Asian Journal of Surgery (2017) xx, 1–7

Available online at www.sciencedirect.com

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journal homepage: www.e-asianjournalsurgery.com

ORIGINAL ARTICLE

Topical diltiazem ointment in post-hemorrhoidectomy pain relief: A meta-analysis of randomized controlled trials

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Received 19 March 2017; received in revised form 25 May 2017; accepted 1 June 2017

KEYWORDS
Hemorrhoidectomy;
Post-hemorrhoidectomy;
Diltiazem ointment;
Calcium channel blocker;

Summary *Background:* Hemorrhoidectomy is commonly associated with postoperative pain. Calcium channel blockers are known to cause relaxation of gastrointestinal smooth muscle and oral diltiazem has also been shown to reduce the resting anal pressure.
Objective: We attempted to analyze efficacy and side effects of topical diltiazem oint. in post-operative pain control.
Methods: This is a meta-analysis of patients who underwent hemorrhoidectomy using topical diltiazem oint. versus placebo (Vaseline) for pain control. Patients with third or fourth degree

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http://dx.doi.org/10.1016/j.asjsur.2017.06.002

Meta-analysis

hemorrhoids undergoing traditional hemorrhoidectomy were included. Procedures took place in the colorectal division of a hospital in 5 countries. Five randomized control trials (RCTs) published between 2005 and 2016 including 227 patients were included our meta-analysis (Diltiazem (calcium channel block) group = 137; Placebo (Vaseline) group = 90). Pain assessment was performed using a standardized Visual Analogue Scale. Any side effects of surgery or medication use, which were noted by the patient or the surgeon, also were recorded.

Results: A total of 227 patients were included in the meta-analysis. The results revealed that Diltiazem ointment was statistically significant in reducing pain within 48 h, at 72 h, and more than 96 h after operation compared to the placebo group. Regarding overall complications (including headache), there was no statistical significance between diltiazem and placebo group.

Conclusions: Topical application of diltiazem effectively relieves pain after hemorrhoidectomy with minimal side effects. Further large studies are needed to substantiate its value in clinical practice.

1. Introduction

An estimation of around 10 million people suffer from hemorrhoids in the U.S.A with a prevalence of around 4.4%. This incidence is nearly 37 hemorrhoidectomies per 100,000 people per year being performed.[1] Hemorrhoidectomy still stands as the most effective treatment for high grade hemorrhoids and postoperative acute pain as an expected result of hemorrhoidectomy has been experienced by thousands of patients all over the world remains its main obstacles.[2–4] The reason for delayed patient discharge after hemorrhoidectomy is commonly due to post-operative pain. However, average time for discharge is believed to be 2 days.[5] Moreover, this matter is important because it involves both cost and social issues in terms of bed occupancy and delayed return to work.

The cause of post-hemorrhoidectomy pain is multifactorial, including spasm of anal sphincter and puborectalis muscles, type of anesthesia, poor and delayed wound healing, surgical technique, type of post-operative analgesia, use of stools softeners and subjective pain threshold have been implicated as potential mechanisms.[7–9] Pain control after hemorrhoidectomy has been constantly under debate and investigation, dreadfully by patients and challenging for surgeons. In current clinical practice, post-operative pain was reduced using narcotics, nonsteroid anti-inflammatory drugs or glyceryl trinitrate ointment but their use is confined to a short period and is associated with frequent side effects such as headaches, hypotension, angina, rebound hypertension, tolerance and allergic skin reaction, anal burning or itching.[5]

Hypertonicity of the internal anal sphincter (IAS) is surmised to play part in the cause of anal fissures and is associated with fissure pain. Spasm of the IAS is thought to be related to the source of pain after hemorrhoidectomy and may be a component of postoperative hemorrhoidectomy pain.[6] Diltiazem, a calcium channel blocker, has been shown to reduce resting anal pressure and relax gastrointestinal smooth muscle.[10–13] Topical application of diltiazem is commonly used to relieve pain and promote wound healing in patients with anal fissure.[14] Five randomized controlled trials (RCTs) have investigated the topical use of Diltiazem after hemorrhoidectomy; however, it has been reported from Sugimoto's study[19] that "total incidence of complications was significantly higher in the diltiazem group than in the placebo group (P = 0.03)", which is the largest trial (patient number: 62) present so far and this result is against all the rest of other studies.[15–18] In order to clarify the issues regarding the safety and benefit of using topical diltiazem ointment in post-hemorrhoidectomy pain control, a meta-analysis of the evidence available to date would be useful to draw a current conclusion.

2. Materials and methods

2.1. Search strategy

This meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[20] A com-prehensive search of published studies was performed in PubMed, Embase and the Cochrane Database (from January 2005 to November 2016). The MeSH and main keywords were as follows: "post-hemorrhoidectomy pain", "post-operative anal pain" or "Topical agent", "nifedipine ointment", "diltiazem ointment" or "calcium channel blocker". Based on these MesH and main keywords, we formulated the search strategy (for PubMed and Embase) as following: (Topical agent OR nifedipine ointment OR diltiazem ointment OR calcium channel blocker) AND (post-hemorrhoidectomy pain OR post-operative anal pain). All the relevant studies which described an effect of topical diltiazem on posthaemorrhoidectomy pain were checked carefully (including the reference lists of relevant studies). We have included the "nifedipine ointment" in the initial search due to it is an old drug and is frequently used as a control by many investigators to compare with a group of other calcium channel blockers (diltiazem may be

Please cite this article in press as: Huang Y-J, et al., Topical diltiazem ointment in post-hemorrhoidectomy pain relief: A meta-analysis of randomized controlled trials, Asian Journal of Surgery (2017), http://dx.doi.org/10.1016/j.asjsur.2017.06.002