

Systematic Analysis of Efficiency and Safety of Dexamethasone and Cimetidine in the Treatment of Gastroenteritis

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ABSTRACT. *The purpose of this study is to determine the efficiency and safety of two drugs in the treatment of gastroenteritis by META analysis, and to establish a preliminary evaluation system. PubMed (1966-2018.1), CochraneLibrary (1996-2018.1), Embase (1974-2018.1), CNKI (1994-2018.1), VIP (1989-2018.1) and CBM (1978-2018.1). Exclusion criteria and quality was evaluated and data were extracted. Meta analysis was performed using RevMan 5.0 software. A total of 16 RCTs were enrolled. The quality of the study was moderate. A total of 1333 patients with ulcerative colitis were enrolled. Meta-analysis showed that in the total rate, dexamethasone was superior to cimetidine in the treatment of ulcerative colitis. There were 12 RCTs reported adverse reactions, and dexamethasone had fewer adverse reactions. META analysis showed that both efficacy and safety of dexamethasone were better.*

KEYWORDS: *META analysis, gastroenteritis, cimetidine, dexamethasone*

1. Introduction

Gastroenteritis is a common gastrointestinal disease in summer and autumn. It causes the absorption of gastrointestinal mucosa to decrease, the exudation and secretion to increase, resulting in a large number of watery stools. At the same time, inflammation and allergy stimulate gastrointestinal contraction dysfunction and spasm, resulting in abdominal colic [1]. In summary, anti-inflammation and anti-allergy should be the main treatment. Several studies have shown that dexamethasone has anti-inflammatory, anti-allergic and anti-shock effects. Anti-inflammatory effects can reduce and prevent tissue response to inflammation.

Inhibits the aggregation of inflammatory cells, including macrophages and leukocytes, at inflammatory sites, and inhibits phagocytosis, lysosomal enzyme release, and the synthesis and release of inflammatory chemical mediators. It can alleviate and prevent tissue response to inflammation, thereby reducing the expression of inflammation. Cimetidine is a histamine H2 receptor antagonist [2], which can effectively inhibit the secretion of basic gastric acid, as well as anti-allergy and increase immune function. It can effectively reduce the stimulation and injury of gastrointestinal mucosa caused by excessive secretion of gastric acid. It can also resist allergies, enhance the immune function of gastrointestinal mucosa, promote mucosal repair and reduce the invasion and exudation of bacteria and viruses. Cochrane systematic evaluation [3] compared dexamethasone with traditional drugs, the results showed that dexamethasone had better efficacy, and the incidence of adverse reactions had no significant difference. However, there is no evidence-based medical evidence in China. In order to understand the efficacy and safety of dexamethasone and cimetidine in the treatment of acute gastroenteritis, the randomized controlled trials of dexamethasone and cimetidine at home and abroad were comprehensively searched. Cochrane systematic evaluation method was used to analyze the efficacy and safety of dexamethasone and cimetidine in order to provide the basis for clinical treatment.

2. Inclusion and exclusion criteria

2.1 Basic information and limitation

Randomized controlled trials (RCTs) of dexamethasone versus cimetidine in the treatment of gastroenteritis at home and abroad, whether or not allocation concealment or blind method is used. The research literature is full-text and limited to Chinese and English. Randomized controlled trials (RCTs) of dexamethasone versus cimetidine in the treatment of gastroenteritis at home and abroad, whether or not allocation concealment or blind method is used. The research literature is full-text and limited to Chinese and English.

The experimental group was treated with dexamethasone and the control group was treated with cimetidine. The main outcome index is the total effective rate. Secondary outcomes were complete remission rate, recurrence rate and any adverse reactions during treatment.

2.2 Retrieval Strategy

PubMed (1966-2010.1), Cochrane Library (1996-2010.1), EMBASE (1974-2010.1), CNKI (1994-2010.1), VIP (1989-2010.1), CBM (1978-2010.1) were searched by computer. The key words were gastroenteritis, dexamethasone, cimetidine, randomized controlled trials, etc.

Two evaluators read the literature independently. After excluding the test that obviously did not meet the inclusion criteria, they read the full text of the test that

might meet the inclusion criteria to determine whether it really met the inclusion criteria, and then cross-checked it. When they disagreed, they discussed or solicited the opinions of third parties.

2.3 Statistical Analysis Method

The methodological quality of RCT was evaluated according to the bias risk assessment tool recommended in Cochrane System Evaluator Manual 5.0.1.

RevMan 5.0 software provided by Cochrane Collaboration Network was used for statistical analysis. Clinical heterogeneity was analyzed and subgroups were divided according to possible causes. If there is no statistical heterogeneity ($P < 0.1$) among the studies in the subgroup, the fixed effect model should be used; otherwise, if there is heterogeneity ($P < 0.1$), the sources of heterogeneity should be analyzed first. If there is no obvious clinical heterogeneity and no definite source of statistical heterogeneity can be found, the random effect model can be used; if there is obvious clinical or methodological heterogeneity or incomplete data provided, No. When meta-analysis is possible, descriptive analysis is performed. The weighted mean difference (WMD) and its 95% CI were used to represent the continuous variables, and the relative risk (RR) and its 95% CI were used to represent the classified variables. If there is significant statistical heterogeneity due to the different methodological quality of the included studies, the low-quality studies can be removed for sensitivity analysis.

3. Results

3.1 Literature screening results and characteristics of inclusion studies

2258 papers were obtained, including 319 PubMed papers, 293 Cochrane Library papers, 794 Embase papers, 347 CNKI papers, 244 VIP papers and 261 CBM papers. Through reading the title, abstract and full text, 16 RCTs were included, including 6 in English and 10 in Chinese. Six RCTs included 1 333 patients with gastroenteritis, 715 in dexamethasone group and 618 in cimetidine group (Table 1).

Table 1 Basic features of the study

N T/C	Average age (year)		gender(M/F)		Intervention measures		Course of treatment	Baseline comparability	Result
	T	C	T	C	T	C			
19/21	45	34	11/8	12/9	Dexamethasone2.4g/d	cimetidine2g/d	4weeks	yes	①② ③
115/105	38.7±12.9	39.5±14.5	71/44	61/44	Dexamethasone1.5g/d	cimetidine3g/d	8weeks	yes	①③
29/31	42.6±10.3	40.5±14.3	19/10	25/6	Dexamethasone4g/d	cimetidine2g/d	2years	yes	④
44/44	32	33	24/20	23/21	Dexamethasone1g/d	cimetidine2g/d	1year	yes	④
52/57	34.0	34.9	30/22	30/27	Dexamethasone3g/d	cimetidine9g/d	4weeks	yes	①③
19/18	37.6±11.3	36.2±11.2	10/9	7/11	Dexamethasone4g/d	cimetidine4g/d	6weeks	yes	①② ③
25/23	39.2±10.1	37.1±11.2	19/6	17/6	Dexamethasone4g/d	cimetidine4g/d	4weeks	yes	①② ③
61/59	-	-	-	-	Dexamethasone2.4g/d	cimetidine4g/d	6weeks	yes	①② ③
20/20	51±13	48±12	10/10	10/10	Dexamethasone2.4g/d	cimetidine1g,qid	6weeks	yes	①③
30/30	-	-	-	-	Dexamethasone3- 4g/d	cimetidine4- 6g/d	8weeks	yes	①
24/24	-	-	-	-	Dexamethasone4g/d	cimetidine4- 6g/d	8weeks	yes	①
78/72	-	-	-	-	Dexamethasone1.5g/d	cimetidine4g/d	6weeks	yes	①③
32/30	65.16±5.29	65.17±5.08	17/15	17/13	Dexamethasone4g/d	cimetidine4g/d	4weeks	yes	①③
105/30	42.1	43.6	63/42	17/13	Dexamethasone3g/d	cimetidine4g/d	4weeks	yes	①③
36/32	43.6	42.8	20/16	13/19	Dexamethasone3g/d	cimetidine: first four weeks4g/d last four weeks2g/d	8weeks	yes	①③
26/22	36	31	14/12	10/12	Dexamethasone3- 4g/d	cimetidine4- 6g/d	6weeks	yes	①③

T: test group; C: control group; -: undescribed; ① total effective rate; ② complete remission rate; ③ adverse reactions.

3.2 Methodological Quality Assessment Included in the Study

All the 16 RCTs included had methodological quality problems, with moderate quality and moderate probability of bias.

3.3 Meta analysis results

The total effective rate of 14 RCTs reported the total effective rate (marked, effective, remission). There was no statistical heterogeneity among the studies ($I^2=10\%$, $P=0.35$). Therefore, a fixed-effect model was used for meta-analysis. The results showed that there was significant difference in the total effective rate of dexamethasone versus cimetidine in the treatment of acute gastroenteritis [RR =

1.10, 95% CI (1.04, 1.17, P = 0.002]. The total effective rate of dexamethasone group was higher than that of cimetidine group .

Complete remission rate 4 RCTs reported complete remission rate. There was no statistical heterogeneity among the studies ($I^2=0\%$, $P=0.72$). Therefore, a fixed-effect model was used for meta-analysis. The results showed that dexamethasone group was superior to cimetidine group, and the difference between the two groups was statistically significant [RR = 1.82, 95% CI (1.14, 2.91), P = 0.01].

The recurrence rate was reported by 2 RCTs. There was no statistical heterogeneity among the studies ($I^2=0\%$, $P=0.80$). Therefore, a fixed-effect model was used for meta-analysis. The results showed that there was no significant difference in recurrence rate between dexamethasone and cimetidine [RR = 0.86, 95% CI (0.57, 1.29), P = 0.47].

Adverse reactions were reported in 12 RCTs [8,9,12-16,19-23]. There was statistical heterogeneity among the studies ($I^2 = 37\%$, P = 0.09), so the random effect model was used for meta-analysis. The results showed that the adverse reactions of the methadone group were less than those of the cimetidine group, and there was a significant difference between the two groups [RR = 0.56, 95% CI (0.42, 0.73), P < 0.0001].

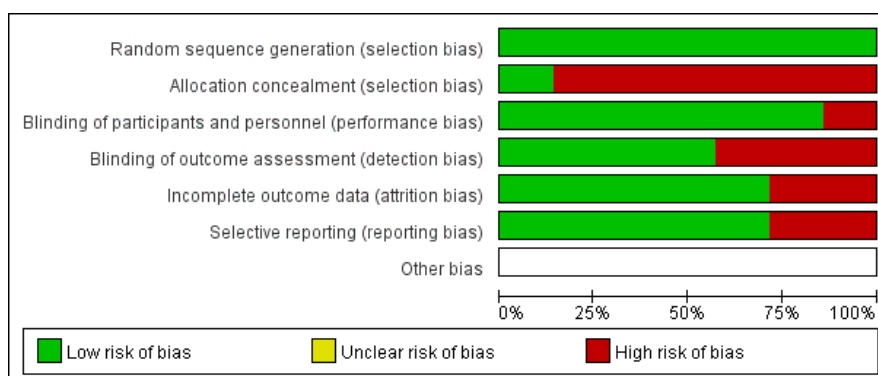


Figure 1. Risk Ratio from Random. 95% C

4. Discussion

4.1 Methodological Quality of Inclusion

The system evaluates L6 RCTs, and the baselines of age and sex are comparable among the studies. Although all the L6 studies were randomized controlled trials, only 3 RCTs [15, 16, 21] used the correct random method, while the remaining 13 RCTs only mentioned randomization and did not describe the specific random method; only 5 RCTs [8, 9, 11-13, 15, 16] used the correct hidden grouping, and the

remaining 11 RCTs did not describe it, so there was a possibility of selective bias. Only seven RCTs [8,9,11-13,15,16] were included in the study. The implementation of the other 11 RCTs was not clear and there was a possibility of measurement bias. According to Cochrane's recommendation of evaluation tools, the quality of 16 RCTs was moderate, and the possibility of bias was moderate.

4.2 Analysis of efficacy and safety

Based on the 16 RCTs included, the results of the system evaluation showed that: (1) dexamethasone was superior to cimetidine in improving the total effective rate of treatment, suggesting that dexamethasone was superior to traditional aminosalicylic acid drugs in the treatment of acute gastroenteritis, which was consistent with Sutherland 61's conclusion; and (2) in the complete remission rate, dexamethasone was also superior to cimetidine. It showed a greater advantage and could effectively alleviate the symptoms and signs of patients with acute gastroenteritis; (3) the recurrence rate was similar, indicating that dexamethasone had no significant advantage in the long-term treatment of acute gastroenteritis; (4) no serious adverse reactions were reported in the included studies. Meta-analysis showed that the incidence of adverse reactions of mesatozine was lower, suggesting that dexamethasone was effective in the treatment of acute gastroenteritis. It has better safety and less side effects. This is inconsistent with Sutherland's report, possibly due to racial differences or differences in the inclusion literature.

4.3 Limitations of System Evaluation and Future Research

There are some shortcomings in the methodological quality of the system evaluation, such as unclear random method, unclear allocation and unclear implementation of blind method, which affect the authenticity of the results. It is suggested that proper random methods, allocation concealment schemes and delaying methods should be adopted in RCT in the future to report missing visits so as to reduce various bias such as selectivity, practicability, measurement and loss. In addition, the incorporation of RCT in dosage is not uniform, the duration of treatment varies, and no long-term follow-up and report of adverse reactions, suggesting that future clinical trials should pay attention to the unification of drug dosage, standardize observation time, and long-term follow-up report of possible serious adverse reactions of drugs. In conclusion, whether dexamethasone is superior to cimetidine in the treatment of acute gastroenteritis remains to be carried out in a large randomized controlled trial with strict design and long-term follow-up to provide scientific evidence for clinical practice.

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