ORIGINAL RESEARCH

Effectiveness of lidocaine patches for pain treatment after total knee arthroplasty

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BACKGROUND: Effective analgesic therapy in the postoperative period of total knee arthroplasty is essential for good surgical outcomes. The current trend is to use multimodal treatment, in which the use of patches with lidocaine as adjuvant therapy has an increasingly relevant role.
OBJECTIVE: To investigate the potential benefits of lidocaine patch association with the basic analgesia regimen for pain relief during the postoperative period of total knee arthroplasty.
METHOD: A retrospective cohort study was performed , with a total of 24 patients in each group, who underwent total knee arthroplasty. Pain levels using a visual analogue scale and opioid intake were controlled from the immediate postoperative to the end of a 28-day interval.
RESULTS: During the postoperative period, pain was less intense in patients who used lidocaine patches. In these same patients, the doses of opioids needed to control pain were lower in 15 of the 28 days analyzed. The relative frequency of nausea was higher in the group that did not use adjuvant therapy. Patients older than 70 years and females predominated.
CONCLUSION: Adjuvant treatment after total knee arthroplasty using lidocaine patches was effective in reducing pain and decreasing the use of opioids in the period analyzed, and represents a good addition to multimodal analgesic therapy.

KEYWORDS: Knee Arthroplasty; Analgesia; Lidocaine.

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INTRODUCTION

Total knee arthroplasty is an effective surgical procedure to combat pain, increase functional capacity and improve the quality of life of patients suffering from gonarthrosis.[1] However, satisfactory analgesic therapy in the postoperative period is an imperative factor for rehabilitation, mobilization, good functional results and early hospital discharge.[2] In contrast, inadequate pain management is strongly associated with the development of chronic pain.[3-6] The persistence of discomfort is severely debilitating and has a direct impact on the patient's quality of life.[3,5]

Despite all the technological advances, adequate pain control is still a challenge in the postoperative period of total knee arthroplasty.[7,8] Modalities in current use, such as opioid-derived analgesics, provide satisfactory relief but may be associated with side effects, sub-medication and serious complications, which often lead to increased drug use, higher hospitalization costs, and longer recovery time.[1,8,9]

Adjuvant local treatments are advantageous because they require lower daily doses to achieve pain relief, and because they act specifically at the affected site,[10] with lower metabolic changes, less drug interactions and reduced systemic side effects.[9] Their use is also associated with reductions in the need for opioids, which lessens adverse effects and

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secondary sedation, often associated with delayed mobilization and recovery of patients.[1,8,9] Lidocaine patches, used as adjuvant topical therapy for pain relief in the postoperative period, are good alternatives for local treatment; they promote better pain management, assist in rehabilitation, increase patient satisfaction and reduce the use of opioids,[11-12] besides being simple and easy to apply.[10] Lidocaine has minimal systemic absorption[1] and rare systemic side effects.[9,10] Impressive results have been reported after major surgical procedures and are roughly equivalent to the use of systemic opioids in relation to pain control.[9,11] Initial studies have shown great improvement with regard to daily pain, as well as recovery of normal function in daily activities, in particular knee flexion and extension.[12]

The management of postoperative pain is critical for optimization in the care of operated orthopedic patients,[13] especially in the case of surgeries normally associated with considerable pain, such as total knee arthroplasty. Thus, the use of lidocaine patches, together with other analgesic techniques, may be an effective solution to the problems that accompany pain management during this period and, consequently, improve rehabilitation conditions of patients.[11,12] They concur toward increasingly effective and beneficial treatment with fewer side effects.

The aim of the present study was to investigate the potential benefits of lidocaine patch association with the basic analgesic regimen for pain relief during the postoperative period of total knee arthroplasty. In addition, we compared pain evolution, opioid use and postoperative complications in patients submitted to total knee arthroplasty with and without the use of lidocaine patches; we also determined the demographic and clinical data of participating patients.

METHOD

General. This is a cohort study. Patients were divided into two groups with 24 entries to each group; patients were selected for entry into each group after being submitted to total knee arthroplasty: Group 1: standard analgesia plus lidocaine patches; Group 2: standard analgesia. Only patients with complete records of analgesics used over the full post-operative period until attainment of pain control after discharge from hospital were included.

Analgesia scheme. The standard analgesia scheme for both groups was as follows: (a) an intra-hospital postsurgical procedure consisting of dipyrone 1g at 6 hour intervals and tramadol 100mg at 8 hour intervals, both given intravenously over the first 24 post-operative hours; (b) dipyrone 1 g at 6 hour intervals and tramadol 100 mg, as required, both given intravenously from 24 to 72 hours postoperative; (c) a post-discharge maintenance analgesia scheme, consisting of oral dipyrone at 6 hour intervals for 15 days and as needed thereafter, plus oral tramadol 50 mg at 8 hour intervals, as rescue for pain control.

Lidocaine patch application. Patients in the test group received patches of lidocaine applied on the sides of the surgical incision so as not to interfere with the wound closure and its dressings. Patches were first applied at the sides of the dry wound, changed according to the manufacturer's recommendations and used for up to 12 hours/day and then removed. This process was repeated as necessary for continued analgesia. Patients were advised to avoid applying heat sources, such as hot compresses, directly upon the patch, as this increases lidocaine absorption and, consequently, might lead to toxicity. The use of lidocaine patches was approved by the Brazilian sanitary vigilance agency (ANVISA) on September 9, 2014. Patches are composed a thin adhesive material measuring 10x14 cm, containing lidocaine at a concentration of 5%. Patch are only available under medical prescription and contain 700 mg of lidocaine in an aqueous base [50 mg of lidocaine per gram of adhesive base].

The inclusion criteria for the study were patients submitted to total knee arthroplasty; age: 55-85 years; primary osteoarthrosis with grades 3-5 in the Ahlbäck classification[14]; pain levels above 5 by the Visual Analogue Scale (VAS).

The exclusion criteria were hypersensitivity to the active substance [lidocaine] or any excipient of drugs used in standard analgesia, wound infection or respiratory tract infection; previous arthroplasty; comorbidities that impede the placement of a prosthesis: decompensated Diabetes Mellitus and cardiac arrhythmia; acute myocardial infarction, stroke, deep venous thrombosis or pulmonary thromboembolism. **Analyzed parameters**.

General data: age (complete years); Gender; Body Mass Index (Kg/m^2); affected side (right or left); diagnosed comorbidities; pain intensity through the visual analogue scale, over the first 24 hours postoperatively. Complications during hospital stay (first 72 postoperative hours)

Analgesic rescue data: dosage and timing of use of the opioid analgesic tramadol (prescribed in the routine and requested by patient) from the immediate postoperative tempo to cessation of use.

Postoperative functional data: the WOMAC questionnaire[15] was applied on the pre-operative period and after 28 days; Supported load on crutches capability or not; range of motion in the operated knee (degrees) tested with a goniometer® on the pre-operative period and after 28 days.

Statistical analysis. Categorical data are expressed in absolute and relative frequency; quantitative data are expressed as means and standard deviation. Statistical analysis proper was preceded by the Shapiro-Wilk test to test the normality of variable distribution for Visual Analog Scale,

opioid rescue and WOMAC score. None exhibited normal distribution; consequently, we used the Mann-Whitney U Test setting statistical significance at $p < 0.05$. A Spearman corelation test was used to determine associations between lidocaine, VAS and opioid rescue. All procedures used the SPSS for MacOSX version 21 software.

This study followed norms established by the Declaration of Helsinki version VII, as well as those set by the Brazilian Ministry of Health Resolution 466/12, which governs studies with human beings. The project was submitted to the Ethics and Research Committee [CEP] of the Faculty of Technology and Sciences under case number 1,348,391 Researchers signed the Investigator's Term of Commitment, the Term of Commitment to Use Data in Patient Records and Databases in Research Projects, and the Subject Confidentiality Statement in the study. Included patients read and signed an approved Informed Consent Form prior to data collection.

RESULTS

The research project started with 48 patients, but there was a loss of follow-up for a total of 3 subjects, secondary to the development of superficial skin infection (2 patients) or respiratory tract infection (1 patient) during the postoperative period; two of the patients belonged to the test group (lidocaine patch) and 1 to the control group. Thus, the study was completed with 45 patients, 22 in the test group, 23 in the control group.

Table 1 displays the perception of pain intensity by the patients of each group through the score provided by the Visual Analogue Scale at different moments of evaluation. Before surgery, the level of pain was virtually identical in both groups. When first measured after surgery, pain had decreased in both groups and remained lower in both throughout the 28 day postoperative period. However, during the entire four-week period, pain levels were systematically lower in the lidocaine treated patients.

Table 2 displays the use of rescue analgesia (opioid tramadol) throughout the post-operative period. The 24-hour value is standard immediate postoperative dosage in our service. The 48-, and 72-hour values refer to the full dose in each day, while the patients were hospitalized; the 14th and 28th day values correspond to the sum of the doses of the previous days as follows: the 14th postoperative day represents patient information about oral opioid use of the previous ten days (4th to 13th day); the 28th day values correspond to patient information about oral opioid use in the last 14 days. First day values are standard of care and allow for no analysis; in the following periods, the dose of opioid analgesics depended on the need of each patient. Significant differences were observed for the 72-hour and 28-day periods: in both cases, the required amount of opioid was significantly smaller for the lidocaine patch group.

Table 3 exhibits Womac scores measured before and 28 days after surgery. WOMAC scores increased significantly for both groups in the postoperative period. However, no difference was found in the lidocaine patch vs. controls, before or after surgery.

No statistically significant difference between the groups with regard to the load supported by the joint with the use of crutches was observed on the 28th postoperative day.

DISCUSSION

The study showed that postoperative pain was less intense in patients who used the lidocaine patch as adjunctive therapy. To the best of our knowledge this is a new contribution in terms of the control of the amounts of opioid pain rescue required by patients.

After total knee arthroplasty, peripheral pain has two basic origins: neurogenic, resulting from nerve injury during the surgical procedure, and inflammatory, secondary to activation of the cascade of events involving cytokines, prostaglandins and other mediators.[16-17] Topical lidocaine therapy does not extinguish the trigger, namely the surgical trauma, but prevents the spread of the pain stimulus.[10,18]

Because lidocaine is a local anesthetic, the amount absorbed in the topical modality under study is negligible,[10,19,20] producing local analgesia without reaching

Table 1. Average score in the Analogic Visual scale of pain in test and control patients during pre- and post-operative phases of total knee arthroplasty

Moment	Groups		p* (95% CI)
	Patch (n=22) average ± std dev	Control (n=23) average ± std dev	
Pre-operative	8.09 ± 0.92	7.74 ± 0.68	0.221 (0.210 - 0.230)
Post-operative 24 hr	3.77 ± 0.97	5.09 ± 1.24	0.001 (0.000 - 0.001)
Post-operative 48 hr	3.86 ± 1.24	4.61 ± 1.15	0.028 (0.020 - 0.030)
Post-operative 72 hr	3.14 ± 0.94	4.87 ± 2.09	0.001 (0.000 - 0.001)
Post-operative 14 days	2.36 ± 1.64	3.87 ± 1.91	0.003 (0.002 - 0.005)
Post-operative 28 days	1.64 ± 1.86	3.22 ± 1.75	0.007 (0.005 - 0.008)

*Mann-Whitney U test. Significant differences (test lower than control) in bold type

Table 2. Rescue analgesia doses used throughout the post-operative phase of a total knee arthroplasty procedure

Opioid (mg) administered at	Groups		P* (95% CI)
	Patch (n=22) mean ± std dev	Control (n=23) mean ± std dev	
24 hours (IV)	400	400	fixed dose: "p" not applicable
48 hours (IV)	204.5 ± 109	145.6. ± 81.1	0.064 (0.590 - 0.690)
72 hours (IV)	113.6 ± 94	260.8 ± 140	0.001 (0.000 - 0.001)
14 days (oral)	470.4 ± 367.6	682.6 ± 432.4	0.084 (0.078 - 0.089)
28 days (oral)	261.4 ± 198.2	532.6 ± 369.5	0.013 (0.011 - 0.016)
Total morphine (except 1st 24-hrs.)	1450 ± 568,8	1621,7 ± 767,3	0,006 (0,004-0,007)

*U de Mann-Whitney U test. Significant differences (test lower than control) in bold type

Table 3. WOMAC scores before and 28 days after total knee arthroplasty in patients treated with Lidocaine patch vs. controls

Moment	Grupos		P* (95% CI)
	Patch (n=22) mean ± std dev	Control (n=23) mean ± std dev	
Preoperative	31.14 ± 8,6	27.39 ± 5.86	0.79 (0,740 – 0.084)
Postoperative 28 days	48.55 ± 6.56	46.9 ± 8.06	0.42 (0.407 – 0.426)
p** (CI 95%)	0.001 (0.000-0.001)	0.001 (0.000-0.001)	

* Mann-Whitney U test. No significant differences

the sensory blockade level.[9,10] This is known as "target peripheral analgesia",[10] which is ideal for recovery after the surgical procedure.

The lower intensity of pain in the patients who used the patch corroborates a report by Husain et al,[12] in a randomized double-blind controlled trial in patients who underwent unilateral placement of a knee prosthesis, in which the Analogue Visual Scale was also applied and produced a similar result, namely a significant decrease in pain levels.

In contrast, Khanna et al[11] also compared pain in the postoperative period of total knee arthroplasty in two groups (lidocaine patch vs. control): however, although they report a statistically significant decrease of pain (through VAS) during the evaluation, they concluded that no additional relief was provided by lidocaine at the end of the study, a questionable interpretation of data, which diverges from our findings.

In this study, there was a statistically significant reduction in the load of opioid required and applied to lidocaine treated patients in most (15 out of 25) postoperative days. As noted above, the quantification of this decline in pain rescue associated to the use of lidocaine patches is the most relevant contribution of this study. Our results show a reduction on pain and analgesic consumption.

In terms of WOMAC scores, there was no statistical significance between lidocaine treated vs. control patients. However, it is known that a poor control of acute pain after total knee arthroplasty is strongly associated with the development of chronic pain in the long term.[21]

While acute pain tends to be proportional to the degree of tissue injury, pain that persists for more than 3 months is considered chronic, exceeding the typical period of tissue recovery and often self-perpetuating as a pathological process.[2] Thus, the absence of any difference between the groups in terms of functional recovery may be the result of the short period of analysis (28 days), while the potentially more prolonged neuropathic pain, which may have a real impact on the functionality is of a more chronic nature.

In addition, studies[2,22] demonstrate that pain does not depend exclusively on the somatic factor: there is also a psychic component that can interfere with its perception, usually associated with anxiety, inability to deal with fear, amplification in the face of illness and feelings of helplessness.[2] This relationship specifically interfered with the WOMAC score in the study by Sullivan et al, who evaluated the influence of pain catastrophization as a chronic pain risk after total knee arthroplasty.[22]

In our study, there was no statistically significant difference between the groups with regard to the load supported by the joint with the use of crutches on the 28th postoperative day. This result may have been secondary to the homogeneity of the motor physiotherapy scheme recommended for the two groups: both were submitted to the same program. In all likelihood, this influenced the gains in joint functionality, which can positively concur to improvement in load bearing. Recovery of the range of motion of the joint is obviously an important factor for the good result of the surgery and patient satisfaction;[23] in our study, the use of lidocaine patches made no difference as regards the mean maximal extension and flexion values .

Adverse reactions due to the use of patches are expected in up to 16% of patients.[9] However, in the sample

studied, there were no cases of side effects during the first 72 hours of follow-up. But complaints of nausea showed an important difference between groups: in the control group, 26.0% presented nausea, compared to only 4.5% in the test group. This is most likely a consequence of the use of opioids, because nausea is a dose dependent effect of opioid usage.[24,25] Thus, the described difference could be associated with the lower consumption of opioids by the experimental group, and, ultimately to the fact that they used the adhesives with lidocaine, presenting better pain control. Pain itself, as an isolated factor, can also induce nausea and vomiting.[26] Thus, lidocaine may have also contributed to the lesser occurrence of nausea through pain control.

The use of lidocaine patches decreases not only the pain, but also the development of side effects secondary to the use of systemic medication. This allows for more comfort to the patient after total knee arthroplasty, as well as reducing the symptomatic management of each side effect with more systemic medications, reducing not only the consumption of drugs but also possibly the costs of hospitalization.[8]

Among the patients followed up, the relative frequency of the female gender was 63.63% in the experimental group and 56.52% in the control group. This finding corroborates the literature in that, in the majority of studies, the relative frequency of women was higher than that of men. In the study by van Egmond, C et al.[27] the relative frequency of women was 60%, a percentage similar to that of the Elmallah R et al study,[28] in which 61.1% of the patients were female, and of the study by Jauregui J et al,[29] which showed that 61.5% of the sample were female.

Age is another factor that is actively related to the period after surgery,[28] being an important predictor of functional outcome.[30] In the study, patients older than 70 years presented a relative frequency of 45.45% in the intervention group and 43.47% in the control group.

One of the factors that are being associated with the less favorable outcome of total knee arthroplasty and the greater intensity of postoperative pain is the presence or absence of comorbidities,[31] including higher values of pain evaluated by the Visual Analogue Scale and reduced WOMAC score.[32]

Limitation of the study include: (a) no blinding was performed as part of the methodology, since the control group did not use placebo patches so that examiners had knowledge about which group the patients belonged to; (b) Information on the amount of opioids used by patients after hospital discharge was brought by the patients themselves; (c) the loss of follow-up of 3 patients, two in the experimental group and one in the control group, due to the development of postoperative infections that were predicted to be exclusion criteria [respiratory tract infection and skin infection]. However, this last limitation did not statistically interfere in the results, due to the distribution of the patients who were excluded regarding the allocation in each group.

Finally, for a more detailed result on the development of chronic pain and follow-up of long-term outcomes, further studies with multicentric analysis and longer assessment periods are needed.

CONCLUSION

Adjuvant treatment after total knee arthroplasty using lidocaine patches effectively reduced pain, opioid pain rescue load and systemic side effects compared to individuals who did not use the patches No difference occurred between the groups regarding the functional score of the maximum supported load and the range of motion of the joint treated surgically.

Thus, the association of patches with lidocaine to standard post-operative total knee arthroplasty is a practical, simple, safe and efficient procedure to promote better pain control during this period, promoting satisfactory gains in comfort and rehabilitation of patients.

CONFLICT OF INTEREST

Authors declare no conflict of interest with regard to this study

AUTHOR PARTICIPATION

DS and MCO: main planning and writing. JGGM, FRPCJ and DS: collected data. DS and MCO: organized references. FRPCJ and DS: organized the data and calculated statistical parameters. COM, DS, JGGM and FRPCJ: organized final data and wrote the discussion. DS, MLA and DFA: performed the surgical acts, revised the Manuscript and provided the intellectual concept.

EFICÁCIA DO TRATAMENTO ADJUVANTE DA DOR PÓS-ARTROPLASTIA TOTAL DO JOELHO UTILIZANDO EMPLASTROS COM LIDOCAÍNA

OBJETIVO: A terapia analgésica eficaz no pós-operatório de artroplastia total do joelho é imprescindível para bons resultados cirúrgicos. A tendência atual é a de se utilizar o tratamento multimodal, no qual a utilização de emplastros com lidocaína como terapia adjuvante tem papel crescente e relevante. Investigar os potenciais benefícios da associação do emplastro com lidocaína ao esquema terapêutico básico de analgesia para o alívio da dor durante o período pós-operatório de artroplastia total de joelho.

MÉTODO: Foi realizado um estudo de coorte retrospectivo cuja população foi a de pacientes submetidos

a artroplastia total do joelho, divididos em dois grupos com 24 integrantes em cada, acompanhados por um período de 28 dias.

RESULTADOS: Durante o pós-operatório analisado a dor foi menos intensa nos pacientes que utilizaram os emplastros com lidocaína. Nesses mesmos pacientes, as doses de opióides necessárias para controlar a dor foram menores em 15 dos 28 dias analisados. A frequência relativa de náuseas foi maior no grupo que não utilizou a terapia adjuvante. Predominaram os pacientes com mais de 70 anos e o gênero feminino.

CONCLUSÃO: O tratamento adjuvante após a artroplastia total do joelho utilizando emplastros com lidocaína mostrou ser eficaz na redução da dor e diminuição do uso de opióides no período analisado, constituindo um bom incremento para a terapia analgésica multimodal.

PALAVRAS-CHAVE: Artroplastia do Joelho; Analgesia; Lidocaina

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