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Original Contribution

Effect of postoperative analgesia on acute and persistent postherniotomy pain: a randomized study☆,☆☆

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☆ The trial was registered on clinicaltrials.gov (NCT01345162; principal investigator, Massimo Allegri) and European Union Drug Regulating Authorities Clinical Trials (EUDRACT) (2009-011-856-23).

☆☆ Full protocol accessible at Bioethics Committee Secretariat–Istituto Di Ricerca e Cura a Carattere Scientifico (IRCCS) Foundation Policlinico S Matteo, Pavia, Italy (e-mail: comitato.bioetica@smatteo.pv.it).

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Abstract
Study objective: The study objective is to identify differences in postoperative pain management according to different analgesic treatments, targeting 2 main pathways involved in pain perception.
Design: The design is a randomized, parallel groups, open-label study.
Setting: The setting is in an operating room, postoperative recovery area, and surgical ward.
Patients: There are 200 patients undergoing open inguinal hernia repair (IHR) with tension-free technique (mesh repair).
Interventions: The intervention is a randomization to receive ketorolac (group K) or tramadol (group T) for 3 days after surgery.
MeasurementsThe measurements are differences in analgesic efficacy (numeric rating scale [NRS]) in the postoperative (up to 5 days) period, chronic pain incidence (1 and 3 months), side effects, and complications.
Main results: We found no differences in analgesic efficacy (NRS value ≥ 4 in the first 96 hours: 26% in group K vs 32% in group T, $P = .43$); the proportion of patients with NRS ≥ 4 was similar in both groups, and the time trajectories were not significantly different (P for interaction = .24). Side effects were higher (12% vs 6%) in the tramadol group, although not significantly ($P = .14$), with a case of bleeding in the ketorolac group and higher incidence of constipation in tramadol group. One patient in each group developed chronic pain.
Conclusions: Ketorolac or weak opioids are equally effective on acute pain and on persistent postsurgical pain development after IHR, and drug choice should be based on their potential side effects and patient's comorbidities. Further studies are needed to standardize the most rational approach to prevent persistent postsurgical pain after IHR.

1. Introduction

Inguinal hernia repair (IHR) is a common surgical intervention performed worldwide [1]. In Italy, the health ministry registered 75,392 procedures in 2010 [2]. Despite minimal postoperative morbidity, PPSP is still the most common and serious long-term problem after IHR and able to influence patients' quality of life [3-5].

The incidence of PPSP after IHR is reported to be approximately 10% [6], but because hernia surgery is very common, a large number of individuals may be affected. Persistent postsurgical pain (PPSP) is a complex condition in which inflammatory, nociceptive, and neuropathic components are involved [7,8]. Among risk factors for PPSP, the severity of acute postoperative pain is often mentioned; individuals prone to experience intense postoperative pain may be the ones most vulnerable to PPSP [9,10]. Despite this, postoperative analgesia remains a challenge; 30% of the patients report severe pain within the first 24 hours, a prevalence that has remained unchanged for almost 10 years [11].

Multimodal analgesia is recommended for postoperative analgesia after hernia repair [12], but no studies have fixed the issue on whether inflammation or descending inhibitory pathways should be preferentially targeted for a more effective acute pain relief and to avoid PPSP.

In this prospective, multicenter single-blind randomized clinical trial, we aimed to determine which analgesic treatment is most effective both in controlling acute postoperative pain and in reducing PPSP occurrence at 1 and 3 months after inguinal hernia repair (IHR); the 2 treatments are paradigmatic of 2 different pathophysiological approaches, one focusing on inflammation, the other focusing on pain modulation through activation of central descending inhibitory activity. Thereby, the 2 treatment groups involved a 3-day administration of either a nonsteroidal anti-inflammatory drug (NSAID), ketorolac, or of a weak opioid combining a central descending inhibitory activity, tramadol. Our secondary aim was to verify any difference in terms of side effects, surgical complications, use of rescue medications, functional activity, and chronic pain incidence.

2. Methods

2.1. Patients' enrollment

After ethical committee approval from the 2 hospitals involved in the study (IRCCS Policlinico S Matteo, Pavia, Italy, and Ospedale di Circolo–Fondazione Macchi, Varese, Italy), the trial was registered on clinicaltrials.gov (NCT01345162; principal investigator, Massimo Allegri) and EUDRACT (2009-011-856-23). The study was designed according to Consolidated Standards Of Reporting Trials (CONSORT) guidelines [13]. All the patients enrolled in the study signed an informed consent. No changes in methods were made after the trial was started.

Adult patients scheduled for monolateral IHR with anterior approach (open, non-videolaparoscopic approach) and tension-free technique (mesh repair), with type 2, 3A, and 3B inguinal hernia (according to Nyhus 1993 classification) [14]; ≥ 18 years; and with American Society of