Original Article

Clinical efficacy of vitamin B in the treatment of mouth ulcer: a systematic review and meta-analysis

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Background: Our study sought to determine the efficacy of vitamin B in treating mouth ulcers.

Methods: The databases PubMed, Web of Science, Embase, Chinese National Knowledge Infrastructure (CNKI), and Wanfang were comprehensively searched to identify relevant articles published between 2010 and 2021. Subsequently, the clinical efficacy of vitamin B in the treatment of mouth ulcers was comprehensively and quantitatively evaluated through meta-analysis.

Results: Totally, 16 studies were finally included in the meta-analysis, including 1,534 patients. Patients who did not receive treatment were taken as controls, while those who were treated with vitamin B alone or vitamin B combined with pantothenic acid were included in the treatment group. In comparison with the control group, the effective rate was higher [odds ratio (OR) =5.24, 95% confidence interval (CI): 3.72 to 7.37, P<0.001] while the recurrence rate was lower (OR =0.194, 95% CI: 0.128 to 0.295, P<0.001) in the treatment group. Additionally, both the ulcer healing time [standardized mean difference (SMD) =–2.15, 95% CI: –2.80 to –1.50, P<0.001] and treatment time (SMD =–2.31, 95% CI: –2.67 to –1.96, P<0.001) in the treatment group were shorter than those of the control group.

Discussion: Vitamin B enables a higher effective rate and lower recurrence rate, accelerates ulcer healing, and shortens the course of treatment. Collectively, vitamin B has a high clinical value in treating patients with mouth ulcers.

Keywords: Vitamin B; mouth ulcers; efficacy; meta-analysis

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Introduction

In dentistry, mouth ulcers are painful mucosal lesions, which are often located in the tongue, gum, cheek, or lip (1). In the general population, the incidence of mouth ulcers is 5–20% (2-4). Although the lesion is harmless and can heal itself, pains and discomfort caused by a mouth ulcer affect eating, drinking, brushing, and even speaking, leading to a decline in the patient's quality of life and work efficiency. The occurrence of mouth ulcers is probably associated with antigen sensitivity, genetic susceptibility, hormones, mucosal integrity, nutritional deficiencies, and stress, but the exact cause is unknown (5). A twin study explained the variation in incidence of a latent phenotype of mouth ulcer, which included a specific environmental factor (10%), a common environmental factor (26%), and a genetic factor (64%) (6). The treatment of mouth ulcers is basically symptomatic, with the purposes of alleviating pain, shortening healing time, reducing ulcer area, reducing recurrence rate, and increasing disease interval. Currently, treatment methods

mainly include systemic and topical corticosteroids, antibiotics, vitamin B complex, adhesives, topical antiseptics, analgesics, anti-inflammatory agents, mouthwashes with active enzymes, cautery, and photobiomodulation (7). Infection and vitamin B deficiency have been reported as possible contributing factors in mouth ulcers (8). Vitamin B, a micronutrient essential to the human body, can be obtained by dietary modification or drug treatment. Due to its advantage of low treatment cost, the treatment of mouth ulcers with vitamin B is worthy of clinical recommendation. This meta-analysis attempted to further investigate the clinical efficacy of vitamin B in treating mouth ulcers.

We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1064).

Methods

Literature retrieval strategy

The databases of PubMed, Web of Science, Embase, Chinese National Knowledge Infrastructure (CNKI), and Wanfang were comprehensively searched to identify relevant articles published between 2010 and 2021. The search terms were: ("vitamin B") AND ("mouth ulcer" OR "oral ulcer") AND ("clinical effect" OR "treatment effect"). The language was restricted to English and Chinese, while the main results were unrestricted to avoid bias.

Literature screening criteria

The inclusion criteria were as follows: (I) published randomized controlled studies on vitamin B in treating mouth ulcers; (II) literature with vitamin B as the treatment option for patients with mouth ulcers; (III) literature with at least one outcome measure such as effective rate, recurrence rate, healing time of ulcers, and treatment time.

The exclusion criteria were as follows: (I) no data on the results required by this meta-analysis provided, and the original text could not be obtained; (II) literature of poor quality, with incomplete data, and duplicate literature; (III) case reports, systematic reviews, expert consensus, non-comparative studies, reviews, and conference abstracts.

Data extraction and quality assessment

Based on the screening criteria, two investigators independently screened titles and abstracts and, if necessary, read full-text. They also independently completed data extraction and quality assessment. Any disagreement between the investigators was resolved through discussion with a third reviewer.

The inclusion criteria for participants were as follows: (I) patients with a definite clinical diagnosis of mouth ulcers; (II) patients who voluntarily read and signed the informed consent; (III) patients with high compliance with clinical studies who were not easily lost to follow-up. The exclusion criteria of participants were as follows: (I) patients with mouth ulcers caused by other clinical treatments or diseases; (II) patients with hematopoietic and coagulation disorders; (III) patients with comorbidities such as chronic diseases or underlying diseases; (IV) patients who were unable to communicate verbally.

The experimental methods included in the study involved random allocation of the participants to the control and treatment groups. The control group received no treatment, while the treatment group received vitamin B alone or vitamin B combined with pantothenic acid.

Statistical analysis

The software Stata 16.0 was utilized for statistical analysis (StataCorp LLC., College Station, TX, USA). Data were presented as odds ratio (OR) and its 95% confidence interval (CI) or standardized mean difference (SMD) and its 95% CI. Assessment of statistical heterogeneity was completed utilizing Cochrane q test and the I^2 test. If there was statistical homogeneity among studies ($P<0.05$ or $I^2>50\%$), the random-effects model (REM) was adopted; otherwise, the fixed-effects model (FEM) was used. Evaluation of publication bias was conducted by funnel plots, and a significant publication bias was suggested by $P<0.05$. Sensitivity analysis was employed to determine the stability of results.

Results

General information of included literature

The literature screening process is shown in *Figure 1*. On completion of the initial search in the databases, 281 studies were identified. Then, 125 duplicates were removed and 10 articles were excluded through reading of titles and abstracts. Next, by reading the full text, studies with incomplete or duplicate data, and studies without vitamin B as a treatment option were excluded. Finally, a total of

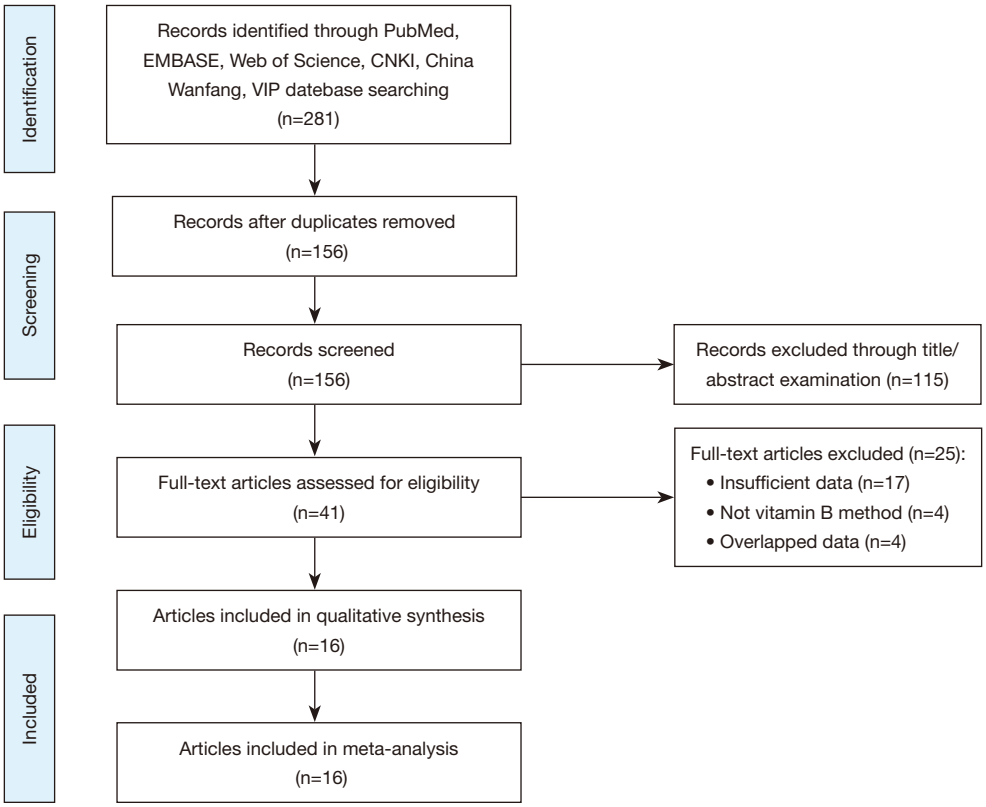

Figure 1 Flow chart of literature screening process. CNKI, Chinese National Knowledge Infrastructure.

16 studies were included in this meta-analysis (9-24). The included studies were all randomized controlled trials (RCTs) in Chinese, including 1,534 patients—767 in the treatment group and 767 in the control group. The basic characteristics of the included literature are shown in *Table 1*.

Meta-analysis results

Clinical efficacy

A total of 16 studies reported the effective rates of the two groups, and 11 studies compared the recurrence rates of the two groups. The FEM was used to analyze the effective rate (I^2=0.00%, P=1.000) and recurrence rate (I^2=0.00%, P=0.955). The results showed that in comparison with the control group, the effective rate of the treatment group was significantly higher (OR =5.24, 95% CI: 3.72 to 7.37, P<0.001) (*Figure 2A*) and the recurrence rate in the treatment group was lower than that in the control group (OR =0.194, 95% CI: 0.128 to 0.295, P<0.001) (*Figure 2B*). Further sensitivity analysis (*Figure 3*) revealed that the results did not change significantly after pooling, suggesting that the result was stable and less likely to be affected by heterogeneity.

Ulcer healing time and treatment time

The REM was used to analyze the ulcer healing time (I^2=90.40%, P<0.001) and treatment time (I^2=64.70%, P=0.015) in six studies. The results showed that the ulcer healing time in the treatment group was reduced by 2.15 days compared with the control group (SMD =–2.15, 95% CI: –2.80 to –1.50, P<0.001) (*Figure 4A*). Further, subgroup analysis of the drugs revealed that in comparison with the control group, the healing time was reduced by 2.06 days in the vitamin B group (SMD =–2.06, 95% CI: –2.97 to –1.16, P<0.001) and 2.35 days in the antibiotic group (SMD =–2.35, 95% CI: –2.73 to –1.98, P<0.001). In comparison with the control group, the treatment time was reduced by 2.32 days in the treatment group (95% CI: 1.96 to 2.67, P<0.001) (*Figure 4B*). Further subgroup analysis showed that when compared with the control group, the treatment time was shorter in both the vitamin B group (SMD =–2.55, 95% CI: –2.89 to –2.22, P<0.001) and antibiotic group (SMD =–1.88, 95% CI: –2.23 to

Table 1 Basic characteristics of included literature

Study	Year	Sample time (year/month)	Cases treat/con	Age (years)		Gender (male/female)		Intervention	Study design	Outcome measures
				Treat group	Con group	Treat group	Con group	Treat group		
Jiang Zhi	2020	2018.02–2019.03	61/61	44.66±10.95	44.02±11.01	31/30	32/29	VB_2, PA	RCT	①+②+③+④
Chen Huiqing	2019	2017.01–2017.12	76/76	37.8±10.9	38.5±11.4	32/44	35/41	VB_2, PA	RCT	①+②+③+④
Zhao Ming	2013	2009.03–2012.03	30/30	27.03±4.53	26.61±4.48	16/14	17/13	VC, VB-cp, PA	RCT	①+②
Zheng Qiang	2015	2013.01–2014.12	34/34	29.74±5.66	29.74±5.66	21/13	21/13	VC, VB-cp, PA	RCT	①+②+③+④
Gu Weihong	2017	2014.06–2015.09	72/72	36.9±4.3	36.8±4.1	41/31	40/32	VB_2, PA	RCT	①+②
Zhang Yuqin	2018	2017.02–2018.02	50/50	34.29±4.76	34.15±4.52	26/24	27/23	VB_2, PA	RCT	①+②
Tang Anbin	2015	2011.06–2014.06	50/50	32.25±5.41	33.68±5.36	26/24	28/22	VB_2, PA	RCT	①+②
Chen Yanqi	2019	2018.04–2019.04	49/49	49.89±1.52	49.90±1.56	27/22	28/21	VC, VB-cp, PA	RCT	①
Liu Xinyi	2018	2017.01–2018.01	40/40	47.2±1.1	45.3±1.2	29/11	28/12	VB_2, PA	RCT	①+②+③+④
Ma Tao	2016	2014.01–2015.07	23/23	36.4±5.8	36.4±5.8	13/10	13/10	VB-cp, PA	RCT	①
Pan Qiping	2018	2017.06–2018.06	36/36	37.29±5.86	37.62±5.98	21/15	19/17	VB_2, PA	RCT	①+②
Xu Zhongwei	2018	2017.02–2017.12	53/53	45.03±2.11	45.68±2.48	28/25	27/26	VC, VB-cp, PA	RCT	①
Huo Liyan	2020	2018.01–2019.01	40/40	32.53±13.39	32.56±14.41	19/21	19/21	VB-cp, PA	RCT	①
Zhang Weiming	2018	2016.07–2017.06	60/60	39.3±8.2	40.2±8.4	33/27	35/25	AB, VB_2, PA	RCT	①
Zang Lei	2018	2014.02–2016.08	48/48	42.86±1.54	42.78±1.48	24/24	28/20	AB, VB_2, PA	RCT	①+②+③+④
Qian Yaqin	2014	2011.02–2013.02	45/45	42.6±1.4	42.8±1.5	25/20	26/19	AB, VB_2, PA	RCT	①+②+③+④

① : total effective rate; ② : recurrence rate; ③ : ulcer healing time; ④ : treatment time. Treat, treatment; Con, control; RCT, randomized controlled trial; NR, not reported; VB-cp, vitamin B complex; VB_2, vitamin B_2; VC, vitamin C; PA, pantothenic acid; AB, antibiotic.

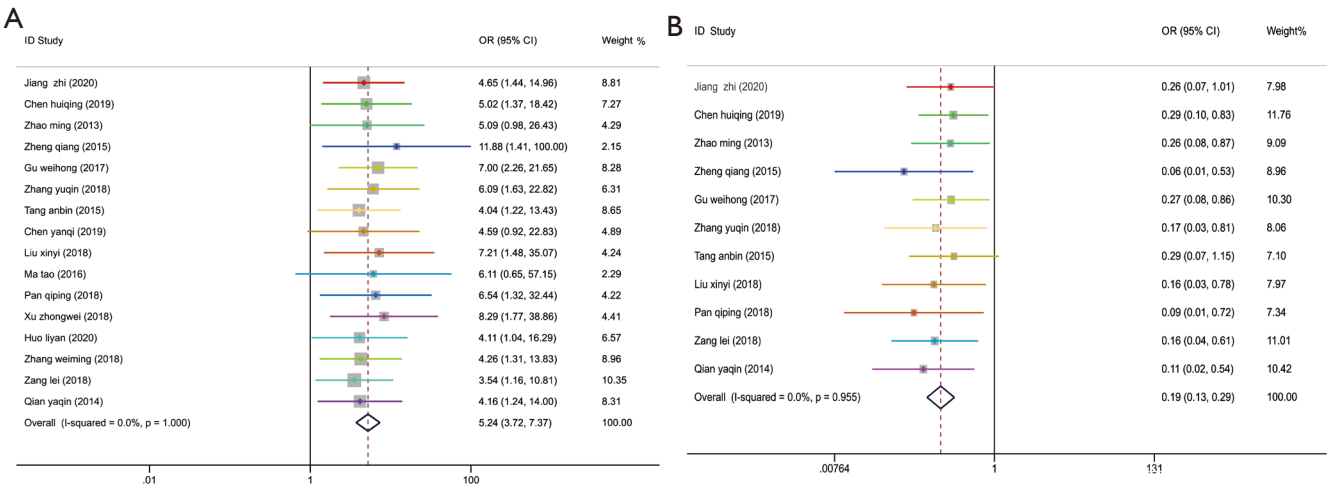

Figure 2 Forest plots of clinical efficacy in the two groups. (A) Forest plot of effective rate in patients with mouth ulcers; (B) forest plot of recurrence rate in patients with mouth ulcers. OR, odds ratio; CI, confidence interval.

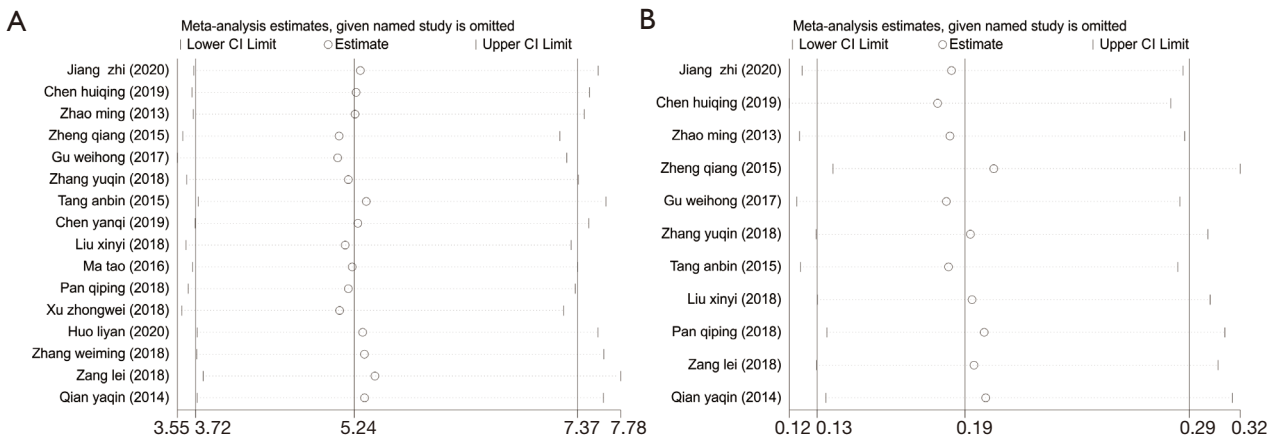

Figure 3 Sensitivity analysis of clinical efficacy in the two groups. (A) Sensitivity analysis of the effective rate in patients with mouth ulcers; (B) sensitivity analysis of the recurrence rate in patients with mouth ulcers. CI, confidence interval.

–1.54, P<0.001). Additionally, the low sensitivity was also supported by the above results (*Figure 5*) and indicated the robustness of the above results.

Publication bias

Funnel plots were employed to determine the existence of publication bias. We used the standard error (SE) (logOR) and logOR of effective rate (*Figure 6A*) and recurrence rate (*Figure 6B*) to construct the funnel plots, and the symmetry of the plots indicated no significant publication bias. This conclusion was only for the six included studies which investigated the healing and treatment time. The remaining 10 articles were deemed to have publication bias by default, so no funnel plots were drawn for them.

Discussion

As a common oral disease with a high recurrence rate, in addition to being affected by genetic genes, mouth ulcers are related to poor dietary and living habits. Mouth ulcers are painful lesions in the oral mucosa, accompanied by peripheral congestion and redness (25). They are also prone to induce complications such as lymphadenopathy, halitosis, and chronic pharyngitis. Vitamin B, one of the essential

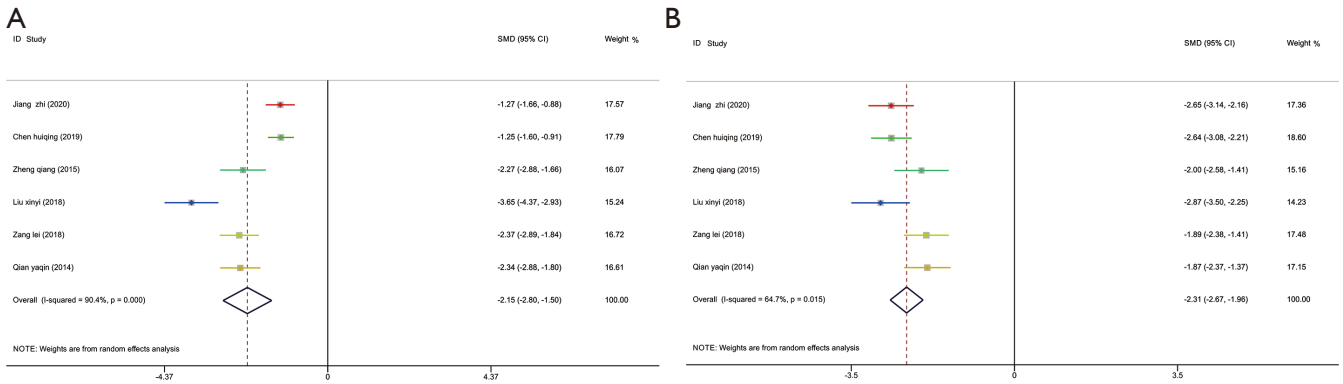

Figure 4 Forest plots of ulcer healing time (A) and treatment time (B). SMD, standardized mean difference; CI, confidence interval.

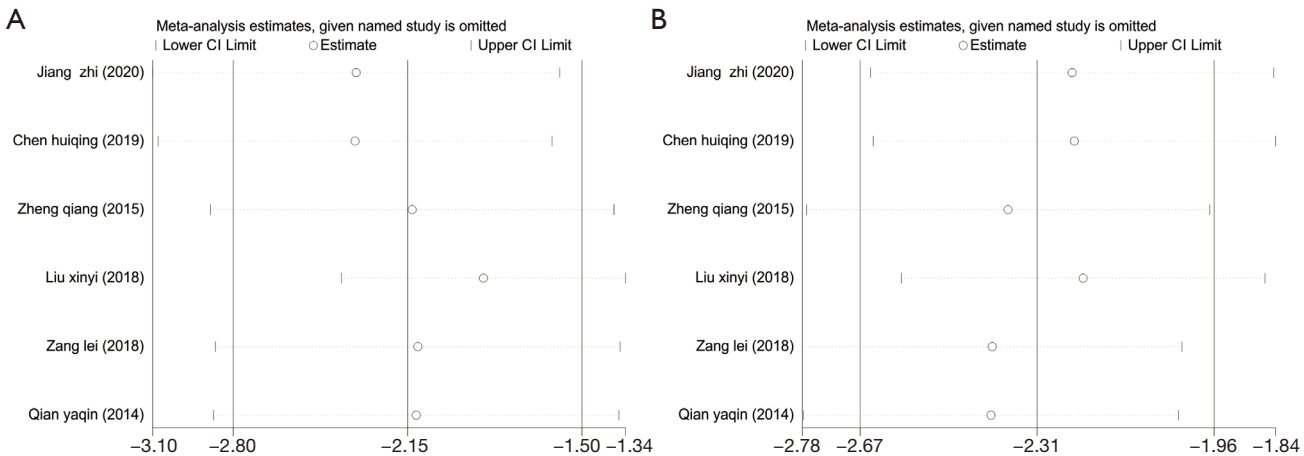

Figure 5 Sensitivity analysis of ulcer healing time (A) and treatment time (B). CI, confidence interval.

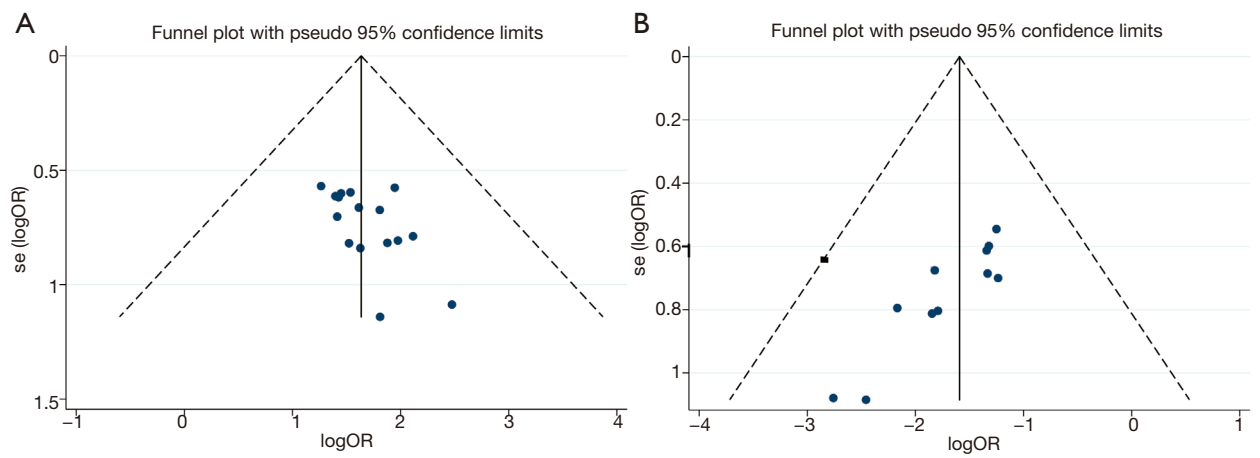

Figure 6 Funnel plots of clinical efficacy in the two groups. (A) Funnel plot of effective rate in patients with oral ulcer; (B) funnel plot of recurrence rate in patients with oral ulcer. SE, standard error; OR, odds ratio.

nutrients for the human body, is effective in wound healing. Vitamin B complex, a compound agent, is usually introduced in the treatment of mouth ulcers; it includes vitamin B_1, vitamin B_2, nicotinamide, pantothenic acid, vitamin B_6, folic acid, and vitamin B_{12}. Vitamin B_1, also called thiamine, is involved in the process of energy conversion in the body and is required for the normal function of muscles and nerves (26). Vitamin B_3, also known as niacin, primarily enables the normal functions of enzymes and participates in hydrogen transfer during biological oxidation (27). Vitamin B_2, known as riboflavin, is closely associated with inflammation in the oral mucosa and genitalia, and has been shown to be important for normal growth, muscle development, and hair (28). Pantothenic acid, which generally refers to vitamin B_5 enables the metabolism of carbohydrates, fats, and proteins and consequent production of energy in the body (29). Vitamin B_6 is involved in the physiological activity of various coenzymes of the body as well as in the metabolism of fats and amino acids (30). Folic acid and vitamin B_{12} (also called cobalamin) are two closely related B vitamins; the involvement of the two in producing red blood cells in the bone marrow has been supported by numerous reports, while their deficiency may lead to anemia (31). This meta-analysis therefore set out to comprehensively and quantitatively investigate whether vitamin B complex treatment has a positive effect on healing mouth ulcers.

In total, 16 included studies reported the effective rate, and 11 studies compared the recurrence rate of the two groups. Through meta-analysis, it was revealed that in comparison with the control group, the effective rate was higher (OR =5.24, 95% CI: 3.72 to 7.37, P<0.001) while the recurrence rate was lower in the treatment group (OR =0.194, 95% CI: 0.128 to 0.295, P<0.001). These results could be taken as confirmation of the effects of vitamin B on improving clinical efficacy and reducing recurrence in patients with mouth ulcers. Similarly, Guan *et al.* suggested that vitamin B can inhibit cholinesterase activity, promote cell regeneration, and reduce mucositis, consequently improving the therapeutic effect (32).

A total of 6 studies compared the ulcer healing time and treatment time. In comparison with the control group, the ulcer healing time was reduced by 2.15 days (95% CI: 1.50 to 2.80, P<0.001) and the treatment time was reduced by 2.32 days (95% CI: 1.96 to 2.67, P<0.001) in the treatment group. The effect is due to the ability of vitamin B to protect sebaceous glands and mucosal tissues, and promote mucosal repair and regeneration, thus shortening the healing time. Meanwhile, vitamin B inhibits the development of inflammation, thus shortening the treatment time (17). Collectively, administration of vitamin B may be clinically suitable for patients with mouth ulcers.

Vitamin B complex is ubiquitous in various daily foods. For instance, vitamin B_1 is present in fruit, vegetables, pork, and beef, and vitamin B_2 is more abundant in animal liver and fish (33). It is possible to obtain the necessary amount of vitamin B required for the human body from dietary sources. Therefore, in the treatment process, in addition to scientific and reasonable vitamin supplements, patients should also be educated to improve their understanding of mouth ulcers, so as to correct their dietary and living habits. Specifically, eating more vegetables, fruits, and meat rich in vitamin B, drinking more water, and doing appropriate exercise can enhance both immunity and physical fitness, consequently promoting the early recovery of patients, and reducing the recurrence rate.

However, our study still had some limitations. First, there was a lack of control for confounding variables. This may have led to the overestimation or underestimation of risk estimation. Second, we did not use Begg's test or Egger's test to assess publication bias, which is an inherent bias in meta-analysis. We only subjectively determined the presence of publication bias by funnel plots. Finally, this study was not registered as a systematic review, which probably reduces the credibility of this study.

Conclusions

In summary, both vitamin B alone or vitamin B combined with pantothenic acid are effective in treating mouth ulcers. In addition to its effectiveness, vitamin B also significantly reduces the possibility of recurrence, accelerates ulcer healing, and shortens the course of treatment. Collectively, vitamin B has a high clinical value in treating patients with mouth ulcers.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-1064

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1064). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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