ISSN 2616-5791 Vol.5, Issue 5: 1-6, DOI: 10.25236/AJMHS.2024.050501

Comparative Study on the Efficacy of Kangfuxin Liquid Combined with Oral Ulcer Powder of Recurrent Oral Ulcers: A Meta-analysis

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Abstract: *This study systematically evaluates the clinical efficacy of Kangfuxin Liquid and Oral Ulcer Powder in treating recurrent oral ulcers. The study utilized computer-based searches via databases such as China National Knowledge Infrastructure (CNKI), VIP, PubMed, EMBASE, Web of Science, and Wanfang, covering literature from January 2013 to January 2024. A meta-analysis was conducted using RevMan 5.4.1, considering the effective rate as the outcome measure, focusing on studies involving treatments that combined Kangfuxin Liquid with Oral Ulcer Capsule Powder to treat Recurrent Oral Ulcers. Six articles, incorporating 828 samples, were selected through the screening process. Analysis results indicate a statistically significant greater efficacy when Kangfuxin Liquid was combined with Oral Ulcer Powder, as compared to the sole use of Oral Ulcer Powder [OR=5.04, 95%CI (2.86, 8.86), P<0.00001]. However, due to potential publication bias in this study, these results should be interpreted with some caution.*

Keywords: *Kangfuxin Liquid; recurrent oral ulcer; oral ulcer powder; Meta-analysis*

1. Introduction

Recurrent Oral Ulcer (ROU) is a pervasive condition that predominantly affects regions of the oral mucosa, including the lips, cheeks, tongue, and soft palate [1]. Its distinctive manifestation comprises round or oval lesions, characterized by radial erythema and edema, and typically overlaid with a gray-white pseudomembrane. Although the disease demonstrates a low mortality rate, the excruciating pain and discomfort caused by ROU substantially impede routine activities such as communication and feeding [2]. Notably, recurrent episodes of ROU can lead to increased susceptibility to malnutrition, particularly in children at developmental stages, due to diminished appetite and impaired efficiency of food intake. Besides, ROU can potentially compromise immunity, leading to an elevated risk of infection by other diseases. Current academic consensus attributes the etiology of ROU to a multitude of factors including immunity, endocrinological factors, genetic predisposition, and psychosocial wellness [3]. However, due to the complexity of ROU's etiology, a definitive therapeutic strategy has yet to be established. Current clinical practices are largely palliative, focusing primarily on pain management and enhancing systemic vitality [4]. Yet, these approaches demonstrate limited efficacy in facilitating wound healing [5]. Previous investigations suggest that traditional Oral Ulcer Powder, a therapeutic modality derived from Traditional Chinese Medicine (TCM), presents a potent treatment avenue for ROU and is increasingly gaining clinical traction [6]. Conversely, Kangfuxin Liquid, a widely-used clinical pharmaceutical for gastric ulcers, has exhibited remarkable anti-inflammatory and hemolytic properties, and cellular reparative potential, as supported by numerous clinical studies [7]. Recently, Kangfuxin Liquid has been repurposed for the management of diverse mucosal lesions, including ROU. Given emerging evidence that supports the hypothesis that synergistic drug regimens may outweigh the therapeutic efficiency of standalone pharmaceuticals [8], this study is intended to investigate if integrating Kangfuxin Liquid into the ROU therapeutic repertoire could potentially hasten recovery rates. This investigation employs an exhaustive review and analysis of pertinent studies conducted over the past decade that explore the therapeutic utility of Kangfuxin Liquid in the context of ROU management. The study aspires to generate impactful data to further underpin future clinical and pharmacological research concerning ROU therapeutic strategies

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2. Method and Data Analysis

2.1 Retrieval strategy

Electronic databases including China National Knowledge Infrastructure (CNKI), VIP Database, PubMed, Web of Science, The Excerpta Medica Database (EMBASE), and WanFang Data were searched for relevant literature. The time frame was set from January 2013 to January 2024. Search terms included "oral ulcer", "Kangfuxin liquid", "oral ulcer powder", "curative effect", "Oral ulcer", "Oral ulcer powder", and "Kangfuxin liquid".

2.2 Inclusion Criteria

Inclusion criteria were as follows: 1) Type of study: randomized controlled trials, 2) Study subjects: patients with ROU without any other oral diseases, 3) Intervention method: the experimental group received Kangfuxin Liquid treatment whereas the control group was treated with Oral Ulcer Powder, 4) Outcome measure: efficacy.

2.3 Exclusion Criteria

Exclusion criteria involved: 1) Review articles, 2) Studies with incomplete data or content, 3) Studies focusing on specific professions or physiological states, 4) Studies that were duplicates, and 5) Studies whose criteria or standards greatly differed from the majority of the literature.

2.4 Literature Screening and Data Extraction

Two reviewers independently screened the literature and extracted data; in the event of a disagreement, a third reviewer made the final decision. Following the preliminary screening by the reviewers, any difference in search results was resolved through discussion with a third reviewer if necessary. Duplicate studies were eliminated and the remaining studies' abstracts were reviewed against the inclusion criteria. A third reviewer then performed a follow-up review to validate the initial screening and data extraction.

2.5 Quality Assessment of the Included Studies

Detailed data from included studies such as authors, publication year, sample size, intervention methods, randomization procedure, duration of treatment, and drop-out rates were extracted. Cochrane's quality assessment tool was then utilized, and a risk bias graph was created using RevMan 5.4.1 software.

2.6 Statistical Analysis

RevMan5.4.1 software was utilized for the statistical analysis of the collected data. Count data were represented through odds ratio (OR) with its 95% confidence interval (CI), while continuous data were expressed as mean difference (MD) with its 95%CI. The heterogeneity of the included studies was analyzed. $I^2 \leq 50\%$ and $P \geq 0.05$ were considered acceptable heterogeneity and analyzed using a fixed-effect model. $I^2 > 50\%$ and $P < 0.05$ were indicative of significant heterogeneity and, in such cases, a random-effects model was implemented.

3. Results

3.1 Literature Screening

Document collection process according to Figure 1. First of all, the initial literature search yielded 387 potential articles. Following the title and abstract review, 124 articles were shortlisted for further investigation. After a comprehensive inspection of the full articles, 29 studies were considered for eligibility. Lastly, 6 studies, that rigorously met the inclusion and exclusion criteria of the study, were chosen for final analysis.

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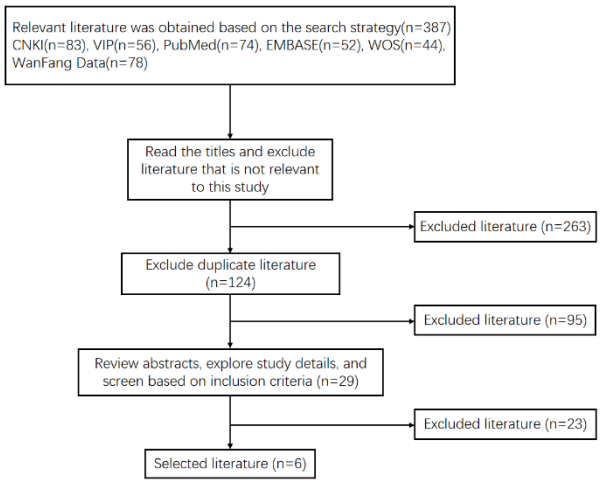

Figure 1: Literature screening process

3.2 Basic characteristics

There were a total of 828 patients in the 6 documents obtained, and there were 414 patients in the control group and the observation group respectively. The treatment duration in all literature is 7 days. The treatment method in one of the documents is the treatment of Oral Ulcer Powder and Kangfuxin Liquid; the treatment method in the remaining article is to first carry out conventional treatment, and then treat Oral Ulcer Powder and Kangfuxin Liquid. All 6 documents include effective rates. See Table 1 for details.

Table 1: Basic Characteristics of Literature

Author	Number of samples	Treatment	Period/d	random method	case exit
	Control group/observation group	Control group/observation group			
Hou Ming Yan 2013[9]	78/78	OUP/ KFXL	7	No mention	None
Li Jiao 2018[10]	56/56	OUP/ KFXL	7	No mention	None
Ma Jiang Min 2018[11]	46/46	OUP/ KFXL	7	random number table	None
Nian Li Yan 2021[12]	118/118	OUP/ KFXL	7	random number table	None
Nie Sen 2020[1]	49/49	OUP/ KFXL	7	random number table	None
Xie Chun 2016[13]	67/67	OUP/ KFXL	7	random number table	None

3.3 Literature Quality Assessment Integration

The Cochrane literature assessment tool was employed to evaluate the quality of the included studies. Four of these studies [1,11–13] utilized a random number table method for their groupings and were categorized as having a low risk of bias. Two other studies [9,10], however, did not mention their specific methods of randomization and were noted as having an unclear risk. None of the included studies explicitly described any measure of allocation concealment, thus their risk in this category was also classified as unclear. In three of the studies [10–12], potential breaches of blinding of researchers and participants were identified, presenting a high risk. Conversely, the remaining three studies [1, 9, 13] did not clarify whether blindings of researchers and subjects were implemented and thus were classified as having an unclear risk. Another three [1, 9, 12] explained their blinding method for outcome assessment and were categorized as low risk, but the other three [10, 11, 13] did not disclose this information, denoting an unclear risk. Despite these variables, the outcome measures obtained in all six studies were consistently in line with the predetermined ones, signifying no discrepancies or reporting bias and indicating a low risk. Furthermore, none of the six studies showed any other potential biases, hence were labeled as low risk. Findings of the literature bias risk analyses are depicted in Figures 2 and 3.

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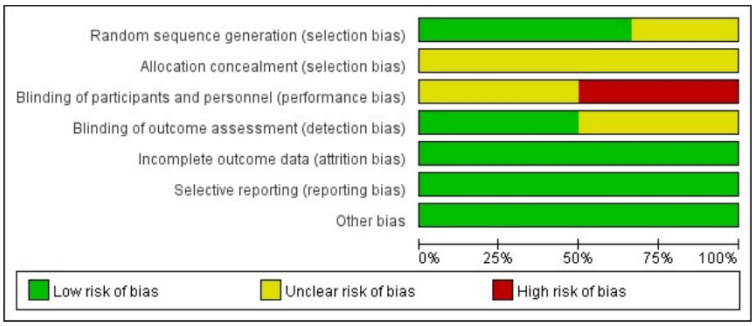

Figure 2: Percentage of included RCTs with the risk of bias

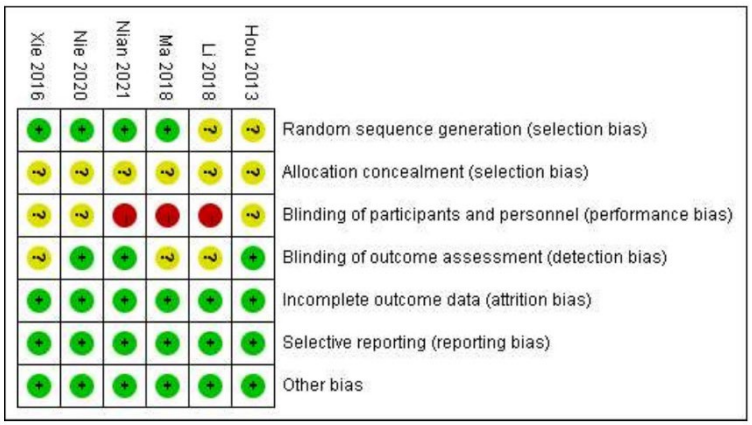

Figure 3: Distribution of risk of bias of included RCTs

3.4 Meta-analysis results

By analyzing the effectiveness of the six included documents, the meta-analysis method was used to analyze the data, and the result is shown in figure 4. The heterogeneity of the data was detected (P=1.00; I^2=0%). The heterogeneity results showed that the heterogeneity between studies was. Therefore, a fixed-effects model was used for meta-analysis. The final results showed that the treatment effect of the observation group was better than that of the control group [OR=5.04, 95%CI (2.86, 8.86), P<0.00001], which means that the new method of rehabilitation The efficacy of the liquid combined with the oral ulcer powder in the treatment of recurrent oral ulcers is more effective than the treatment of the oral ulcer powder alone, and there is a statistical difference.

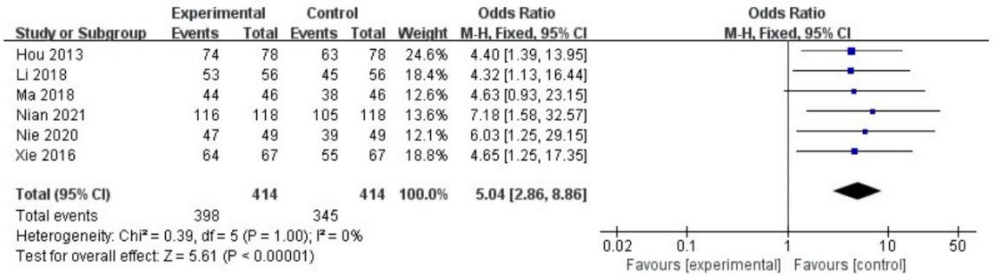

Figure 4: Result of Meta-Analysis

3.5 Publication bias

This study used RevMan 5.4.1 to create a funnel plot of publication bias shown above figure 5 and evaluated publication bias by observing the asymmetry of the funnel plot. The results showed that this study may have publication bias, and the results of this study need to be interpreted with caution.

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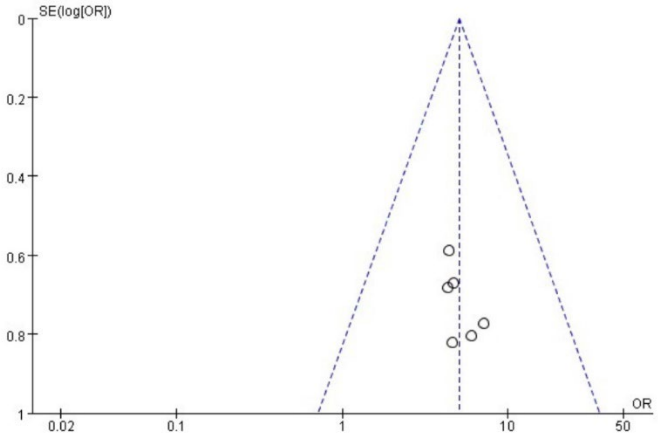

Figure 5: Funnel plot

4. Discussion

The etiology of Recurrent Oral Ulceration (ROU) continues to be debated within clinical circles. ROU manifestation among individuals is highly variable, which many scholars attribute to a complex synergy of diverse factors. These observed causal elements fall broadly into three categories: genetic, environmental, and immunological factors. It is pertinent to note that susceptibility to ROU seems to increase among individuals with compromised immune systems, and habitual or recovering smokers, in addition to those diagnosed with anemia [14]. Some scholarly discourse draws potential linkages between ROU and specific pathogenic microorganisms, evidenced by considerable alterations in the bacterial flora within lesioned areas. Such fluctuations correspond to patients' recovery stage, lending credence to the hypotheses of bacterial pathogen infections being instrumental in oral ulcer development [15]. However, this area remains under-explored within the scientific literature.

In the context of ROU, Traditional Chinese Medicine (TCM) theorizes that inflammation, heat, and pain-inducing conditions are related to heart diseases, while also emphasizing the critical role of the spleen and kidneys. A substantial amount of research implicates 'Fire Evil'—a TCM metaphor—as a primary etiological factor in ROU, emanating from Yin and Yang imbalances, obstruction in the Qi, and blood flow, along with concurrent spleen and stomach damage [16]. As such, TCM perceives ROU treatment as contingent on addressing related patient conditions — imbalances of heat in the heart and spleen, Yin deficiency, excess heat, and spleen and stomach dampness [17,18]. Our research focuses primarily on Periplaneta americana extract, lauded in TCM for its diuretic, anti-inflammatory, circulation, and blood stasis activation potency. Formulas such as Xinmailong Injection, derived from this extract, have demonstrated marked improvement in cardiac rhythm and myocardial contractility [19]. Concurrently, Kangfuxin Liquid—a TCM compound—exhibits the ability to heal ulcer wounds, fortify the immune system, and effectively prevent recurrence [20]. This research integrates six papers investigating the effectiveness of combined Kangfuxin Liquid and Oral Ulcer Powder treatment for ROU. The synthesized findings substantiated that this combined treatment yielded better efficacy. However, the potential publication bias in this appraisal, owing to the significant inclusion of Chinese literature, necessitates a cautious interpretation of the results. It is also important to acknowledge the widespread use of Kangfuxin Liquid within China. Consequently, upcoming research must consider broadening the timeline of the referenced literature and include subgroup analyses of diverse therapy combinations to mitigate publication bias.

References

[1] Nie Sen. Clinical efficacy of Kangfuxin Liquid combined with Oriental Ulcer Powder in the treatment of recurrent aphthous ulcer [J]. Contemporary Medicine, 2020, 26(23): 91–93.
[2] Li Xiaoyan, Ge Guolan. Analysis of the efficacy of Kangfuxin Liquid combined with cimetidine in the treatment of recurrent oral ulcers [J]. Journal of Practical Traditional Chinese Medicine Internal Medicine, 2020, 34(9): 83–85.
[3] Wang Ling. Clinical effect of three drugs combined to treat oral ulcers[J]. Chinese Pharmacoeconomics, 2024, 19(2): 99–103.

ISSN 2616-5791 Vol.5, Issue 5: 1-6, DOI: 10.25236/AJMHS.2024.050501

[4] Yu Jiaoling, Na Jie. Observation on the clinical efficacy of Kangfuxin Liquid in the treatment of recurrent oral ulcers [J]. Chinese Modern Drug Application, 2021, 15(4): 139–142.
[5] Zhu Fandi, Zou Jiaxin, Zhu Yunge. The efficacy of Bingbo Powder combined with Montmorillonite Powder in the treatment of recurrent oral ulcers [J]. Modern Medicine and Health, 2023, 39(23): 4010-4012+4017.
[6] Liu Yanxia. Analysis of the efficacy of traditional Chinese medicine Ulcer Powder in the treatment of recurrent oral ulcers [J]. Huaihai Medicine, 2017, 35(5): 588–590.
[7] Hu Liang. Analysis of the clinical efficacy of Kangfuxin Liquid in the treatment of gastric ulcer and its effect on inflammatory factors, oxidative stress and gastric mucosal repair [J]. Modern Diagnosis and Treatment, 2023, 34(17): 2543- 2545+2556.
[8] Li Xiang, Shen Chen. Li Qiangou's clinical experience in treating recurrent oral ulcers[J]. Global Chinese Medicine, 2024, 17(2): 269–272.
[9] Hou Mingyan. Observation on the effect of Kangfuxin Liquid combined with Oriental Ulcer Powder in the treatment of recurrent aphthous ulcer [J]. Journal of Bethune Military Medical College, 2013, 11(6): 556–557.
[10] Li Jiao. Clinical efficacy of Kangfuxin Liquid combined with Oriental Ulcer Powder in the treatment of recurrent aphthous ulcer [J]. Heilongjiang Medicine, 2018, 31(6): 1294–1296.
[11] Ma Jiangmin, Xu Lemeng, Zhang Peng. Clinical study of Kangfuxin Liquid as an adjuvant treatment for recurrent oral ulcers in the elderly [J]. Chinese Journal of Geriatric Stomatology, 2018, 16(3): 154–156.
[12] Nian Liyan. Clinical analysis of the combined use of Kangfuxin Liquid and Oral Ulcer Powder in the treatment of recurrent aphthous ulcers [J]. Chinese Modern Drug Application, 2021, 15(14): 10–12.
[13] Xie Chun, Dai Lin, Liu Jian. Clinical observation on the treatment of recurrent aphthous ulcer with Kangfuxin Liquid combined with Orchid Ulcer Powder [J]. Chinese Pharmacy, 2016, 27(8): 1101–1103.
[14] Huang Dongmei. How to treat and prevent recurrent oral ulcers[J]. Gansu Science and Technology News, Gansu Science and Technology News, 2024: 008.
[15] Zha Biqing, Zhou Yiran, Chen Jing, et al. Dynamic analysis of oral flora in patients with recurrent oral ulcers [J]. Modern Preventive Medicine, 2023, 50(12): 2289-2294+2304.
[16] Liu Shuyi, Zhang Fengwu, Wang Liping. Zhang Fengwu's experience in treating oral ulcers based on "Yin Fire Theory" [J]. Chinese Medicine Herald, 2023, 29(5): 154–156.
[17] Chao Chun'e. Clinical study on the pathogenesis and treatment of recurrent oral ulcers [J]. Chinese Contemporary Medicine, 2010, 17(3): 16–17.
[18] Zhang Xuesong. Pathogenesis and treatment of recurrent oral ulcers[J]. Chinese and Foreign Medical Research, 2012, 10(32): 107–108.
[19] Wang Pengwei, Yang Fei, Cao Wenqiu. Research progress on the clinical application of Periplaneta americana extract Kangfuxin Liquid at home and abroad [J]. Today's Pharmacy, 2023, 33(10): 784–788.
[20] Luo Shichao. Clinical study on the treatment of chronic hypertrophic pharyngitis using traditional Chinese medicine cautery method combined with Kangfuxin liquid gargle[D]. Guangxi University of Traditional Chinese Medicine, 2023.