Original Article

A systematic review and meta-analysis: effects of glucocorticoids on rheumatoid arthritis and systemic lupus erythematosus

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Background: Meta-analysis was performed to explore the efficacy of glucocorticoids in the treatment of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), to provide a theoretical basis for the clinical treatment of patients.

Methods: Relevant literatures from the establishment of the database to December 31, 2020, were searched from databases such as PubMed. The literatures with randomized controlled trial of the clinical efficacy of glucocorticoids in the treatment of RA and SLE were screened for meta-analysis.

Results: Eleven documents were included, including 1,298 participants. It was found that the cardiovascular system [mean difference (MD) =1.23; 95% confidence interval (CI): 0.64 to 2.34; Z=0.62; P=0.53], respiratory system (MD =1.87; 95% CI: −0.66 to 5.29; Z=1.18; P=0.24), nervous system (MD =1.22; 95% CI: 0.25–5.84; Z=0.25; P=0.8), visual impairment (MD =1.41; 95% CI: 0.79–2.52; Z=1.15; P=0.25), endocrine system (MD =8.53; 95% CI: 2.71–26.88; Z=3.66; P=0.0003), digestive system (MD =1.41; 95% CI: 0.76–2.63; Z=1.09; P=0.28), genitourinary system (MD =1.06; 95% CI: 0.35–3.17; Z=0.1; P=0.92), blood system (MD =2.96; 95% CI: 0.62–14.26; Z=1.35; P=0.18), Z=0.48; P=0.63), infection status (MD =1.36; 95% CI: 0.98–1.87; Z=1.86; P=0.06), clinical efficacy (MD =1.79; 95% CI: 1.27–2.52; Z=3.32; P=0.0009), pain (MD =1.16; 95% CI: 0.76–1.78; Z=0.68; P=0.5), and joint swelling score (MD =0.03; 95% CI: −0.38 to 0.45; Z=0.15; P=0.88) of experimental group after treatment were all superior versus controls. However, the skin and mucous membranes (MD =0.87; 95% CI: 0.55–1.37; Z=0.61; P=0.54), musculoskeletal (MD =0.85; 95% CI: 0.43–1.66; Z=0.48; P=0.63), radiation injury (MD =−1.93; 95% CI: −3.68 to −0.18; Z=2.17; P=0.03), and C-reactive protein (CRP) level (MD =−8.66; 95% CI: −10.16 to −7.16; Z=11.34; P<0.00001) of experimental group were inferior to those of control group.

Discussion: Glucocorticoids in the treatment of RA and SLE can improve the clinical efficacy, but it was easy to cause multiple system adverse reactions. Therefore, the clinical treatment should follow the doctor's advice.

Keywords: Glucocorticoid; placebo; rheumatoid arthritis; systemic lupus erythematosus; clinical efficacy

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Introduction

Rheumatoid arthritis (RA) is a chronic and systemic disease of inflammatory synovitis with unknown etiology. Its prominent clinical manifestation is recurrent symmetrical multiple arthritis, with the hands, wrists, feet, and other joints most often affected. Early manifestations are redness, swelling, heat, pain, and dysfunction. Later, joint may appear different degrees of rigidity and deformity, and there

is bone and skeletal muscle atrophy. RA is a disease with a high rate of disability (1). The incidence of RA is about 1% in the world and 0.4% in China. Generally, RA occurs between 25 and 55 years old, and the incidence of RA in women is 2–3 times higher than that in men, which can seriously affect the heart, lungs, kidneys, and other related organs. So-called RA is not just inflammatory changes in the joints, but systemic and widespread lesions (2). Systemic lupus erythematosus (SLE) is an autoimmune inflammatory connective tissue disease that affects multiple organs, which is also a noninfectious, nonneoplastic, persistent systemic disease that occurs mostly in young women. Its immune characteristics include lupus erythematosus cells (LEC), antinuclear antibodies (ANA), immune complexes (IC), decreased complement levels, immunoglobulin and complement deposition in tissues, anticoagulants in circulation, and other autoantibodies. The clinical symptoms of SLE involve almost every system and organ in the body. The clinical features are multiple organ damage, complex and diverse, and the disease alternately occurs to relieve and worsen. In addition, the initial symptoms are not typical. Some patients may have no skin manifestations throughout the course of the disease. Early, mild, and atypical cases of SLE are increasing (3). Skin and mucous membrane damage mainly occurs in patients after illness, and some patients have skeletal muscle, heart, and other involvement manifestations (4). The principles of clinical treatment of the above two diseases are preventing infection, protecting body function, and reducing inflammation (5).

Traditional treatment is limited to symptomatic treatment and immunosuppressive therapy is used only when severe complications occur. The most common clinical treatment drug is glucocorticoid, which is a type of regulatory molecule in the body. It regulates the development, growth, metabolism, and immune function. It is widely used and effective anti-inflammatory and immunosuppressive agent. Glucocorticoids are often the first choice in emergency or critical situations (6), which can prevent the occurrence of the immune inflammatory response and pathological immune response and are effective for almost any type of allergic disease. However, if the use of this drug is prolonged, its adverse reactions become obvious.

At present, Meta-analysis studies on glucocorticoid therapy for RA mainly focus on the effect on bone mineral density and other indicators of patients, as well as the effect on the complication rate after treatment of SLE. There are relatively few meta-studies on the efficacy and safety of glucocorticoids in patients with RA and SLE. To further study the efficacy of glucocorticoids, clinical randomized controlled studies of glucocorticoids in the treatment of RA and SLE were screened in this work. Meta-analysis was performed to conduct a systematic analysis of curative effect, to evaluate the clinical efficacy of glucocorticoids in the treatment of RA and SLE.

We present the following article in accordance with the RPISMA reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1485).

Methods

Inclusion and exclusion criteria of documents

Inclusion criteria: (I) the participants were patients who had been clinically diagnosed with RA and SLE; (II) randomized controlled trial published in English databases; (III) the treatment method of experimental group was glucocorticoids, and the intervention measure of controls was placebo treatment; the baseline data were comparable between group; (IV) those who failed conservative treatment; (V) the evaluation indicators of the research outcome included postoperative satisfaction of patients and adverse reactions.

Exclusion criteria: (I) non-RCT studies such as retrospective studies, case reports, and cohort studies; (II) research objects were animals, cells, and so on; (III) unpublished documents such as degree thesis or non-English documents; (IV) operation method of experimental group was non-glucocorticoid or other treatment; (V) research subject was the trial of RA and SLE combined with other diseases; (VI) research data were incomplete and the corresponding effect indicator could not be calculated.

Document retrieval

We searched PubMed, Embase, MEDLINE, Ovid, Springer, and Web of Science. The search deadline was 31 December 2020. Documents including RCTs of glucocorticoids in the treatment of RA and SLE were screened. The search terms consisted of subject terms and keywords, including “Glucocorticoid”, “Rheumatoid arthritis”, “Systemic lupus erythematosus”, and “Clinical efficacy”. Either “And” or “or” was used for joint search among search terms, and the document search was carried out by two researchers independently.

Document screening

Document screening was performed by two researchers independently. After finishing the document search, NoteExpress 3.2 (Aegean Software Corp., Beijing, China) was used to establish a document database and the retrieved documents were checked for duplicate documents. After elimination of duplicate documents, the remaining documents were manually screened by two researchers. Screening involved reading the titles and abstracts of the articles first, and elimination of documents that obviously unqualified. Then, full documents were read to determine whether they would be included for meta-analysis. During screening, any disagreement was resolved through discussion. A third party was invited to decide if a consensus was still not reached.

Data extraction

The two researchers made a data record table regarding the basic information of the document, participant characteristics, intervention measures, outcome indicators, and bias evaluation. The data were independently pre-extracted from the documents. The extraction process was carried out independently by the two researchers. The extraction was then cross-examined. During the extraction process, if disagreement occurred, it was discussed and resolved between the two researchers. If consensus weren't reached, a third party was contacted to decide after arbitration. The data extracted from the included documents mainly included: (I) document title, first author (only one name), time of publication, and the research area; (II) participants' age, sample size, and baseline comparability; (III) research plan design, implementations, intervention measures and control measures, and anti-bias measures; (IV) outcome indicators and data.

Quality assessment

The bias risk assessment criteria provided in the Cochrane Handbook for Systematic Reviews of Intervention 5.0.2 were adopted. The evaluation tool evaluated the quality of the included document from the generation of random sequences, blinding for patients and trial personnel, blinding for outcome assessors, whether research data was complete, whether there were selective reporting results, and whether there were other sources of bias. Any discrepancies between researchers regarding document evaluation were resolved through discussion, or a third party was invited to arbitrate.

Statistical analysis

The Cochrane Handbook for Systematic Reviews of Interventions 5.0.2 was adopted to evaluate the risk of document bias. STATA 11.0 (StataCorp., College Station, TX, USA) was employed to merge the statistics of the included documents. Review Manager (RevMan) 5.3 (Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014) was employed to meta-analyze the combined statistics and draw forest and funnel plots. Binary variables in count data took relative risk (RR) as the effect size, and the 95% CI was calculated. For continuous variables in measurement data, if the detection indicator units were the same, the weighted mean difference (MD) was taken as the effect size. If the detection indicator units were not the same, the standardized mean difference (SMD) was taken as the effect size. When research results of various documents could be combined, the document was meta-analyzed. The I^2 test was used to evaluate the heterogeneity of the included documents. The greater the I^2, the greater the heterogeneity. If I^2>50% and the source of heterogeneity could not be explained, the random effects model (REM) was adopted to combine effect sizes for meta-analysis. If I^2<50%, which meant that the heterogeneity of the document was good, the fixed effects model (FEM) was used to combine effect size for meta-analysis. If the research data were less than 2 items and meta-analysis could not be performed, descriptive analysis was made. The combined effect size test adopted Mann-Whitney U test and 95% CI. The U test result was expressed as a P value, and P<0.05 meant remarkable differences. Binary variables were tested with 95% CI. 95% CI >1 or <1 meant considerable differences. 95% CI containing 1 meant that the difference was not substantial. Continuous variables were tested by 95% test. 95% CI >0 or <0 meant remarkable differences.

Results

Document search results

A total of 1,057 documents were found upon preliminary inspection. Among these, there were 531 related documents from PubMed, 261 from Embase, 120 from MEDLINE, 47 from Springer, 38 from Ovid, and 60 from Web of Science. After the preliminary search was finished, all 1,057 documents were imported into NoteExpress 3.2, and 185 documents remained after elimination of duplicates. Then, the two researchers read the titles and abstracts of the remaining documents and screened the documents.

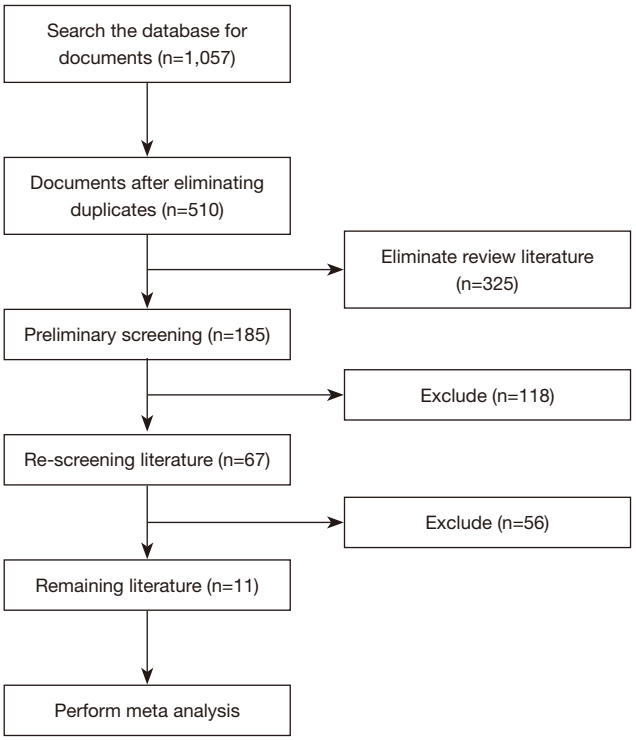

Figure 1 Document retrieval process.

After the screening, 67 documents remained. Finally, the two researchers read and cross-examined the full text of the document, followed by screening and exclusion where appropriate. Eleven documents were included in this study, all of which were publicly published RCT studies, published before 2020 (*Figure 1*, *Table 1*). There were 1,298 study subjects, and baseline data such as the age between groups were comparable.

Bias risk assessment

The Cochrane Handbook for Systematic Reviews of Interventions 5.0.2 was used to evaluate the risk of bias. We employed RevMan 5.3 to output the risk of bias map. The risk of bias assessment items included the following: (I) random sequence generation. The 11 documents (7-17) included in this study all described the specific grouping method as "according to different surgical treatments" and were suggested as low risk. (II) Allocation concealment. None of these studies mentioned whether there was "allocation concealment", suggesting unclear risk. (III) Participant blinding. A total of 7 of the 11 documents mentioned that "patients were aware and provided written informed consent" but did not mention whether blinding method was used for the experimenters, suggesting unclear risks. (IV) Blinding of the outcome assessor. All 11 documents did not mention whether outcome assessor was blinded, suggesting that the risk was not clear. (V) Result data integrity. All the outcome data were complete, suggesting low risk. (VI) Selective reporting. There was no selective reporting among the 11 documents, indicating low risk. (VII) Other risk of bias. The number of participants in experimental group and control group was inconsistent in 1 document (16), indicating a high risk, and it could not be determined whether there were other biases in the other 10 documents, suggesting unclear risk (*Figures 2,3*).

Cardiovascular system

Four documents analyzed the cardiovascular system of participants after treatment. A total of 565 patients with RA and SLE were included, with 278 cases in experimental group and 287 cases as controls. Heterogeneity test (I^2=49%, P=0.12) revealed that the heterogeneity among the studies was small, so FEM was utilized for analysis, and the analysis results were presented in *Figure 4*. The combined effect showed that (MD =1.23; 95% CI: 0.64–2.34; Z=0.62; P=0.53). The diamond in the forest plot was on the right of vertical line (VL), which suggested that the incidence of adverse effects of the cardiovascular system in patients with RA and SLE after glucocorticoid treatment was higher versus control group.

Respiratory system

Four studies in this study analyzed the respiratory system of participants. 493 patients with RA and SLE were included, there were 248 in experimental group and 245 in control. Heterogeneity test results (I^2=0%, P=0.64) indicated no heterogeneity among the studies, so FEM was adopted, and the analysis results are illustrated in *Figure 5*. The combined effect was (MD =1.87; 95% CI: −0.66 to 5.29; Z=1.18; P=0.24). The diamond in the forest plot was on the right of VL, indicating that the incidence of adverse respiratory reactions in patients with RA and SLE after glucocorticoid treatment was superior to control group.

Nervous system

Four literatures in this study analyzed the nervous system of participants. Five hundred and thirty-two patients with RA and SLE were included, 268 were in experimental group

Table 1 Basic features of included documents

First author	Year of publication	Group	Sample size	Counter measure
Fortin	2008	Experimental	41	Glucocorticoid
		Control	45	Placebo
Everdingen	2002	Experimental	40	Glucocorticoid
		Control	41	Placebo
Capell	2004	Experimental	84	Glucocorticoid
		Control	83	Placebo
Choy	2008	Experimental	117	Glucocorticoid
		Control	115	Placebo
Wassenberg	2005	Experimental	80	Glucocorticoid
		Control	86	Placebo
Islam	2012	Experimental	13	Glucocorticoid
		Control	24	Placebo
Kirwan	1995	Experimental	61	Glucocorticoid
		Control	67	Placebo
Goes	2013	Experimental	117	Glucocorticoid
		Control	119	Placebo
Miyawaki	2013	Experimental	30	Glucocorticoid
		Control	18	Placebo
Everdingen	2003	Experimental	40	Glucocorticoid
		Control	40	Placebo
Carneiro	1999	Experimental	18	Glucocorticoid
		Control	19	Placebo

and 264 in control. The heterogeneity test results (I^2=58%, P=0.07) suggested certain degree of heterogeneity, so REM was utilized for analysis, with the results displayed in *Figure 6*. It was revealed that the combined effect was (MD =1.22; 95% CI: 0.25–5.84; Z=0.25; P=0.8). The diamond in the forest plot was on the right of VL, which meant that the incidence of neurological adverse reactions in patients with RA and SLE after glucocorticoid treatment was higher relative to control group.

Visual damage

In this study, five studies analyzed the visual impairment of participants. Six hundred and thirteen patients with RA and SLE were included, with 308 in experimental group and 205 as controls. The heterogeneity test results (I^2=0%, P=0.89) illustrated that there was no heterogeneity among the studies, so FEM was adopted for analysis. The combined effect was (MD =1.41; 95% CI: 0.79–2.52; Z=1.15; P=0.25) (*Figure 7*). The diamond in the forest plot was located on the right of VL, showing that the visual impairment of patients with RA and SLE after glucocorticoid treatment was superior to that of controls.

Endocrine system

In this study, four documents analyzed the endocrine system of participants. Three hundred seventy cases of RA and SLE patients were included in this meta-analysis, with 179 cases in experimental group and 191 cases as controls.

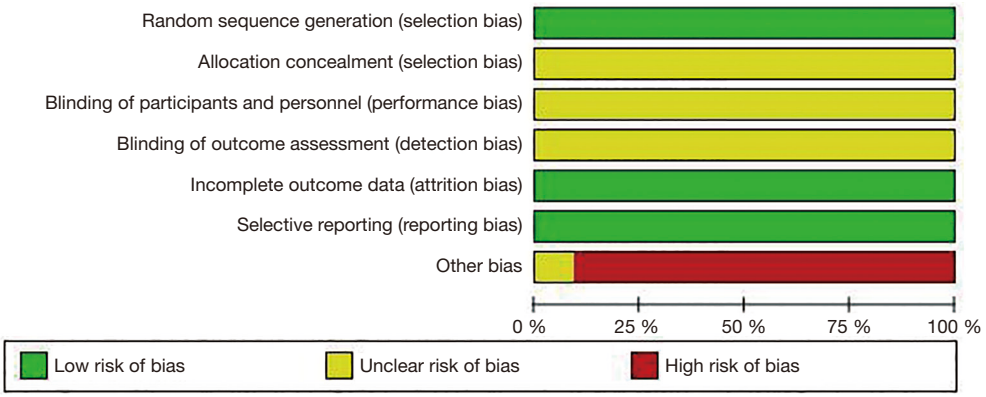

Figure 2 Risk bias evaluation results.

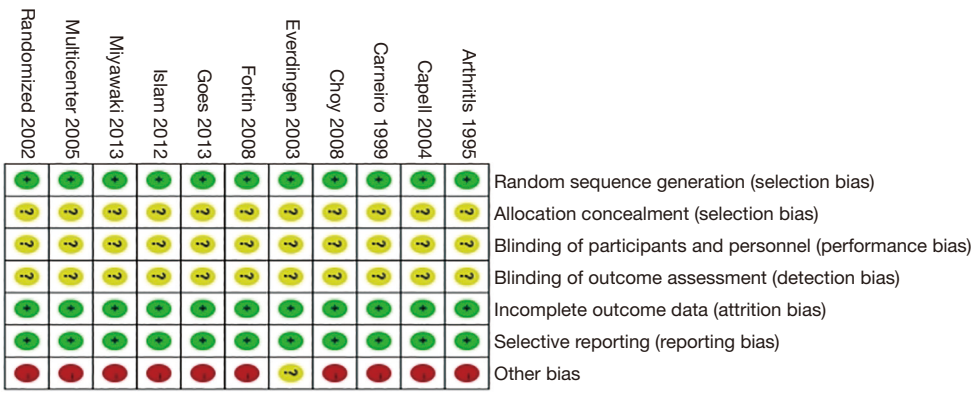

Figure 3 Risk assessment of bias in included documents.

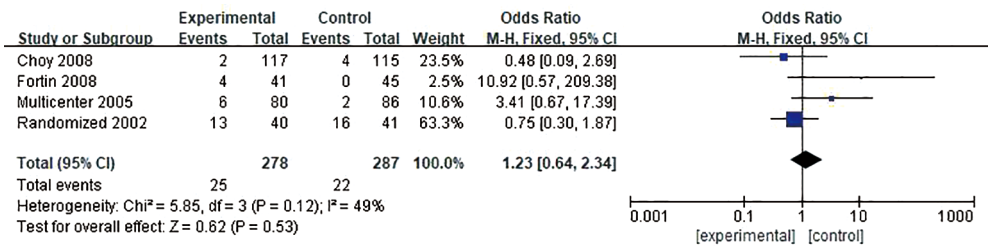

Figure 4 Forest plot of adverse effects of glucocorticoid treatment on cardiovascular system. CI, confidence interval; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

The heterogeneity test results (I^2=0%, P=0.47) found no heterogeneity among the studies, so FEM was utilized, and the results are presented in *Figure 8*. The combined effect was (MD =8.53; 95% CI: 2.71–26.88; Z=3.66; P=0.0003). The diamond in the forest plot was located on the right of VL, which suggested that the incidence of adverse endocrine system reactions in patients with RA and SLE after glucocorticoid treatment was higher versus controls.

Digestive system

Five literatures analyzed the digestive system of participants. Six hundred and two patients with RA and SLE were included, with 291 in experimental group and 311 as

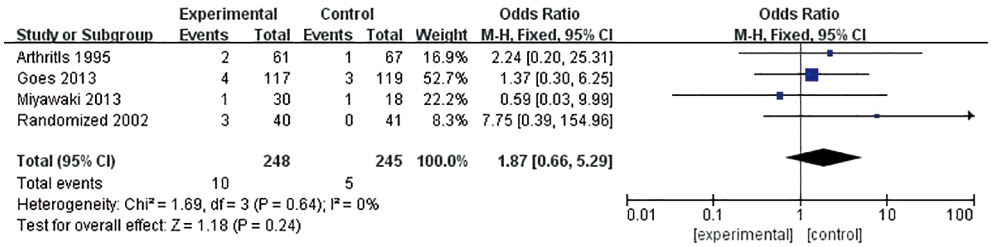

Figure 5 Forest plot of adverse effects of glucocorticoid treatment on the cardiovascular system.

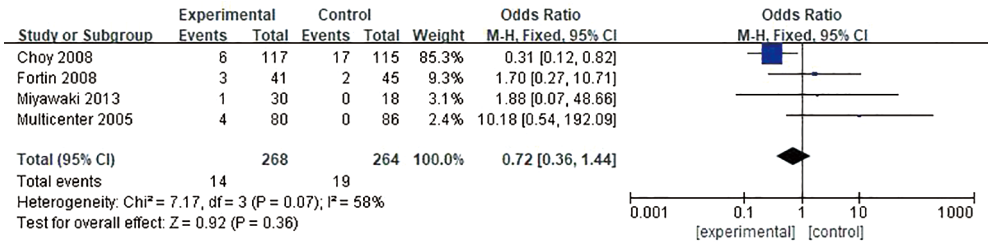

Figure 6 Forest plot of adverse reactions of the nervous system.

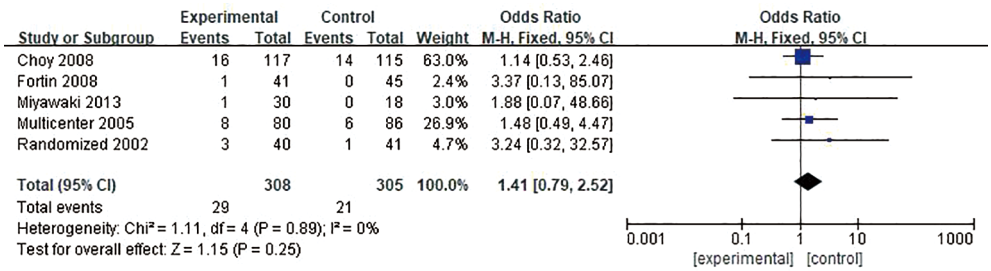

Figure 7 Forest plot of glucocorticoid treatment of visual impairment.

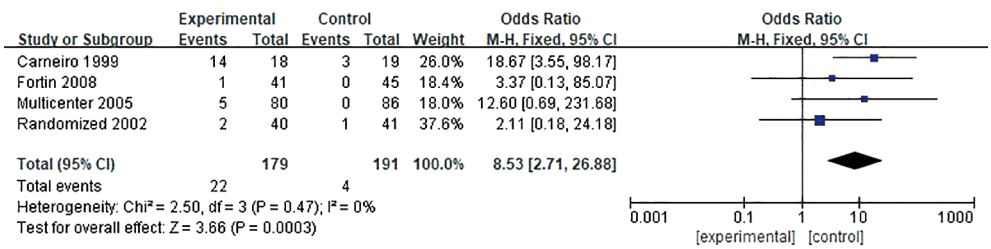

Figure 8 Forest plot of adverse effects on the endocrine system.

controls. The heterogeneity test results (I^2=57%, P=0.05) revealed heterogeneity among the studies, and REM was adopted for analysis (*Figure 9*). The combined effect was (MD =1.41; 95% CI: 0.76–2.63; Z=1.09; P=0.28). The diamond in the forest plot was on the right of VL, showing that incidence of adverse digestive system reactions in patients with RA and SLE after glucocorticoid treatment was superior to control group.

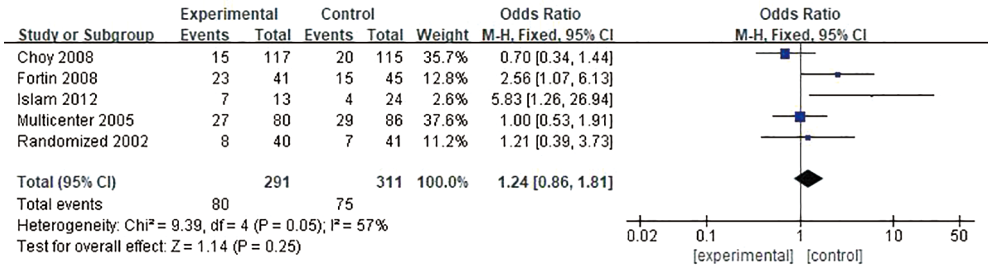

Figure 9 Forest plot of adverse digestive system reactions.

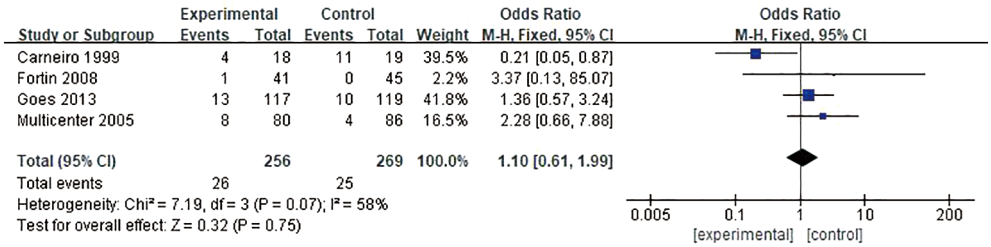

Figure 10 Forest plot of adverse reactions in the urogenital system.

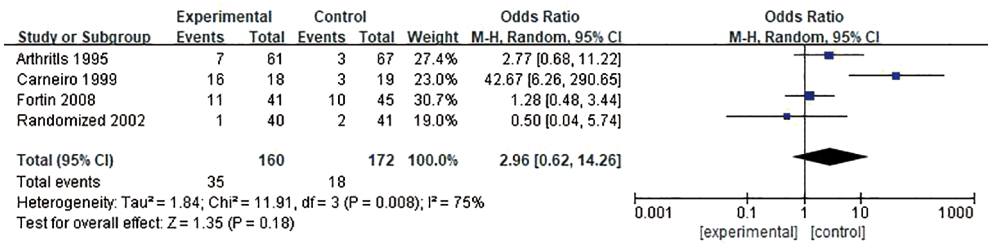

Figure 11 Forest plot of adverse effects on the blood system.

Genitourinary system

Four documents analyzed the genitourinary system of participants. Five hundred and twenty-five patients with RA and SLE were included. Among which, 256 were in experimental group and 269 in control. The heterogeneity test results (I^2=58%, P=0.07) revealed a certain degree of heterogeneity. Therefore, REM was utilized, and the results are illustrated in *Figure 10*. The combined effect showed that (MD =1.06; 95% CI: 0.35–3.17; Z=0.1; P=0.92). The diamond in the forest plot was on the middle of the VL, which meant that the incidence of urogenital adverse reactions after glucocorticoid treatment of RA and SLE patients was greatly lower relative to controls.

The blood system

In this study, four studies analyzed the blood system of participants. Three hundred thirty two patients with RA and SLE were included, with 160 in experimental group and 172 as controls. The heterogeneity test results (I^2=75%, P=0.18) presented certain heterogeneity among the studies. Therefore, REM was utilized, and the analysis results are illustrated in *Figure 11*. It was found that combined effect was (MD =2.96; 95% CI: 0.62–14.26; Z=1.35; P=0.18). The diamond in the forest plots was on the right of VL, showing that the incidence of hematological adverse reactions in patients with RA and SLE after glucocorticoid treatment was superior to that of

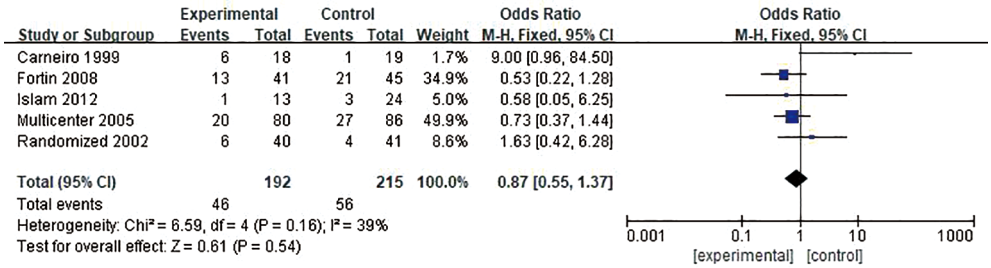

Figure 12 Forest plot of skin and mucosal damage.

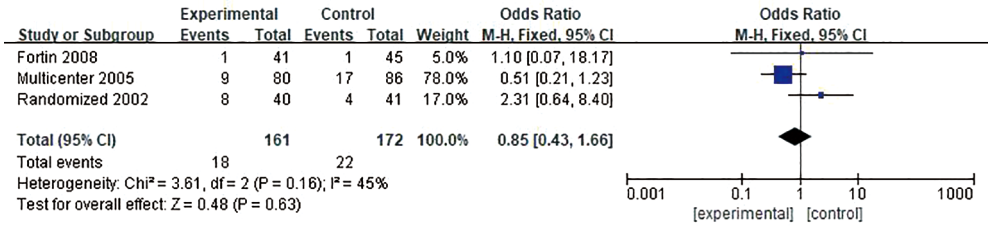

Figure 13 Forest plot of musculoskeletal adverse reactions.

control group.

The skin mucous membrane

In this study, five studies analyzed the skin and mucous membranes of participants. Four hundred and seven patients with RA and SLE were included. There were 192 in experimental group and 215 in control. The heterogeneity test results (I^2=39%, P=0.16) showed small heterogeneity among the studies. Then, FEM was adopted, and the analysis results are presented in *Figure 12*. Combined effect was (MD =0.87; 95% CI: 0.55–1.37; Z=0.61; P=0.54). The diamond in the forest plot was located to the left of the VL, suggesting that the skin and mucosal damage of patients with RA and SLE after glucocorticoid treatment was lower versus controls.

Musculoskeletal

Three literatures analyzed the musculoskeletal condition of participants. Three hundred thirty three patients with RA and SLE were included, with 161 in experimental group and 172 as controls. The heterogeneity test results (I^2=45%, P=0.16) revealed that the heterogeneity among the studies was small. Therefore, FEM was adopted (*Figure 13*). The combined effect revealed that (MD =0.85; 95% CI: 0.43–1.66; Z=0.48; P=0.63). The diamond in the forest plot was located to the left of the VL, which meant that the incidence of musculoskeletal adverse reactions in patients with RA and SLE after glucocorticoid treatment was lower than that in controls.

Infection

Six documents analyzed the infection of participants. 929 patients with RA and SLE were included, with 456 in experimental group and 473 as controls. The heterogeneity test results (I^2=0%, P=0.87) showed no heterogeneity among the studies; therefore, FEM was adopted, and the analysis results are illustrated in *Figure 14*. The combined effect showed that (MD =1.36; 95% CI: 0.98–1.87; Z=1.86; P=0.06). The diamond in the forest plot was on the right of VL, which indicated that the infection rate of patients with RA and SLE after glucocorticoid treatment was higher in contrast to controls.

Radiation damage

Three documents analyzed the radiation injury of patients. 375 patients with RA and SLE were included, with 181 cases in experimental group and 194 as controls. Heterogeneity test results (I^2=83%, P=0.002) found certain heterogeneity among

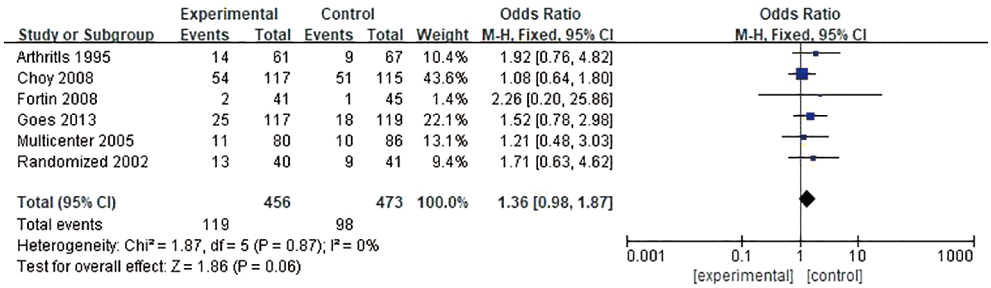

Figure 14 Forest plot of infection.

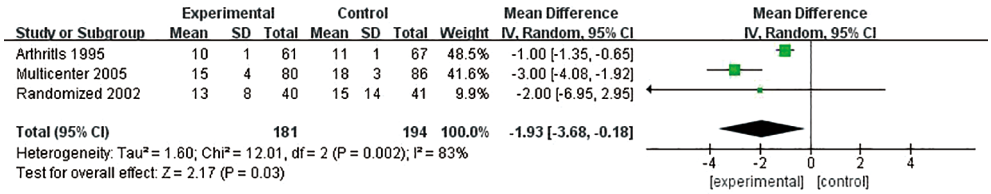

Figure 15 Forest plot of incidence of radiation injury.

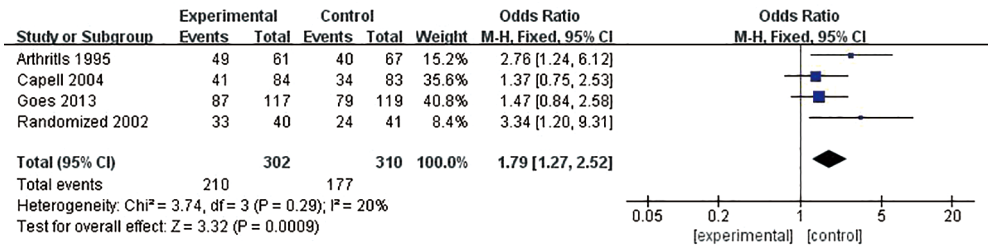

Figure 16 Forest plot of the clinical efficacy of glucocorticoids in the treatment of RA and SLE patients. RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

the studies. Thus, REM was utilized for analysis (*Figure 15*). It was revealed that combined effect was (MD =−1.93; 95% CI: −3.68 to −0.18; Z=2.17; P=0.03). The diamond in the forest plot was on the left of VL, revealing that the incidence of radiation injury in patients with RA and SLE after glucocorticoid treatment was inferior to that in control group.

Clinical curative effect

Four documents analyzed the clinical efficacy of participants. Six hundred and twelve patients with RA and SLE were included. Among which, 302 cases were in experimental group and 310 in control. Heterogeneity test results (I^2=57%, P=0.05) showed heterogeneity among the documents. REM was adopted, and the analysis results are presented in *Figure 16*. Combined effect was (MD =1.79; 95% CI: 1.27–2.52; Z=3.32; P=0.0009). The diamond in the forest plot was on the right of VL, suggesting that the clinical efficacy of glucocorticoids in the treatment of RA and SLE patients was superior to that of controls.

Pain

Three articles analyzed participant pain. 350 patients with RA and SLE were included, with 175 cases in experimental and control group each. The heterogeneity test results (I^2=29%, P=0.25) indicated that the heterogeneity among the studies was small. FEM was adopted for meta-analysis (*Figure 17*). It was revealed

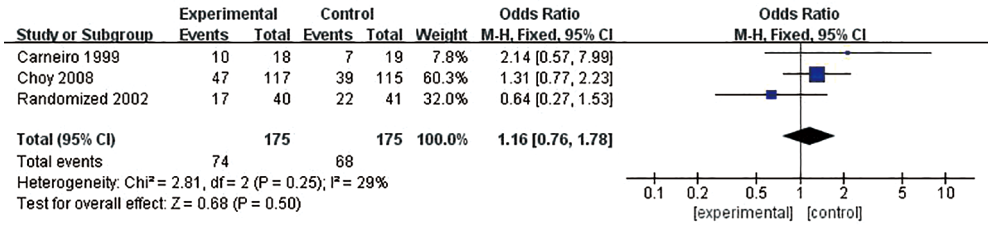

Figure 17 Forest plot of pain.

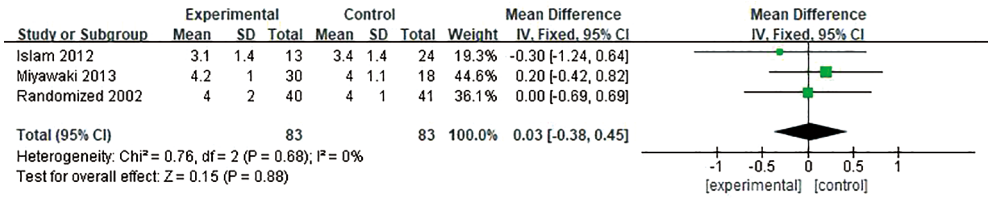

Figure 18 Forest plot of joint swelling scores.

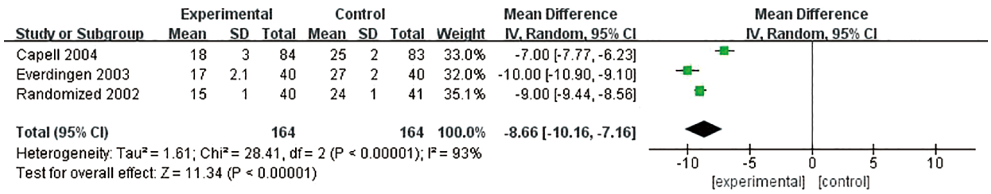

Figure 19 Forest plot of CRP levels. CRP, C-reactive protein.

that combined effect was (MD =1.16; 95% CI: 0.76–1.78; Z=0.68; P=0.5). The diamond in the forest plot was on the right of VL, which meant that the patients with RA and SLE had more pain after glucocorticoid treatment than control group.

Joint swelling score

Three studies analyzed participants' joint swelling scores. 166 patients with RA and SLE were included. There were 83 cases in experimental and control group each. The heterogeneity test results (I^2=0%, P=0.68) suggested that the heterogeneity among the studies was relatively small. FEM was utilized for analysis (*Figure 18*). The combined effect was (MD =0.03; 95% CI: −0.38 to 0.45; Z=0.15; P=0.88). The diamond in the forest plot was located on the right of VL, showing that the joint swelling scores of patients with RA and SLE after glucocorticoid treatment were higher versus control group.

C-reactive protein levels

Three documents analyzed the levels of C-reactive protein (CRP) in participants. 328 patients with RA and SLE were included. There were 164 cases in experimental group and control group each. The heterogeneity test result (I^2=93%, P<0.00001) indicated that there was heterogeneity. REM was utilized for analysis (*Figure 19*). It was found that combined effect was (MD =−8.66; 95% CI: −10.16 to −7.16; Z=11.34; P<0.00001). The diamond in the forest plot was on the right of VL, which meant that the CRP level of patients with RA and SLE after glucocorticoid treatment was inferior to that of controls.

Publication bias analysis

Using Rev Man 5.3, the results of glucocorticoid treatment for RA and SLE and postoperative adverse reaction indicators were analyzed for publication bias, as shown in *Figure 20*. The results showed that the occurrences of adverse

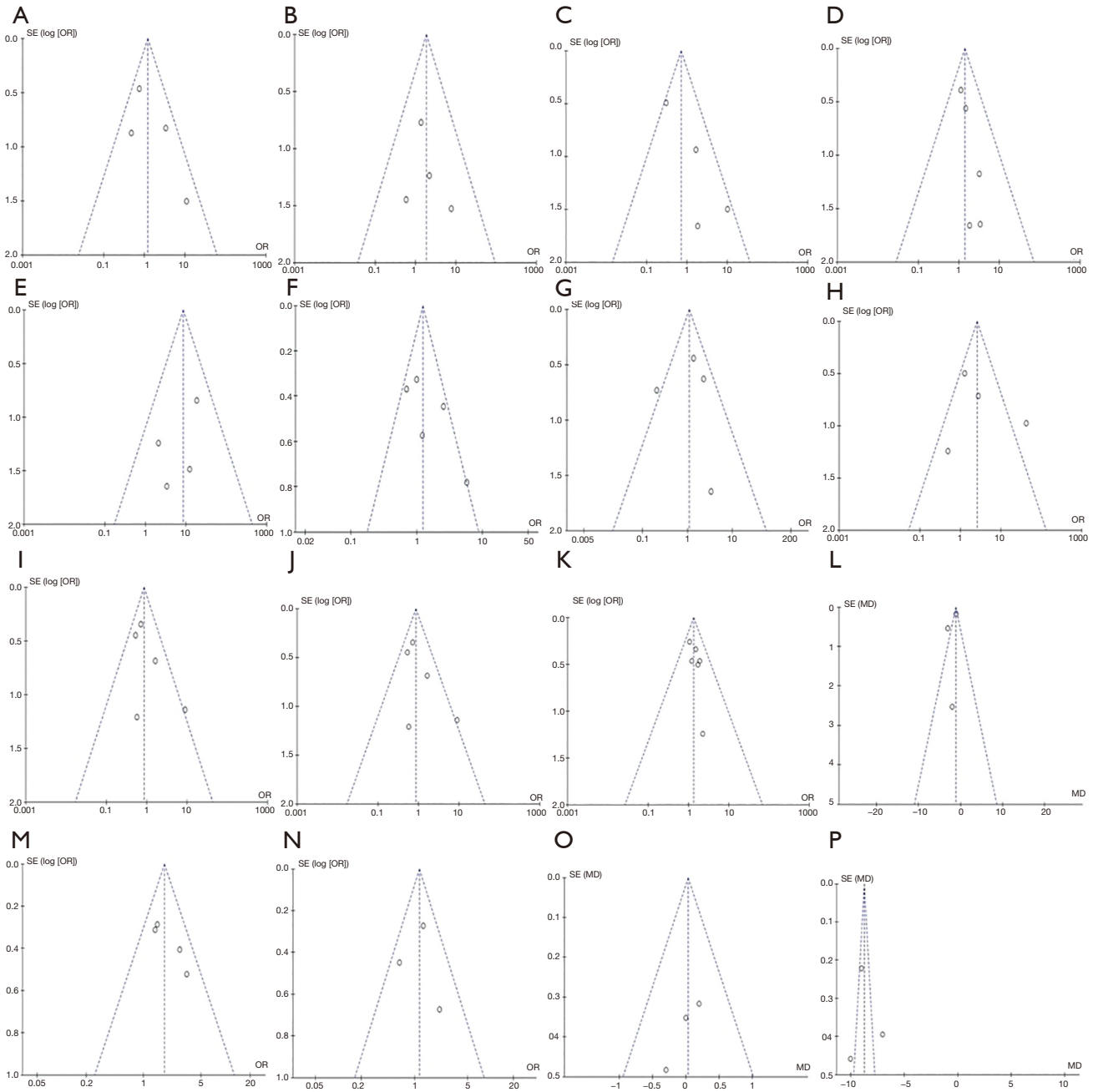

Figure 20 Funnel plot of various evaluation indicators. (A) Cardiovascular system disease; (B) respiratory system, (C) nervous system; (D) visual impairment; (E) endocrine system; (F) digestive system; (G) genitourinary system; (H) blood system, (I) skin mucous membrane; (J) musculoskeletal; (K) infection; (L) radiation injury; (M) symptom improvement; (N) pain; (O) swelling joint score; (P) CRP level. CRP, C-reactive protein.

reactions in participants' cardiovascular system, respiratory system, nervous system, visual impairment, endocrine system, digestive system, urogenital system, blood system, skin and mucous membranes, musculoskeletal, infection, radiation injury, symptom improvement, pain, and swollen joints score were basically distributed within the credible interval, and the document bias was low. In funnel plot of participants' CRP levels, some scattered points were scattered outside the

credible interval, and the distribution was relatively scattered, indicating certain publication bias in the included documents.

Discussion

RA is a systemic and heterogeneous autoimmune disease, mainly characterized by symmetric multiarticular inflammation. As the disease progresses, the patient gradually develops chronic inflammation of the joints, leading to destruction of the joints and bone, swelling and even deformity of the joints, and ultimately the loss of function. SLE is a chronic, multiple organ-involved autoimmune disease. In the past two decades, great progress has been made in the treatment of SLE, and the survival rate of patients has improved significantly. However, complications such as osteonecrosis, osteoporosis, atherosclerosis, and lacunar dysfunction may occur during the treatment of SLE. Osteonecrosis is one of the most serious complications of SLE. Studies found that SLE is more prone to osteonecrosis than other autoimmune diseases such as RA. Both RA and SLE are typical autoimmune diseases. From the results of biochemical examinations, rheumatoid factor can be positive in both RA and SLE. From the perspective of clinical manifestations, joint swelling and pain can occur in both diseases (18-20). There are similarities in the clinical treatment of RA and SLE, among which glucocorticoid treatment is essential (21). As a type of regulatory molecule, it can treat primary or secondary (pituitary) adrenal insufficiency, and physiological doses of hydrocortisone or cortisone are taken as supplement or replacement therapy (22). Glucocorticoid is still the drug of choice in the treatment of primary nephrotic syndrome. Due to the pharmacological characteristics of glucocorticoid, it has a great negative effect on the bone metabolism of patients and may certainly lead to osteoporosis. Glucocorticoid can also be used for various allergic diseases, such as angioedema, acute urticaria, contact dermatitis, serum sickness, anaphylactic shock, severe blood transfusion reaction, thrombocytopenic purpura, and severe bronchial asthma (23,24). However, the drug has significant side effects, which can reduce the body's immunity and hinder tissue repair and healing. For children, care should be taken with the administration of glucocorticoids (25).

Current studies on glucocorticoid in the treatment of RA and SLE have limitations such as small sample size and different efficacy evaluation indexes. To systematically evaluate the clinical efficacy of glucocorticoids in the treatment of RA and SLE, eleven studies were included in this meta-analysis. The results showed that, except for the diamond plots of skin and mucous membranes, musculoskeletal, radiation damage, and CRP, which are distributed on the left, the diamond plots of other indicators were on the right side. In addition, it was found that the therapeutic effect of glucocorticoid was higher in experimental group than that of control group, which also confirmed the effect of glucocorticoid. Studies have suggested that glucocorticoids, as cell cycle non-specific drugs, are characterized by a dose-dependent effect, meaning that increasing the dose would increase the efficacy, but at the same time the toxicity would also increase. Therefore, intermittent administration of large doses is the best choice for therapeutic effects (26). If patients need to take the medicine for prolonged periods because of their own disease situation, they must consult with a skilled physician to ascertain their minimum maintenance dose. The long-term use of glucocorticoids is damaging to the body (27). Patients who take long-term medications need to closely monitor whether adrenal glucocorticoids are causing abnormal reactions in the body. During the medication period, blood pressure and blood lipids should also be checked regularly, along with routine eye checks (28-30). When glucocorticoids are adopted, it is advised to supplement calcium and vitamin D, because the drug may affect bone density and development. Therefore, if calcium and vitamin D are not supplemented simultaneously, osteoporosis and fractures are likely to occur (31).

Conclusions

In this study, eleven documents were included for meta-analysis of glucocorticoid treatment of RA and SLE, involving 12,982 patients with RA and SLE. It was revealed that glucocorticoids can significantly improve the clinical efficacy of patients compared with placebo, but that it also brought different degrees of side effects to patients, reflecting the duality of glucocorticoid therapy. This study had some limitations, which was manifested in the large publication bias of some documents. In addition, due to differences in the research directions, some indicators contained a few samples, and the results were not sufficiently accurate. Therefore, in future work, it remains necessary to recruit larger samples and high-quality glucocorticoids to verify its clinical effects for RA and SLE.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1485). 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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