

Review Article



Efficacy of Diosmin on Post-Hemorrhoidectomy Pain: A Systematic Review of Clinical Trials

Mansour Rezaei¹ , Ramin Azhough^{2,*}

¹Assistant Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

²Associated Professor of Surgery, Department of General Surgery, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran



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ABSTRACT

Introduction: Diosmin is effective in inhibiting the inflammatory response pathways and improving the acute and chronic symptoms of hemorrhoids. Very few studies have been conducted in this field, and the effectiveness of this drug in different studies has not been presented in a single study so that it can be used or not used based on its results. Therefore, the present study aims to investigate the effectiveness of Diosmin on pain after hemorrhoidectomy in the form of a systematic review of clinical trial studies.

Methods: The present study was a systematic review that was designed and conducted based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement. The search was done in SID, Magiran, Embase, PubMed, Cochrane Library, Scopus, and Web of Science databases by following the entry and exit criteria and the keywords such as pain, hemoroide, hemorrhoidectomy, Diosmin, surgery, and post-operative.

Results: 824 patients participated in these 4 randomized clinical trial studies (with a high quality). The instrument used to assess pain intensity in all studies was the Visual Analogic Scale. Diosmin tablets were prescribed in two forms: 500 mg (in three studies) and 300 mg (in one study) after hemorrhoidectomy. In three studies, Diosmin tablets led to a reduction in pain intensity after hemorrhoidectomy, and in one study, no significant difference was seen.

Conclusion: The results of our study indicated that the use of 500 mg Diosmin oral tablets can lead to a reduction in pain intensity after hemorrhoidectomy. Due to the lower number of studies, the results of this study should be used with caution.

*Corresponding Author: Ramin Azhough, (bikaran_mmm@yahoo.com)

Introduction

Hemoroide is one of the most common complications of surgery in the anorectal area, which manifests itself in the form of pain, bleeding, and mass discharge from the anus [1]. One of the most important reasons why patients with hemorrhoids avoid surgery is the fear of pain [2]. Controlling pain in the first hours after surgery, in addition to increase patient satisfaction, will also lead to a decrease in the urinary retention and constipation [3].

Currently, to reduce the pain after hemorrhoidectomy, the systemic narcotics such as pethidine and morphine are used, which in addition to be difficult to obtain by the medical system, lead to respiratory apnea, respiratory depression, decreased bowel movements, increased nausea and vomiting, and addiction [4-6]. Therefore, if a drug with less systemic effects is used for patients, the acceptance rate of surgery will increase [7]. Therefore, many patients will seek treatment for the disease before suffering from hemoroide complications [8]. Diosmin is effective in inhibiting the inflammatory response pathways and improving the acute and chronic symptoms of hemoroide [9,10]. Very few studies have been conducted in this field, and the effectiveness of this drug in various studies has not been presented in a single study so that it can be used or not used based on its results. Thus, the present study aims to investigate the effectiveness of Diosmin on pain after hemorrhoidectomy in the form of a systematic review of clinical trial studies.

Material and Methods

Study Design: The current study is a systematic review type conducted in the second quarter of 2022 based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement, following the entry/exit criteria and after searching in valid databases.

Search strategy: The search was performed in SID, Magiran, Embase, Pubmed, Cochrane Library, Scopus, and Web of Science databases, following the inclusion and exclusion criteria. Keywords were selected based on Mesh and

included pain, hemoroide, hemorrhoidectomy, Diosmin, surgery, and Post-Operative. Both researchers of this study searched the mentioned databases independently and based on the mentioned keywords. The search for articles in the period from the beginning of 1990 to the end of 2021 was between written and online studies in English and Persian.

The minimum Kappa coefficient for two researchers in the selection of articles was set at 70%, and for the articles that were not selected by one of the two researchers, the strategy of "reviewing the articles at the same time by both researchers" was carried out, which means that the article with the presence of both researchers was reviewed at a single time and placed with a two-person discussion that led to the final decision about that article. Finally, articles with full text were included in the study as the final articles. After finding articles with full-text, their sources were also examined to obtain all related articles, and then the obtained articles were subjected to the final review and included in the study.

Inclusion and exclusion criteria of studies: The inclusion criteria of studies in this systematic review include "studies whose target population was patients over 18 years old, randomized clinical trial studies, and studies that investigated post-hemorrhoidectomy pain after taking Diosmin" and criteria exclusion also included "articles without full-text, non-English language articles, failure to provide useful reports, or presenting results in an incorrect manner, low quality articles, and lack of relevance to the topic of the systematic review".

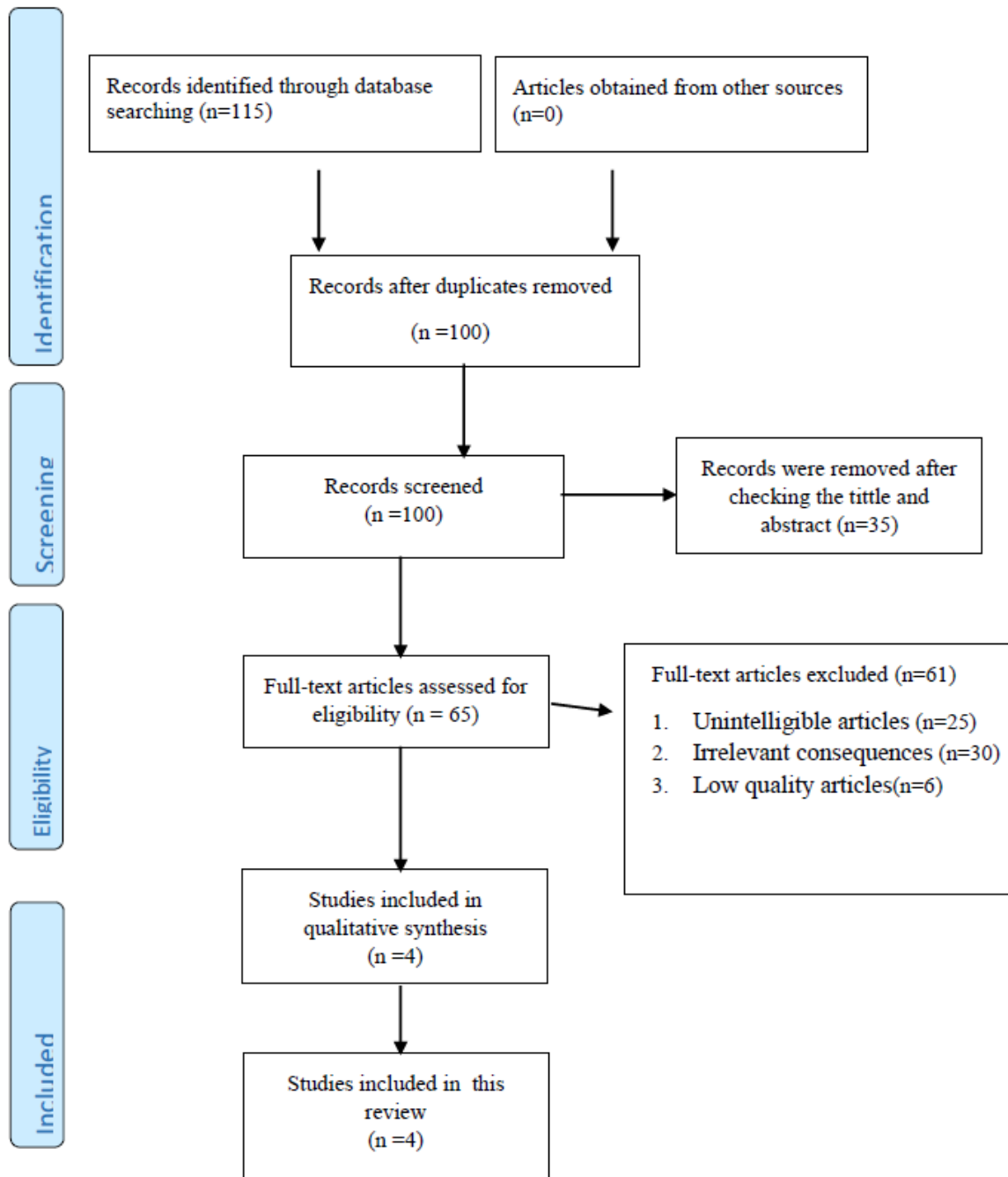
Evaluation of the quality of articles: The methodological quality of each study was scored based on the guidelines recommended by Cochrane for reviews of the clinical trial studies. Each category was evaluated as high quality, low quality, and uncertain quality.

Extraction of information: The variables extracted from each article included the name of the author, the year the study was published, the country where the study was conducted, the number of participants in the study, the tools used in the study, and the final result of the study. Medium and high quality studies were included in this study.

Statistical analysis: Since this study was conducted as a systematic review, no special statistical software was needed. The information extracted from each study was recorded and evaluated in Excel software.

Results

In the initial search, a number of 115 studies were found, and after their examination in different stages, including the review of texts and abstracts, the review of outcomes, the review of reported results, and the review of general conclusions, finally 4 studies were included in this systematic review (Flowchart 1).



Flowchart 1 The process of the studies reviewed in this review

The preliminary data analysis indicated that 824 patients had participated in these 4 randomized clinical trial studies. The period of published studies varied from 2012 to 2021. The tool used to assess pain intensity in all studies was the Visual Analogic Scale. Diosmin tablets were prescribed in two forms: 500 mg (in three studies) and 300 mg (in one study) after hemorrhoidectomy. In three studies, Diosmin tablets led to a reduction in pain intensity after hemorrhoidectomy, and in one study, no

significant difference was seen. The quality of all four studies was high. A summary of the articles included in this systematic review is presented in the following table.

Due to the heterogeneity of the results of the studies (different drug doses, duration of drug use, and pain intensity assessment times), it was not possible to conduct a meta-analysis for these results, and the results were presented as a systematic review.

Table 1 Summary of articles included in this systematic review

The quality of the article	Final result	Duration of intervention in each group	A tool used to assess pain intensity	Sample size	Country	First author/year
Top	The intensity of pain in the internal sphincterotomy group was significantly lower than other groups at all times.	The first group: internal sphincterotomy The second group: 500 mg of medicine 4 times a day The third group: 1000 mg of Paracetamol	Visual Analog Scale The intensity was checked and compared on the first, third and ninth days.	90 patients Three groups of 30 people	Italy	salvatore/2012 [11]
Top	The intensity of pain in the intervention wedge was significantly lower than the control group.	Intervention group: one 500 mg tablet daily for three days Control group: only used routine drugs	Visual Analog Scale Being on the third day	92 patients in two groups of 46 people	Iran	Alvandipoor / 2017 [12]
Top	The intensity of pain in the intervention group and in all three times was significantly lower than the control group.	Intervention group: one 300 mg tablet only once after surgery Control group: placebo pill	Visual Analog Scale 7, 15, and 30 days after surgery	182 patients in two groups of 91 people	Italy	Visconte / 2016 [13]
Top	The corresponding drug led to a decrease in pain intensity in both groups (within-group results).	Diosmin drug 500 mg twice a day for three days was given to both groups.	Visual Analog Scale 1, 4, and 7 days after surgery	460 patients in two groups of 230 people	Egypt	Abo-Ryia / 2021 [14]

Discussion

Pain is one of the most important early and problematic side effects after hemorrhoidectomy surgery, which is very annoying, so that some people do not consider it as a surgery complication, but consider it a predictable consequence of this operation [15,16]. One of the most important reasons why patients with hemorrhoids avoid hemorrhoidectomy surgery is the fear of pain after surgery [17,18]. Likewise, the improper post-operative pain relief is one of the main reasons for prolonging the patient's stay in the hospital and delaying the patient's start after hemorrhoidectomy. Pain control, especially in the first 24 hours after the operation, in addition to increase patient satisfaction, will also reduce the complications prevalence such as urinary retention and constipation. Today, newer treatment methods without pain or with less pain are of interest for doctors and patients, and most patients with hemorrhoids are looking for these methods [19,20].

So far, a lot of research has been done on reducing pain after hemorrhoidectomy, including intrasphincteric injection of ketorolac, intradermal injection of fentanyl, intradermal injection of morphine, injection of morphine intravenously, or in the epidural space, and injection of local anesthetics, and also its use is a topical nitroglycerin ointment after surgery [21,22]. The number of researches and methods carried out shows the lack of a clear and reliable method to reduce pain after surgery and demonstrates that there is still pain relief for patients after hemorrhoidectomy in the early stages after surgery (the acute pain) and in the stages, the patient's rehabilitation remains a problem [23,24]. Currently, the common method of pain control in these patients is the use of systemic narcotic drugs, which have the important side effects such as respiratory depression, headache, nausea, and vomiting [25]. In general, to reduce the pain after hemorrhoidectomy, a method should be used with the least complications. The other pain relief methods such as spinal, epidural, and caudal anesthesia are associated with pain reduction in the early stages after the operation,

but the rate of complications such as the urinary retention is higher in them [26].

Based on the summary of the results of this study, it was found that taking oral Diosmin, in addition to relief the patient's pain after surgery and reducing the use of injectable pain medications, is not associated with the side effects of narcotic drugs [27]. Diosmin 500 mg tablets are used for the treatment of internal and external hemorrhoids, as well as reducing the severity of reddening after surgery. Diosmin pill controls inflammation in the body by reducing prostaglandin levels [28]. This drug treats hemorrhoids and pain after hemorrhoidectomy. It is very useful and reduces inflammation in the body. In this way, blood circulation is improved and leads to the natural healing of internal wounds [29]. This pill is very effective for treating the blood vessel disorders. The low number of clinical trial studies, different degrees of hemorrhoids, different methods of surgery, and low homogeneity of the studies included in this systematic review were some of the limitations of this study, which are recommended to be resolved in the future studies. Conducting the first systematic review and using high-quality studies were also strengths of this study [30].

Conclusion

The results of this study indicated that the use of oral Diosmin tablets at the rate of 500 mg can lead to a decrease in pain intensity after hemorrhoidectomy. Due to the small number of studies, the results of this study should be used with caution.

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