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Comparison of efficacies of vegetable oil based and polyethylene glycol based bisacodyl suppositories in treating patients with neurogenic bowel dysfunction after spinal cord injury: A meta-analysis

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Original Article

ABSTRACT

Background/Aims: We performed a meta-analysis to compare the efficacies of vegetable oil based bisacodyl (VOB) and polyethylene glycol based bisacodyl (PGB) suppositories in treating patients with neurogenic bowel dysfunction (NBD) after spinal cord injury (SCI).

Materials and Methods: Relevant clinical studies (up to February 2014) were retrieved through the following databases: PubMed, MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CCTR), Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Wanfang, and VIP database for Chinese Technical Periodicals. Data were analyzed using the standardized weighted mean difference (SMD) and its 95% confidence interval (CI). P-values <0.05 were considered statistically significant.

Results: A total of 3 studies were included in the meta-analysis. The SMD and its 95% CI were not calculated owing to unreported standard deviations in the individual studies. The average and p-values of statistical difference indicated that the total bowel care time ($p<0.05$), time to flatus ($p<0.05$), and defecation period ($p<0.05$) were shorter in patients treated with PGB than in patients treated with VOB. No significant difference was observed in time to clean up ($p>0.05$) between patients in the PGB and VOB groups.

Conclusion: Based on the results, we conclude that the PGB suppository could act faster than the VOB suppository in the treatment of NBD in patients with SCI.

Keywords: Spinal cord injury, neurogenic bowel dysfunction, suppository, vegetable oil based bisacodyl, polyethylene glycol based bisacodyl

INTRODUCTION

Spinal cord injury (SCI) is a damage to the thick bundle of nerves that runs from the brain to the lower back (1). Adverse consequences include damage to motor and sensory nervous integrity associated with varying degrees of paraplegia, as well as autonomic nervous system dysfunction including neurogenic bowel dysfunction (NBD), neurogenic bladder dysfunction, and sexual dysfunction (2,3). Subsequently, changes in bowel motility and sphincter control ability may lead to constipation, fecal incontinence, and other complications (4,5). NBD is a major problem for SCI patients (6,7). Nearly half of SCI patients (49.6%) have moderate to severe degrees of NBD (8). NBD is also a major physical and psychological problem linked to the diminished quality of life among SCI patients (9). Moreover, the pain caused by intestinal problems have been perceived to be no less than the pain caused by the loss of athletic ability (10). Hence, the improvement of bowel function is critical for SCI patients.

There are many approaches for the successful management of neurogenic bowel, such as drug treatment, abdominal massage, dietary fiber intake, electrical or magnetic stimulation, pulse water irrigation, and conservative treatment (11-13).Suppositories containing a stimulant laxative ingredient are commonly used for bowel management in SCI patients (14). The bisacodyl (bis (p-acetoxyphenyl)-2-pyridylmethane) is a stimulant laxative widely used in treating constipation (15). It acts directly on the mucous membrane, stimulating the sensory nerves for a parasympathetic nerve reflex

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response, and thereby increases intestinal tract secretion and movement (16,17). Bisacodyl was first used as a laxative in 1953 due to its structural similarity to phenolphthalein, and has since been used for the successful management of NBD (14). Polyethylene glycol based bisacodyl (PGB) and vegetable oil based bisacodyl (VOB) are the 2 types of suppositories used to treat NBD after SCI. The water-miscible PGB suppositories have been reported to provide faster relief of constipation associated with neurogenic bowel dysfunction compared with VOB suppositories (18). However, due to a small sample size and different research conditions in each of these reports, a firm conclusion could not be drawn about the efficacies of PGB and VOB for the treatment of NBD in patients with SCI. Thus, we performed a meta-analysis to compare the efficacy of the 2 suppositories in treating NBD patients with SCI in order to provide a reference for clinical decision making.

MATERIALS AND METHODS

Literature retrieval

We retrieved relevant articles (up to February 2014) by a systematic literature search on the databases US National Library of Medicine, National Institutes of Health (PubMed), MEDLINE (National Library of Medical, Bethesda, Maryland), EMBASE (Elsevier, Amsterdam, Netherlands), the Cochrane Central Register of Controlled Trials (CCTR), Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Wanfang, and VIP (VIP Database for Chinese Technical Periodicals). The following keywords were used to search the articles: "SCI" or "spinal cord injury," "bowel dysfunction," "suppository," and "randomized controlled trial" or "clinical trial."

Inclusion and exclusion criteria

Studies provided all the following criteria were included in the meta-analysis: (1) the experimental design was a randomized controlled trial (RCT) or a controlled clinical trial (CCT); (2) the subjects were patients with NBD after SCI; (3) the treatment was suppositories; (4) the studies compared the efficacy of VOB and PGB suppositories; (5) the subjects were divided into 2 groups according to suppository type (VOB group and PGB group); and (6) the studies obtained informed patient consent.

A study was excluded if: (1) the study was a non-therapeutic clinical study or an animal experiment; (2) the SCI patients did not have spinal fractures; and (3) there was no available data. In addition, reviews, repeated articles, and retrospective articles were excluded.

Data extraction

Two investigators independently evaluated the quality of the articles and extracted the following information: first author's name, year of publication, region, sample size, age and gender of subjects, study design, and outcomes. Disagreements were resolved by discussion until a consensus was reached.

Statistical analysis

Data were analyzed using Review Manager (RevMan, Computer program, Version 5.2., Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2012) The standardized weighted mean difference (SMD) and its 95% confidence interval (CI) were applied in the analysis of continuous data. For dichotomous data, we used the relative risk (RR) and 95% CI. P-values less than 0.05 were considered statistically significant.

RESULTS

Literature search

A total of 27 potentially relevant articles were obtained from the initial literature search. Of these, 19 obviously unrelated articles were excluded after review of the title and abstract Among the remaining 8 articles, 2 duplicate publications and 3 studies with unavailable data were omitted. As a result, 3 articles (14,18,19) were selected for this meta-analysis (Figure 1).

Characteristics of the included studies

The characteristics of the included studies are shown in Table 1. Two studies were published in 1997 (18,19) and one in 1998 (14). All studies were carried out in the United States. The age of patients in the 3 studies ranged from 21 to 81 years. Table 2 shows the general characteristics of each study. In 2 studies (14,18), the dosages of PGB and VOB were 10 mg while in the study of Frisbie et al. (19) the dosage was not reported. There were 238 trials in

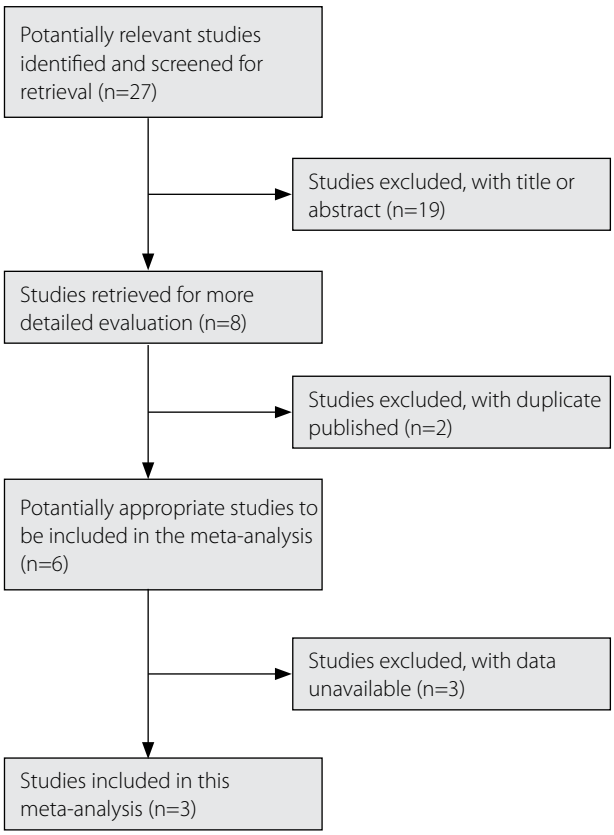

Figure 1. Flow diagram of literature search and study selection.

Original Article

Table 1. Characteristics of the included studies

First author	Year	Region	Sample size	Average age (y)	Section of spinal cord injury	Complete/incomplete spinal cord injury number
Stiens (14)	1998	USA	14	53.4	Upper motor neuron lesion	10/4
House (18)	1997	USA	15	45 (26-61)	9 cases of cervical vertebrae 6 cases of thoracic vertebra	11/4
Frisbie (19)	1997	USA	19	64 (41-81)	15 cases of cervical vertebrae 4 cases of thoracic vertebra	15/4

Table 2. General characteristics of the VOB and PGB groups

	Dosage		Number of trials		
Study	PGB	VOB	PGB	VOB	Efficacy indicators
Stiens 1998 (14)	10 mg	10 mg	81	84	Time to flatus, defecation period, clean up, and total bowel care time
House 1997 (18)	10 mg	10 mg	43	43	Time to flatus, defecation period, clean up, and total bowel care time
Frisbie 1997 (19)	NP	NP	114	57	Total bowel care time

PGB: polyethylene glycol based bisacodyl; VOB: vegetable oil based bisacodyl; NP: Not provided

the PGB group and 184 trials in the VOB group. The efficacy indicators included time to flatus, defecation period, time to clean up (end stool flow until end of clean up), and total bowel care time (suppository insertion until end clean up).

Comparison of total bowel care time between PGB and VOB groups

All the included studies (14,18,19) compared the total bowel care time between the 2 groups. However, the standard deviation of the data in each study was not presented, and SMD and its 95% CI of total bowel care time could not be calculated in this meta-analysis. The total bowel care time was significantly different between the 2 groups ($p<0.05$), and the total bowel care time of patients was significantly less in the PGB group than in the VOB group (Table 3).

Comparison of time to flatus between the PGB and VOB groups

The time to flatus data were reported in 2 included articles (14,18) The average time to flatus in each group and p-value of the statistical difference between the PGB and VOB groups are shown in Table 4. Similarly, the standard deviation for this efficacy indicator was not presented in each study; consequently, the SMD and its 95% CI of time to flatus were not calculated in this study. The time to flatus was significantly different between the 2 groups ($p<0.05$), and the time to flatus of patients was shorter in the PGB group than in the VOB group.

Comparison of defecation period between PGB and VOB groups

Two included studies (14,18) analyzed the defecation period of the patients. The average defecation period in each group and p-value ($p<0.01$ or $p<0.05$) of the statistical difference between the PGB and VOB groups are shown in Table 5. The SMD and its 95% CI of defecation period were not shown owing to the lack of standard deviation of the data in each study. The defecation period was significantly different between the 2 groups ($p<0.05$), and the defecation time of the patients was shorter in the PGB group than in the VOB group.

Table 3. Comparison of the total bowel care time between the VOB and PGB groups

Study	VOB group (min)	PGB group (min)	p value
Stiens 1998 (14)	102	51.2	<0.01
House 1997 (18)	74.5	43	<0.01
Frisbie 1997 (19)	144	66	<0.01
Total			<0.01

PGB: polyethylene glycol based bisacodyl; VOB: vegetable oil based bisacodyl

Table 4. Comparison of the time to flatus between the VOB and PGB groups

Study	VOB group (min)	PGB group (min)	p value
Stiens 1998 (14)	31	12	<0.01
House 1997 (18)	32	15	<0.05
Total			<0.05

PGB: polyethylene glycol based bisacodyl; VOB: vegetable oil based bisacodyl

Comparison of time to clean up between the PGB and VOB groups

Two included articles (14,18) compared the time to clean up in the 2 groups. The SMD and its 95% CI could not be calculated owing to the lack of standard deviation of the data. The average time in each group and p-value of the difference between the PGB and VOB groups are shown in Table 6. There was no significant difference ($p>0.05$) in the time to clean up between the 2 groups.

Table 5. Comparison of the defecation period between the VOB and PGB groups

Study	VOB group (min)	PGB group (min)	p value
Stiens 1998 (14)	58	32	<0.01
House 1997 (18)	36	20	<0.05
Total			<0.05

PGB: polyethylene glycol based bisacodyl; VOB: vegetable oil based bisacodyl

Table 6. Comparison of the time to clean up between the VOB and PGB groups

Study	VOB group (min)	PGB group (min)	p value
Stiens 1998 (14)	1.9	3.2	>0.01
House 1997 (18)	6.7	5.5	>0.05
Total			>0.05

PGB: polyethylene glycol based bisacodyl; VOB: vegetable oil based bisacodyl

DISCUSSION

Neurogenic bowel dysfunction is a common problem for patients with SCI, myelomeningocele (MMC), multiple sclerosis, and Parkinson's disease (12,20,21). There are several treatment modalities for the successful management of NBD including administration of rectal agents such as suppositories. The application of VOB and PGB suppositories and their comparative efficacies in NBD treatment have been reported previously (14,18,19). However, these studies were carried out with small sample sizes and some limitations. In view of this, the present study pooled these articles to statistically analyze the efficacies of VOB and PGB suppositories in treating NBD patients with SCI.

Based on the meta-analysis results, we found that the total bowel care time, time to flatus and the defecation period were significantly less in patients treated with PGB than in patients treated with VOB. There was no significant difference in time to clean up between the 2 groups. PGB, which is a water-soluble suppository, allows the bisacodyl to be activated by the body's own moisture shortly after insertion (22), while VOB, which is a micro-melting suppository, takes a longer time to work because it needs to be melted by the body's heat (23). This may be the reason for the faster effect of PBG compared with VOB. Moreover, the solid dispersion in polyethylene glycol-polyethylene 80 mixture has been found to increase the bioavailability of a poorly water-soluble drug (24) and polyethylene glycol 400 has a marked accelerating effect on small intestinal liquid transit, which in turn has implications for the formulation of poorly water-soluble drugs with polyethylene glycol 400 (25). These benefits of polyethylene glycol were based on its water-soluble and organic solvents. These characteristics of polyethylene glycol and vegetable oil may well explain the faster effect of PGB suppositories than VOB suppositories in the treatment of NBD in patients with SCI.

A recent literature review also reported that the total bowel care time for NBD patients treated with the PGB suppository was significantly shorter than that with the VOB suppository (26). Additionally, more indicators such as time to flatus, defecation period, and time to clean up were used to compare the efficacy of PGB and VOB in the present study, which was the advantage of this meta-analysis.

This meta-analysis has some limitations. First, only 3 studies were included in this meta-analysis and, as the overall sample size was small, additional studies with large sample sizes are warranted to verify the present results. Second, the SMD and its 95% CI of each indicator could not be calculated owing to the lack of standard deviation of the data. Without the weight analysis, the results may be affected by the different characteristics of participants in studies. A more appropriate statistical method must be used to analyze the data. Third, bias caused by confounding factors (age and gender of the subjects, study regions, and design) was not analyzed owing to the lack of data.

In conclusion, we have determined that PGB suppositories could act faster than VOB suppositories in the treatment of NBD in patients with SCI. In order to further evaluate the efficacy and safety of PEG and VOB suppositories, more high-quality randomized controlled trials with large sample sizes are required.

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