Group 1 (n = 36) composed of parturients who will have continuous support and will be encouraged as to walking, adopting a variety of positions with the use of the Swiss ball and receiving massage in the lower back for 30 min; Group 2 (n = 36) composed of parturients who will also have continuous support and will be encouraged as to ambulation, adoption of a variety of position using the Swiss ball and will receive the application of TENS for 30 min and Group 3 (n = 36) composed by parturients who will have continuous support and will be encouraged as to walking, adopting a variety of position with the use of the Swiss ball and will receive application of TENS placebo for 30 min. The outcomes assessed in the study will be: pain intensity assessed by the Visual Analogue Scale of pain applied before, immediately after, 30 minutes and 1 hour after interventions; Delivery Experience and Satisfaction Questionnaire (QESP) applied 12 to 24 hours after delivery, data regarding delivery (type of delivery, total duration of labor and possible obstetric complications) and neonate (weight, height, possible complications, score Apgar in the first and fifth minutes). **Discussion**: With this research, it is expected to understand the effects of

the intervention through TENS electrostimulation, added to other non-pharmacological pain relief measures, in women in labor.

Trial registration: Brazilian Registry of Clinical Trials (REBEC), number RBR-68kh6j approved on March 17, 2020.

Keywords

Pain, labor, non-pharmacological pain relief measures, electrostimulation.

Introduction

Background and rationale {6a}

Labor, although natural and physiological, is a period that can be marked by stress, pain, anxiety, suffering, fear, anguish for women [1]. Thus, the World Health Organization (WHO) recommends the use of non-pharmacological pain relief measures such as ambulation, kinesiotherapy or maternal mobility, exercise on a Swiss ball, massage, breathing exercises, relaxation techniques, hot bath with the aim of reducing pain, promoting an active posture of the parturient, with greater autonomy for women [2].

Non-pharmacological methods of pain relief can be used alone or together by the multidisciplinary team that make up the hospital structure (physiotherapists, nurses, nursing technicians, doctors and doulas), depending on the parturient's choice and the hospital infrastructure [3, 4 , 5, 6]. Some studies have demonstrated the effectiveness of walking and massage therapy in reducing pain and increasing pain tolerance [7,8,9]. Besides that, studies with other methods such as breathing and relaxation techniques, maternal mobility, Swiss ball exercises, massage and hot bath have observed a decrease in the use of medications, a decrease in anxiety and stress, a decrease in the duration of the active phase of labor and greater body perception of the parturient [10, 11, 12].

A non-pharmacological method that has been investigated is the use of Transcutaneous Electrical Stimulation (TENS). This is an apparatus by means of electrical stimulation has a pain reduction action and can be used during labor [13, 14]. There are two theories that explain the action of TENS in reducing pain. The first is the theory that was proposed by Melzack and Wall in 1965 that explains the action of TENS through the theory of the pain gate. Thus TENS provides electrical stimulation through the through the skin, sensory stimuli which will be taken to information to the brain via afferent fibers to the dorsal horn of the Aß marrow [15, 16]. Thus there is a blockage of pain impulses to the brain such as fiber transmits the information faster than the fibers responsible for transmission of pain [15, 16]. Another theory is explained by the release of endogenous opioids by the brain, as is the case of the release of beta-endorphins, which have an analgesic effect [15, 16].

The use of TENS during labor has its placement of electrodes at the levels of the vertebrae T10-L1 and S2-S4 [14, 17]. The sensation that the patient will report is tingling or tickling, and cannot cause muscle contraction or pain during the process. Studies have demonstrated the safety of the method for mother and fetus and positive effects in decreasing pain during work, decreasing the use of complementary analgesia, decreasing anxiety, decreasing labor time and improving satisfaction [13, 14, 15, 16, 17, 18, 19].

Despite the number of studies on the use of TENS in labor and its wide use in clinical practice, systematic reviews on the subject make it clear the low quality of studies so far [18, 20]. Thuvarakan et al [20], in a meta-analysis, found only a small effect of pain reduction during childbirth with the use of TENS, it is not possible to say whether the results were affected by the low quality of the studies.

Furthermore, the reality of clinical practice is the use of the methods of non-pharmacological pain relief together in an attempt to promote greater relief to women. However, the current scientific evidence comes mostly from studies that have evaluated the isolated effects of the techniques [12]. Thus, it is important to analyze the possible additional effect of using TENS in addition to other non-pharmacological pain relief techniques through a clinical trial with greater methodological control. These results may contribute to the physiotherapist's clinical practice in obstetrics, justifying or not the investment in equipment in maternity hospitals.

Objectives {7}

The aim of this randomized clinical trial is to verify the effects of non-pharmacological pain relief measures added or not to the application of TENS on pain, satisfaction with delivery, duration of labor and birth conditions of newborns.

Trial design {8}

This is a single-blind randomized controlled trial to compare three randomized groups in parallel (1:1:1). This article has been written in accordance with the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines.

Methods: Participants, interventions and outcomes

Study setting {9}

The trial will be carried out in the facilities of the Hospital Municipal Modesto de Carvalho, in the city Itumbiara-GO, Brazil.

Eligibility criteria {10}

Participants presenting the following features will be included in the trial:

- Pregnant women in active labor;
- Low-risk pregnancies;
- Women with a gestational age of 37-42 weeks;
- Gestation with a single fetus and this one in the cephalic position.

Exclusion criteria

Patients presenting the following features will be excluded from the trial:

- having a wound or inflammation in the cutaneous areas of application of the TENS electrodes;
- presence of a pacemaker;
- inability to understand verbal commands.

Who will take informed consent? {26a}

The signed informed consent form will be obtained from each patient prior to their participation in the study. The evaluator will acquire consent during hospitalization. The evaluator will explain all stages of the study and the volunteers who agree to participate will sign the term.

Additional consent provisions for the collection and use of participant data and biological specimens {26b}

Not applicable. There will be no biological sample collection in this study.

Interventions

Explanation for the choice of comparators {6b}

In clinical practice, non-pharmacological pain relief resources are used together, in an attempt to promote better results. However, they were not found in literature studies verified by

comparing the non-pharmacological measures of pain relief isolated and already recommended by WHO and combined application of TENS, if such action would an enhancement in diminishing pain of pregnant women during labor. Therefore, it was decided to compare non-pharmacological pain relief measures, with the same measures added to the use of TENS and placebo.

Intervention description {11a}

The intervention of the three groups will occur during the first active phase of labor, from admission, which happens when the parturient has 4 cm of cervical dilation, until the beginning of the expulsive period. The three groups will receive continuous support from professionals, encouraging walking and the adoption of vertical postures. In addition, parturients in Group 1 will be positioned on a Swiss ball so that they receive massage in the dorsal region for 30 min. Classic massage movements will be used, such as: superficial sliding, deep sliding, kneading, friction and rolling. Farmax brand almond oil will be used as a way to facilitate manual maneuvers.

Group 2 women will be submitted to intervention using TENS electrostimulation using the portable Neurodyn Ibramed portable TENS equipment. They will be positioned seated on the Swiss ball and four silicone electrodes that will be fixed with masking tape in the thoraco-lumbar region, at the levels of T10-L1 and S2-S4. A frequency of 100 Hz, pulse width of 100µs will be used, with intensity depending on the sensitivity of each patient for 30 minutes [17].

Women in Group 3 will undergo placebo intervention. They will be positioned and will have electrodes fixed in a similar way to group 2. However, the equipment will remain with the intensity button deactivated, without current flow.

Figure 1- Image of electrode placement in the thoraco-lumbar region

Figure 2- Image of the portable TENS Neurodyn Ibramed

Criteria for discontinuing or modifying allocated interventions {11b}

The criterion for discontinuation is withdrawal of patient consent prior to publication of the results.

Strategies to improve adherence to interventions {11c}

As this is an intervention that happens only during labor, the researchers will explain in detail the procedure for participating in the project and the need for

data collection after delivery.

Relevant concomitant care permitted or prohibited during the trial {11d}

During the protocol are allowed oral and intravenous medications as indicated by the doctor, with the exception of analgesic medication. Maternal mobility, bathing, total freedom for the mother in labour are allowed as recommended by the World Health Organization for women in labour.

Provisions for posttrial care {30}

Researchers are responsible for any harm that occurs as a result of the study. Thus, the researchers will provide for participants' health care needs that arise as a direct consequence of trial participation.

Outcomes {12}

Primary outcome measure

Primary outcome measure is assess the intensity of pain using the Visual Analogue Scale (VAS). It is a simple one-dimensional instrument, used worldwide to assess pain intensity. It is characterized by a 10 cm long horizontal line where 0 represents no pain and 10 the worst imaginable or severe pain. They will be evaluated before the intervention, immediately after the intervention, 30 minutes after and 1 hour after the intervention, will also be evaluated in the immediate puerperium (12-24 hours after delivery). All measurements will be performed in the period between uterine contractions.

Secondary outcome measures

The secondary outcomes of the study are evaluate satisfaction with childbirth, using the Childbirth Experience and Satisfaction Questionnaire (QESP). This consists of a self-report

questionnaire, with a total of 104 questions, which refer to the expectations, experience, satisfaction and quality of the woman's experience related to labor, delivery and immediate postpartum. This consists of a self-report questionnaire, with a total of 104 questions, which refer to the expectations, experience, satisfaction and quality of the woman's experience related to labor, delivery and immediate postpartum. It is composed of relative Lickert questions divided into eight subscales that comprise it: (1) conditions and care provided, (2) positive experience, (3) negative experience, (4) relaxation, (5) support, (6) support partner, (7) concerns and (8) postpartum. The higher the score obtained in each of the subscales, the more positive the perception of women in the dimension assessed by the subscale. The administration time for this questionnaire is approximately 30 minutes [21]. The questionnaire will be applied in the immediate postpartum period (12-24 hours) after delivery.

After delivery, information on the type of delivery, total delivery duration and possible obstetric complications will be collected from the participants' medical records. Besides that, data will be collected on the newborn: weight, height, possible complications, Apgar score in the first and fifth minutes.

Participant timeline {13}

Initially, volunteers will be numbered to avoid the risk of being identified. Soon after admission to the hospital, they will answer the standard anamnesis composed of questions about gynecological, obstetric and health history, lasting approximately 10 minutes.

Before the start of the intervention, the volunteer will be asked to mark on the VAS line the intensity of her pain at the moment. Immediately after, 30 minutes, 1 hour after the interventions with the use of massage, TENS or placebo, the request for indication of pain intensity will be repeated.

After 12 to 24h of the completion of the delivery, the volunteer will be visited by the researcher in the rooming-in and will be applied again to VAS and also the Questionnaire of Experience and Satisfaction with Delivery (QESP).

Data regarding childbirth, including: type of delivery, total duration of labor and possible obstetric complications, will also be collected by consulting medical records. As for the neonate, weight, height, possible complications, Apgar score in the first and fifth minutes will be collected.

The schematic diagram of the participant timeline can be seen in Figure 3.

Sample size {14}

Based on a previous study Báez-Suárez et al [14], considering a difference between groups of 1.5 and the standard deviation of 1.61, considering an alpha of 0.05 and the test power of 0.80 , the minimum sample size in each group is 36 participants.

Figure 3: Flow diagram of the trial design

Recruitment {15}

Participants will be recruited from Modesto de Carvalho Municipal Hospital, in the city Itumbiara-GO, Brazil. This hospital has an average of 67 births per month, with a vaginal birth rate of around 43.51%. No advertising is permitted for recruitment and no inducements will be given for the recruitment of patients in the study.

Assignment of interventions: allocation

Sequence generation {16a}

Participants will be randomized in a 1:1:1 ratio to the three groups, group 1 (active posture and massage in lumbar region for 30 minutes), group 2 (active posture and TENS application in

lumbar region) and group 3 (active posture and TENS placebo application in lumbar region for 30 minutes), by computer-generated random numbers.

Concealment mechanism {16b}

A researcher not involved in the data collection will assign the groups by the sealed envelope method. The opaque envelopes will be numbered and kept locked away, available only to the study researchers.

Implementation {16c}

After including the participant, the researcher responsible for the interventions will open the envelope with the lowest number available to determine which group the participant belongs to.

Assignment of interventions: Blinding

Who will be blinded? {17a}

The researcher in charge of the interventions to be applied to the participants will be blind to the assessments. The researcher in charge of the evaluations and the one accounting for data processing will be blind for treatment allocation. Patients will not be totally blind to the procedure because of the difficulties set by differences between techniques, but participants in the placebo group will not have information about the operation of the equipment.

Procedure for unblinding if needed {17b}

The loss of blinding should not be carried out unless there is a threat to

the participant's safety as a consequence of the study procedures.

Data collection and management

Plans for assessment and collection of outcomes {18a}

A trained researcher will perform all assessments during labor and after delivery. VAS is a simple one-dimensional instrument, used worldwide to assess pain intensity. Studies demonstrate that the Visual Analogue Scale is valid, reliable and suitable for measuring pain in the clinical part as in the evaluation of obstetric pain, as well as being reliable for measuring acute pain [22, 23, 24].

To assess the delivery experience, the Childbirth Experience and Satisfaction Questionnaire (QESP) was chosen. This was built and validated in Portuguese and has good internal consistency and a test-retest fidelity index [21].

Plans to promote participant retention and complete follow-up {18b}

Participants will be followed up during their usual hospitalization after delivery that lasts 48 hours in this hospital.

Data management {19}

Following the institution's protocols, all data will be considered anonymous, and participants will be identified by numbers. All source documents will be stored in locked file cabinets with secure and limited access. The data will be transferred to a secure online data cloud through double-checking between researchers. Only the research group has an individual password to access the data.

Confidentiality {27}

The study will be conducted in accordance with Brazilian rules and regulations. All data generated in this study will remain confidential. Only the research team has access to the study data. Access to data will only be provided in the event of audits or regulatory regulation by the institution.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Not applicable as no biological samples will be collected.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

Obstetric, gynecological, sociodemographic data, among others, will be compiled and collected using the statistical program Statistical Package for Social Sciences (SPSS Statistics version 23) and tabulated in the Excel program. The Shapiro-Wilk test will be applied to test the normality of the data, whether the data follow a normal distribution or follow a non-normal distribution.

The data will be presented to the normality of these, according to the quantitative variables that are normally distributed and continuously will be presented as average (standard deviation). Continuous quantitative variables without normal distribution will be presented in median (interquatile range). Categorical variables will be assessed as frequencies and percentages.

For parametric data, comparison between the groups will be carried out

using the analysis of variance (ANOVA) test. Significance values lower than 0.05, at the 95% confidence interval, will be interpreted as statistically significant. The clinical relevance of recorded values will be confirmed through effect-size calculations (Cohen d) based on significant differences. The following effects will be taken into account: 0.00 to 0.49, low; 0.50 to 0.79, medium; and above 0.80, high [33].

Interim analyses {21b}

No interim analysis will be performed.

Methods for additional analyses (e.g., subgroup analyses) {20b}

None planned.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Any missing data and the reason for the missing data will be described for each group. If necessary, a multiple imputation model will be applied.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

The datasets analyzed during the study will be available from the corresponding author upon reasonable request.

Oversight and monitoring

Composition of the coordinating center and trial steering committee {5d}

The researchers involved in the study (see on title page) form the coordinating center responsible for study coordination, monitoring, data acquisition and management and statistical analysis.

Composition of the data monitoring committee, its role and reporting structure {21a}

This study will not have a data monitoring committee, as it is a short-term trial with minimal known risks.

Adverse event reporting and harm {22}

This study involves minimal known risks but the researcher responsible for the evaluation will question the participants about possible adverse effects. Any harm detected will be reported to the institution's research ethics committee.

Frequency and plans for auditing trial conduct {23}

No audits are planned because this trial is academic.

Plans for communicating important protocol amendments to relevant parties (e.g., trial participants, ethical committees) {25}

According to national regulations, major modifications of the protocol require a formal amendment to the protocol and are to be approved by the

institution's research ethics committee and modified in the Brazilian Registry of Clinical Trials.

Dissemination plans {31a}

The trial results will be submitted for publication in relevant journals and presented at conferences in the area of physiotherapy, gynecology and obstetrics. In addition, the results will be published on the university's social media using accessible language so that it is known to the population.

Discussion

The sensation of pain during labor is feared by pregnant women and may be one of the factors that keep women away from the decision for vaginal delivery. Thus, health professionals look for ways to relieve pain and improve the delivery experience of women. Non-pharmacological methods of pain relief are widely used during childbirth because they have benefits without side effects or contraindications [25].

Despite its widespread use, there is a lack of scientific evidence to support the use of some techniques, including TENS. Thuvarakan et al [20], in a meta-analysis, observed that the studies presented a difficulty in a detailed description with regard to randomization with the most appropriate methods, as was done the allocation, masking and blinding of the study. Thus it was detected that many studies had limitations that compromise the quality of the studies, therefore, their conclusions.

With this research, it is expected to contribute to understanding the effects of the intervention through TENS electrostimulation, in addition to other non-pharmacological pain relief measures, in women in labor. Furthermore, with the dissemination of the conclusions obtained in this study through publication in scientific journals and events in the area, health professionals will have important information for conducting pain management through non-pharmacological pain relief measures during the labor.

Trial status

The study was registered at the Brazilian Registry of Clinical Trials (REBEC) (number RBR-68kh6j) on March 17, 2020. Recruitment for study began in April 01,2020, and the planned recruitment completion date is February 28, 2022.

Declarations

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Authors' contributions {31b}

NTD and VSPB developed protocol concept and design. VSPB accounted for volunteers' randomization and randomized allocation into the groups. NTD will participate in the application of the protocol adopted for the project. PRS, TAC review this manuscript elaborated by NTD.

NTD, PRS, TAC, VSPB, APMRB and CRCA will interpret the collected data. RMCP still performed sample calculation. NTD elaborated the manuscript based on the critical contributions by VCPB. All authors read and approved the final manuscript. All named authors adhere to the authorship guidelines of Trials. All authors have agreed to publication.

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