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Review Article

The effect of methotrexate in combination with mifepristone on ectopic pregnancy: a meta-analysis

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Abstract: Background: Methotrexate and methotrexate combined different doses of mifepristone are mainly applied in ectopic pregnancy. To compare their effects and confirm the effective measures, we performed this meta-analysis. Methods: Thirty-six randomized controlled studies (divided into 3 sub-studies) comparing the effects of methotrexate and methotrexate combined different doses of mifepristone were selected in this meta-analysis. The success rate, gastrointestinal reaction, hepatic lesion, leukocytes decrease, blood ß-HCG drops ≥15%, and bag piece narrows ≥30% were considered in this study. Results: Compared with the control group, the cure rates of the treatment group in 3 sub-studies were higher (sub-study 1, OR=3.66, 95% CI 2.56-5.23, P<0.00001; sub-study 2, OR=3.66, 95% CI 2.56-5.23, P<0.0001 OR=3.66, 95% CI 2.56-5.23, P<0.0001; sub-study 3, OR=3.71, 95% CI 2.49-5.52, P<0.00001). In sub-study 2, the rate of blood ß-HCG drops ≥15% (OR=7.45, 95% CI 3.12-17.81, P\0.00001) and bag piece narrows ≥30% (OR=3.23, 95% CI 1.79-5.85, P\0.0001) of treatment group were higher than the control group. Besides, the gastrointestinal reaction, leukocytes decrease, hepatic lesion of the control group and treatment group in 3 sub-studies had no significant difference. Conclusions: Methotrexate and methotrexate combined mifepristone treatment were effective in ectopic pregnancy. The latter is more effective while its adverse reaction did not increase. The dosage of 200 mg/d of mifepristone compared with 150 mg/d or 100 mg/d was more effective, and their adverse reactions had no significant difference.

Keywords: Methotrexate, mifepristone, ectopic pregnancy

Introduction

Ectopic pregnancy is common in the field of obstetrics and gynecology, and frequently occurred among pregnant in recent years. In the past, patients always went for a doctor with acute abdominal pain, when surgery was the only option in most situations. However, surgical complications, such as postoperative infection and pelvic adhesion, as well as the recurrence of ectopic pregnancy increase the risk of infertility. Thus, an effective and minimally invasive therapy is what doctors and patients really concerned.

More and more ectopic pregnancy patients got early diagnosed due to the improving and application of vaginal ultrasound, diagnostic curettage and beta-human chorionic gonadotropin (β-HCG) detection. This provided opportunities for conservative treatment with medicines. Conservative treatment is not only beneficial for keeping tubal function, but also avoiding complications after surgeries, which may be helpful to the recovery of the patients. In recent years, conservation treatment was widely used for ectopic pregnancy in China. The efficacy of methotrexate in combination with mifepristone was evaluated in clinical practice. This combination induces the death and absorption of the ectopic pregnancy embryo tissue. It is thus regarded as a quite safe, effective and less adverse reactions method.

Methotrexate (MTX) is an inhibitor of dihydrofolate reductase, which affects DNA synthesis by blocking the biosynthesis of purine and pyrimidines base. MTX is thus used for inhibiting the proliferation of nourish cells and reducing the secretion of blood β-HCG, and finally promoting the necrosis, exfoliation and absorption of embryonic tissue.

Mifepristone is a new steroidal antiprogestogen drug, acting at the receptor level. It can competitively combine with progesterone receptor

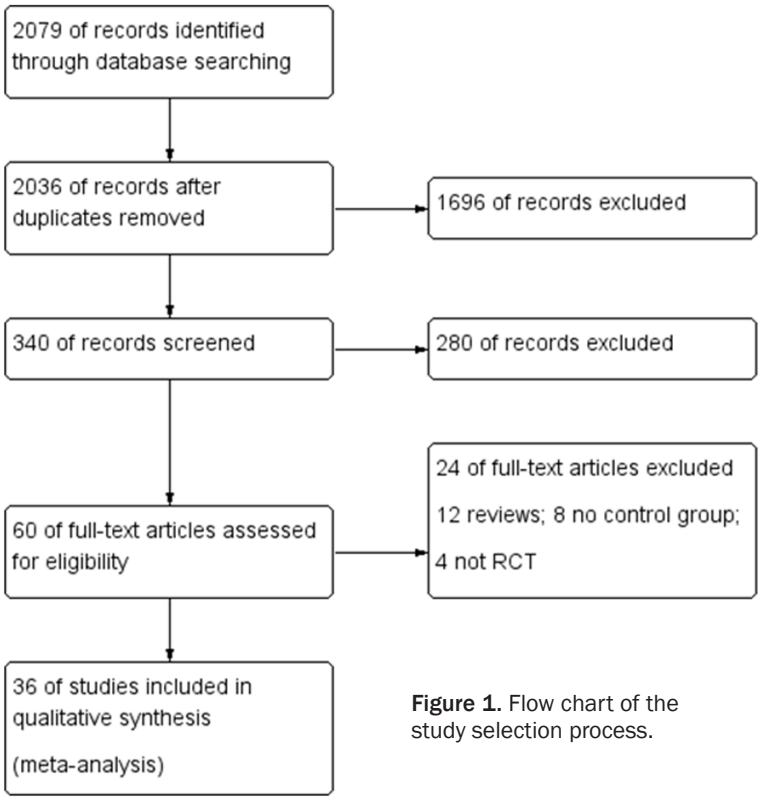

Figure 1. Flow chart of the study selection process.

and glucocorticoid receptor, inhibit the activity of progesterone, and lead to cell degeneration and nuclear fission decrease of decidua and chorion. Moreover, mifepristone promotes the release of endogenous prostaglandin, which will trigger uterine contraction, cervix softening and dilation to assist in ectopic embryonic tissues discharging.

MTX in combination with mifepristone has been proved to have many advantages in different clinical studies. This combination therapy is efficient even with small dose drugs and much more convenient. Furthermore, medical treatment is helpful for patients to avoid injuries from surgeries, and is benefit for reserving tubal function. It is particularly good for young patients with the desire to have a baby.

Clinical studies have confirmed that the combined use of methotrexate and mifepristone on ectopic pregnancy has a lot of benefits, such as small drug dose, simple use, double killing of the embryonic tissue. At the same time, it can avoid the surgical trauma, remain the fallopian function, shortens the recovery period. It is especially suitable for young patients with fertility requirement. In the treatment process, strengthen the psychological care of patient, making patients cooperate actively, close observation of disease and strengthen the diet is the key to success.

Methods

Search strategy

A literature search was made in Medline/PubMed, the Cochrane databases, the China Biological Medicine Database, China National Knowledge Infrastructure (CNKI) and Wan-Fang med-online without language or publishing time limitations. According to "PICO" principle, the key words of this research were designed as "methotrexate" or "mifepristone" or "ectopic pregnancy". All included studies were randomized controlled trials up to 2014.

Inclusion and exclusion criteria

Inclusion criteria were:

① randomized controlled trials (each group sample size >20); ② a description of study design and reasonable statistical analysis method; and ③ details of the therapeutic methods (treatment/trail group: MTX combined different doses of mifepristone; control group: MTX alone) and clinical outcomes. ④ details about the cure rates and adverse reactions.

Exclusion criteria were:

① reviews, non-randomized controlled trials, or meta-analyses; ② small sample size; study time or research methods do not conform to this study.

Data extraction

Two authors (Wan and Xiang) extracted data from included studies, independently. The data below were extracted:

① basic information of the study; ② number of patients; ③ basic information of patients; ④ treatment methods of control group and treat-

Table 1. Characteristics of the included studies

Study	Year	Study tape	Interventions		Age (years)		Size (n)		Cure (n)		Gastrointestinal reaction		Leukocytes decrese		Hepatic lesion	
			Control (MTX/im)	Experimental (MTX/im, Mife/po)	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp
PY Zheng [1]	2011	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	26.7±4.8	27.9±4.9	30	30	25	28	-	-	-	-	-	-
MY Li [2]	2007	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	20-38	20-38	40	46	35	40	28	30	5	3	0	0
XR Tang [3]	2014	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	20-36	20-36	43	43	31	40	5	6	2	1	3	1
YZ Cai [4]	2008	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	19-41	20-40	60	60	51	57	-	-	-	-	-	-
XY Chen [5]	2012	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	17-40	17-40	30	35	22	32	3	10	-	-	1	2
DN Zhang [6]	2011	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	25.1±4.8	24.9±4.8	130	132	36	56	-	-	-	-	-	-
F Wang [7]	2008	RCT	50 mg/(m^2, d)	50mg/(m^2, d), 100 mg/d	-	-	30	30	16	26	-	-	-	-	-	-
QM Shi [8]	2014	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	22-31	24-32	54	54	41	52	-	-	-	-	-	-
XY Wang [9]	2011	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	20-40	20-40	51	51	32	45	-	-	-	-	-	-
YH Ou [10]	2011	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	21-41	21-41	20	28	12	25	-	-	-	-	-	-
SH Guan [11]	2011	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	17-43	17-43	40	40	28	34	3	4	4	3	1	2
ZR Li [12]	2014	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	21-36	23-34	40	40	27	38	-	-	-	-	-	0
HP Zhang [13]	2010	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	20-42	20-42	24	24	18	22	3	2	-	-	1	0
CL Zhang [14]	2014	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	19-40	20-41	20	20	15	18	2	1	-	-	2	1
MC Yuan [15]	2014	RCT	50 mg/(m^2, d)	50 mg/(m^2, d), 100 mg/d	19-37	19-37	49	49	42	47	2	2	-	-	1	2

ment group; ⑤ outcome data, as defined above.

When disagreement arose, a third author (Huang) was consulted as an arbiter.

Study quality

The quality of each study was assessed by two authors (Wan and Xiang) independently, by using the tool of "risk of bias graph in Review Manager 5.3". This is a specific tool for randomized clinical trials. Huang, the third author, was also the one who resolved disagreements between the two reviewers.

Statistical analysis

Statistical analysis was conducted by Review Manager Software 5.3 (Cochrane Collaboration, Oxford, UK). The fixed-effect model or random-effect model were used according to the significant heterogeneity results. Heterogeneity was tested by the chi-squared test. If $P>0.10$ or $I^2<50\%$, the fixed-effect model was used, or else, the random-effect model was used. The funnel plots was used to assess the publication bias of included studies.

Results

We totally identified 2,079 related studies following the search strategy described above. All identified studies were preliminary screened through browsing their title and abstract. Finally, there were 36 studies selected for meta-analysis based on the inclusion and exclusion criteria (**Figure 1**). In the 36 studies, there were 1570 patients in total in the treatment group and 1462 patients in the control group, all from China. The 36 selected studies were divided into 3 sub-studies according to the dosage of mifepristone: 1) sub-study-1: 100 mg/d, 15 studies (**Table 1**); 2) sub-study-2: 150 mg/d, 13 studies (**Table 2**); 3) sub-study-3: 200 mg/d, 8 studies (**Table 3**).

The cure rates

Thirty-six studies reported the cure rates, 15 of sub-study 1, 13 of sub-study 2, 8 of sub-study 3, these included 1570 patients in the treatment group and 1462 patients in the control group. Both of the three sub-studies showed that the cure rates of treatment group were higher than control group (sub-study 1, OR= 3.66, 95% CI 2.56-5.23, P<0.00001; sub-study 2, OR=3.66, 95% CI 2.56-5.23, P< 0.0001; sub-study 3, OR=3.71, 95% CI 2.49-5.52, P<0.00001) (**Figures 2**-**4**).

Gastrointestinal adverse reactions

Gastrointestinal adverse reactions was reported in 16 sixteen studies, 7 of sub-study 1, 5 of

Table 2. Characteristics of the included studies

Study	Year	Study tape	Interventions		Age (years)		Size (n)		Cure (n)		ß-HCG drops ≥15%		Bag piece narrows ≥30%		Gastrointestinal reaction		Hepatic lesion	
			Control (MTX/im)	Experimental (MTX/im, Mife/po)	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp
LJ Liu [16]	2008	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	18-31	18-31	20	24	15	20	-	-	-	-	-	-	-	-
JH Zheng [17]	2014	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	20-42	20-42	29	29	18	28	-	-	-	-	1	1	1	0
HY Zheng [18]	2007	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	19-45	19-45	64	70	40	60	-	-	-	-	-	-	-	-
SG Li [19]	2007	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	-	-	30	30	24	26	-	-	-	-	-	-	-	-
Q Fu [20]	2009	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	18-40	18-40	45	55	30	50	-	-	-	-	35	40	1	2
JX Zhou [21]	2008	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	30.0±5.2	30.0±5.2	50	50	43	46	-	-	-	-	-	-	-	-
LM Lv [22]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	-	-	30	30	21	28	21	28	17	27	-	-	-	-
CX Gu [23]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	22-39	21-36	22	34	15	29	-	-	-	-	-	-	-	-
RF You [24]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	24-37	24-37	36	42	28	38	-	-	-	-	14	6	-	-
SH Wu [25]	2011	RCT	50 mg/(m²,d)	50 mg/(m², d), 150 mg/d	21-38	21-38	34	36	22	32	15	31	14	28	6	8	4	5
CP Ma [26]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	22-38	22-38	40	45	32	43	-	-	22	31	2	3	-	-
CF He [27]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	-	-	28	28	14	24	21	27	-	-	-	-	-	-
J Wei [28]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 150 mg/d	22-35	22-35	28	30	23	28	-	-	-	-	-	-	-	-

Table 3. Characteristics of the included studies

Study	Year	Study tape	Interventions		Age (years)		Size (n)		Cure (n)		Gastrointestinal reaction		Leukocytes decrease		Hepatic lesion		Oral ulcer	
			Control (MTX/im)	Experimental (MTX/im, Mife/po)	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp	Ctrl	Exp
F Yang [29]	2007	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	27.3±3.8	27.6±4.3	45	49	33	45	6	8	1	2	4	4	2	3
D Zhang [30]	2005	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	20-43	18-45	78	81	49	72	-	-	-	-	-	-	-	-
YY Ren [31]	2014	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	23-46	23-46	30	30	17	24	10	11	3	3	-	-	3	4
SJ Ou [32]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	-	-	20	20	14	18	7	4	-	-	2	2	-	-
LJ Xia [33]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	22-35	22-35	31	31	23	27	4	5	2	1	1	2	1	0
YQ Hu [34]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	22-42	22-42	66	83	49	73	-	-	-	-	-	-	-	-
ZM Gao [35]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	23-36	21-34	45	45	33	43	-	-	-	-	-	-	-	-
YL Wang [36]	2011	RCT	50 mg/(m², d)	50 mg/(m², d), 200 mg/d	18-45	18-45	30	46	20	41	-	-	-	-	-	-	-	-

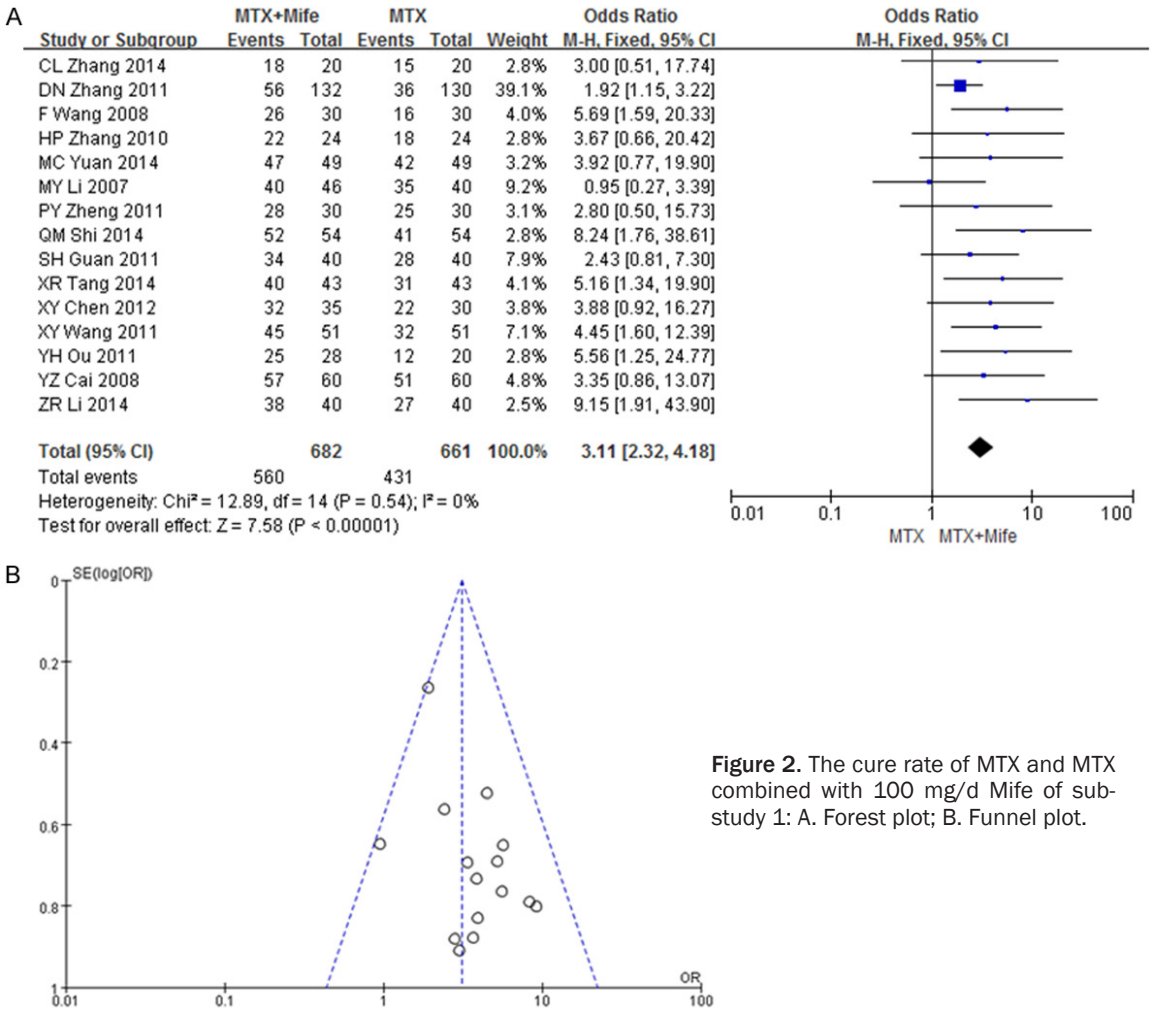

Figure 2. The cure rate of MTX and MTX combined with 100 mg/d Mife of sub-study 1: A. Forest plot; B. Funnel plot.

sub-study 2, 4 of sub-study 3. These included 594 patients in the treatment group and 556 patients in the control group. There was no significant difference between the treatment group and the control group (sub-study 1, OR=1.15, 95% CI 0.68-1.94, P=0.60; sub-study 2, OR=0.69, 95% CI 0.40-1.19, P=0.18; sub-study 3, OR=1.02, 95% CI 0.55-1.87, P=0.95) (**Figures 5-7**).

The incidence of hepatic lesion

Twelve studies reported hepatic lesion, 6 of sub-study 1, 3 of sub-study 2, 3 of sub-study 3, included 431 patients in the treatment group and 367 patients in the control group. No significant difference was founded between the treatment group and the control group (sub-study 1, OR=1.12, 95% CI 0.38-3.29, P=0.83; sub-study 2, OR=1.07, 95% CI 0.36-3.24, P=0.90; sub-study 3, OR=1.10, 95% CI 0.38-3.17, P=0.86) (**Figures 8-10**).

The incidence of leukocytes decrease

Three studies in sub-study 1 and three studies in sub-study 3 reported data on leukocytes decrease, these included 239 patients in the treatment group and 229 patients in the control group. The incidence of leukocytes decrease had no significant difference among the treatment group and control group (sub-study 1, OR=0.57, 95% CI 0.21-1.53, P=0.27; sub-study 3, OR=0.98, 95% CI 0.30-3.16, P=0.97) (**Figures 11**, **12**).

Blood ß-HCG drops ≥15% and bag piece narrows ≥30%

Blood ß-HCG drops ≥15% and bag piece narrows ≥30% were reported in 4 studies of sub-study 2. The combined results showed that the blood ß-HCG drops ≥15% and bag piece narrows ≥30% in the treatment group were much higher than control group (blood ß-HCG drops

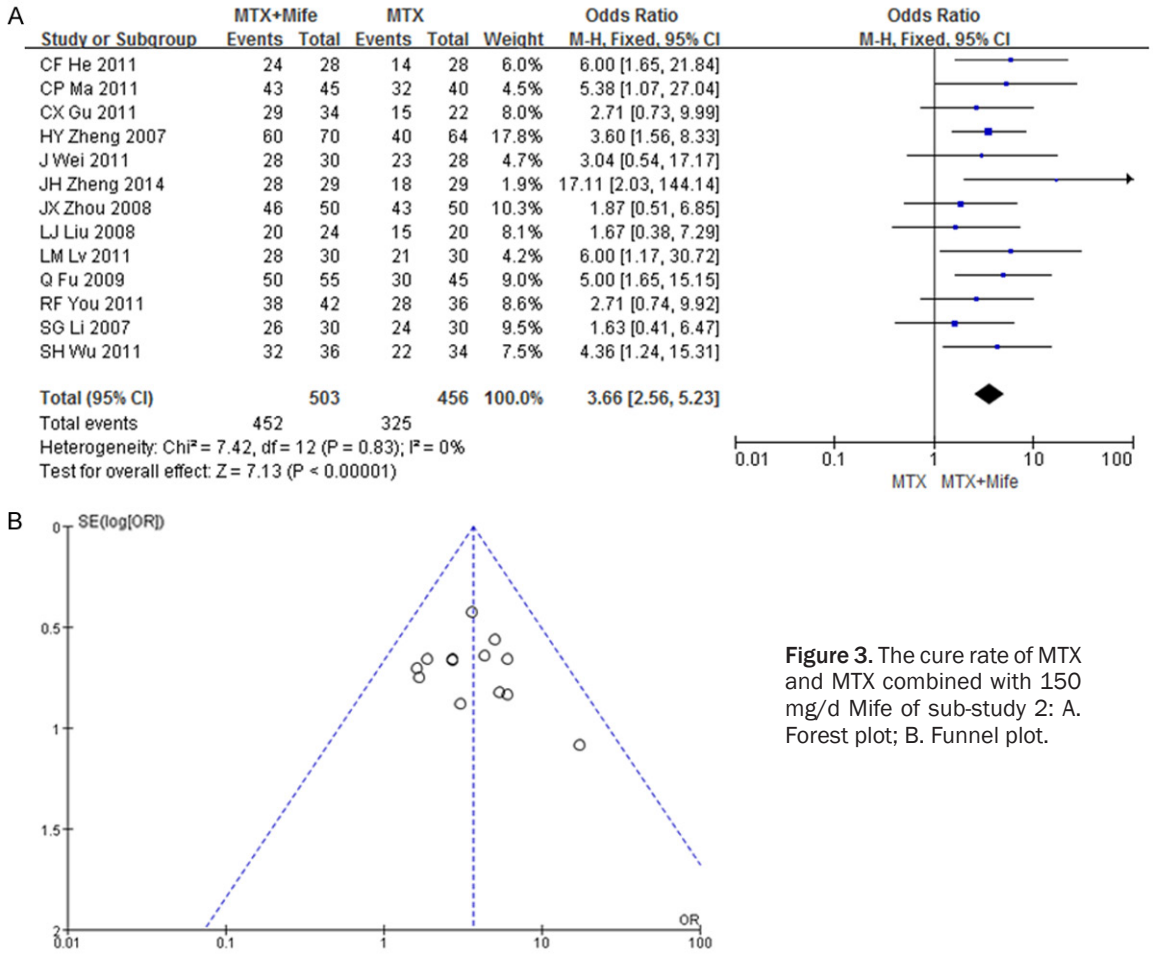

Figure 3. The cure rate of MTX and MTX combined with 150 mg/d Mife of sub-study 2: A. Forest plot; B. Funnel plot.

≥15%, OR=7.45, 95% CI 3.12-17.81, P< 0.00001; bag piece narrows ≥30%, OR=3.23, 95% CI 1.79-5.85, P<0.0001) (**Figures 13**, **14**).

The incidence of oral ulcer

Three studies in sub-study 3 reported data on oral ulcer, these included 110 patients in treatment group and 106 patients in control group. The incidence of oral ulcer had no significant difference among the treatment group and control group (OR=1.13, 95% CI 0.38-3.38, P=0.83) (**Figure 15**).

Discussion

Thirty-six literatures included in this study were randomized controlled trials, both of the treatment group and control group were treated by a single intramuscular injection of 50 mg/(m^2, d) MTX. Additionally, the treatment group were treated by variant doses of mifepristone, which were divided as follows: 15 literatures using a dose of 100 mg/d, 13 literatures using a dose of 150 mg/d and 8 literatures adopted to 200 mg/d. This study was thus divided into three sub-studies based on the doses of mifepristone. The first sub-study used a treatment of MTX combined 100 mg/d mifepristone, the second sub-study used a treatment of MTX combined 150 mg/d mifepristone, while the third sub-study used a treatment of MTX combined 200 mg/d mifepristone. By extracting the relevant information and data, we analyzed the cure rate, the incidence of gastrointestinal adverse reaction, the incidence of hepatic lesion, the leukocytes decrease, blood ß-HCG drops ≥15% and bag piece narrows ≥30% of each sub-study respectively. Moreover, the cure rates and side effects were compared to evaluate the impact of different doses of mifepristone combined with same dose of MTX of ectopic pregnancy.

The combined results of the three sub-studies revealed that the cure rates of MTX in combination with mifepristone treatment of ectopic

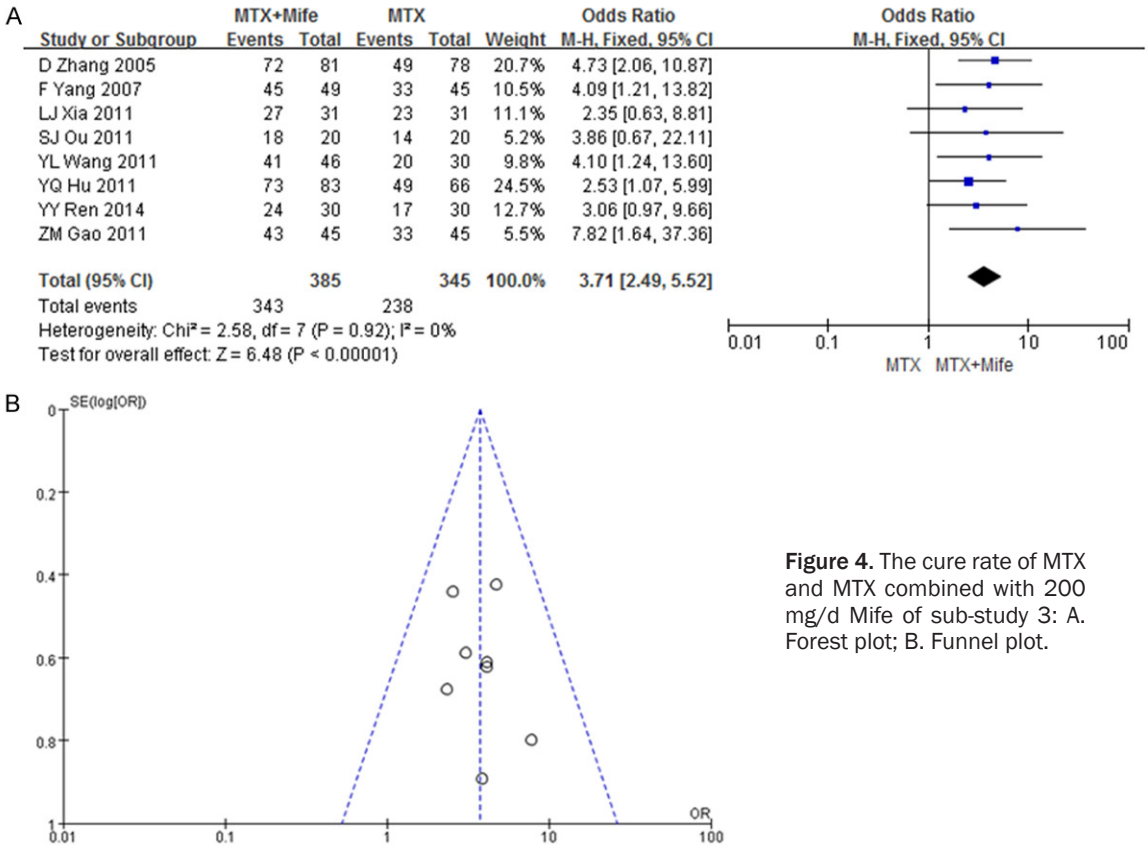

Figure 4. The cure rate of MTX and MTX combined with 200 mg/d Mife of sub-study 3: A. Forest plot; B. Funnel plot.

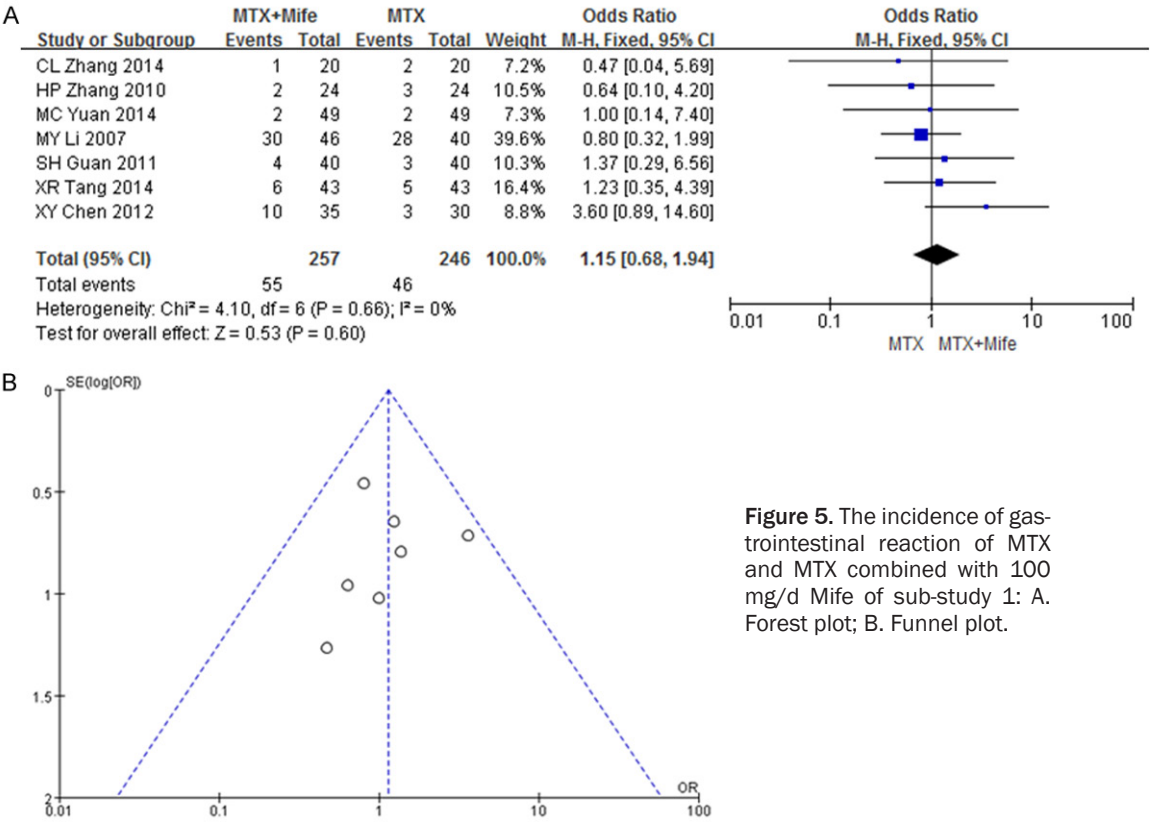

Figure 5. The incidence of gastrointestinal reaction of MTX and MTX combined with 100 mg/d Mife of sub-study 1: A. Forest plot; B. Funnel plot.

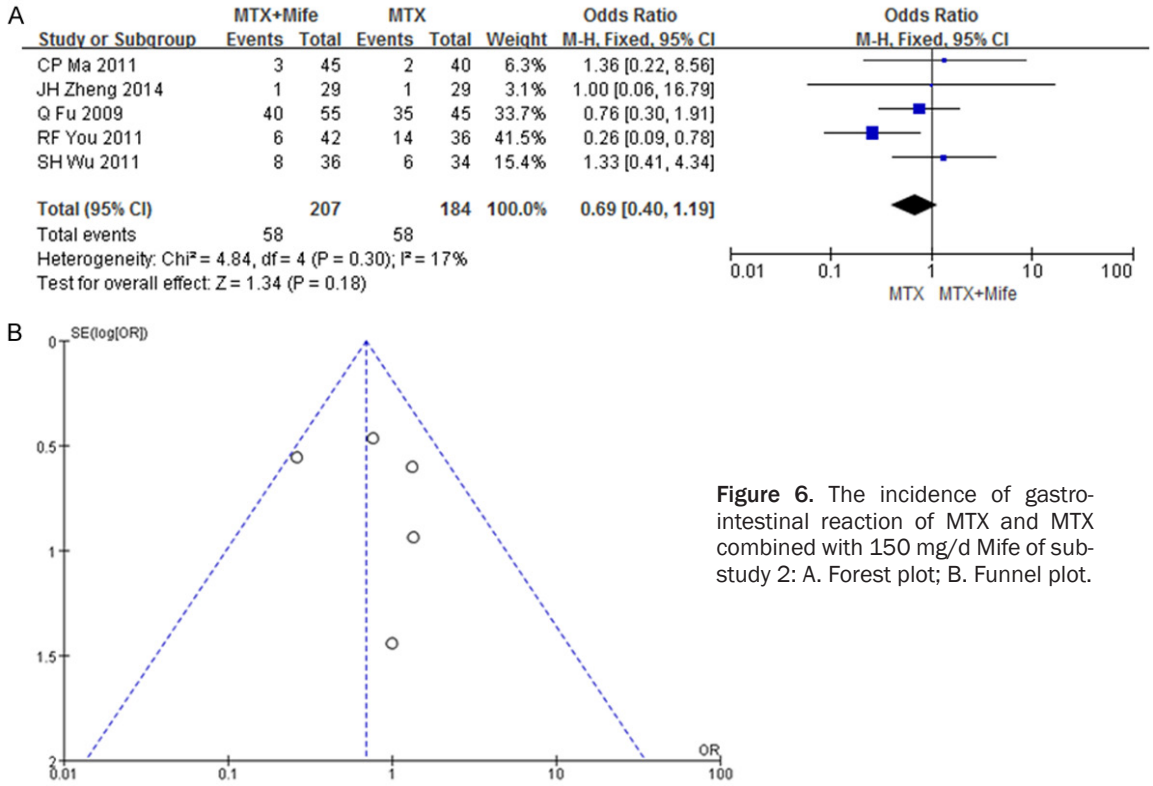

Figure 6. The incidence of gastrointestinal reaction of MTX and MTX combined with 150 mg/d Mife of sub-study 2: A. Forest plot; B. Funnel plot.

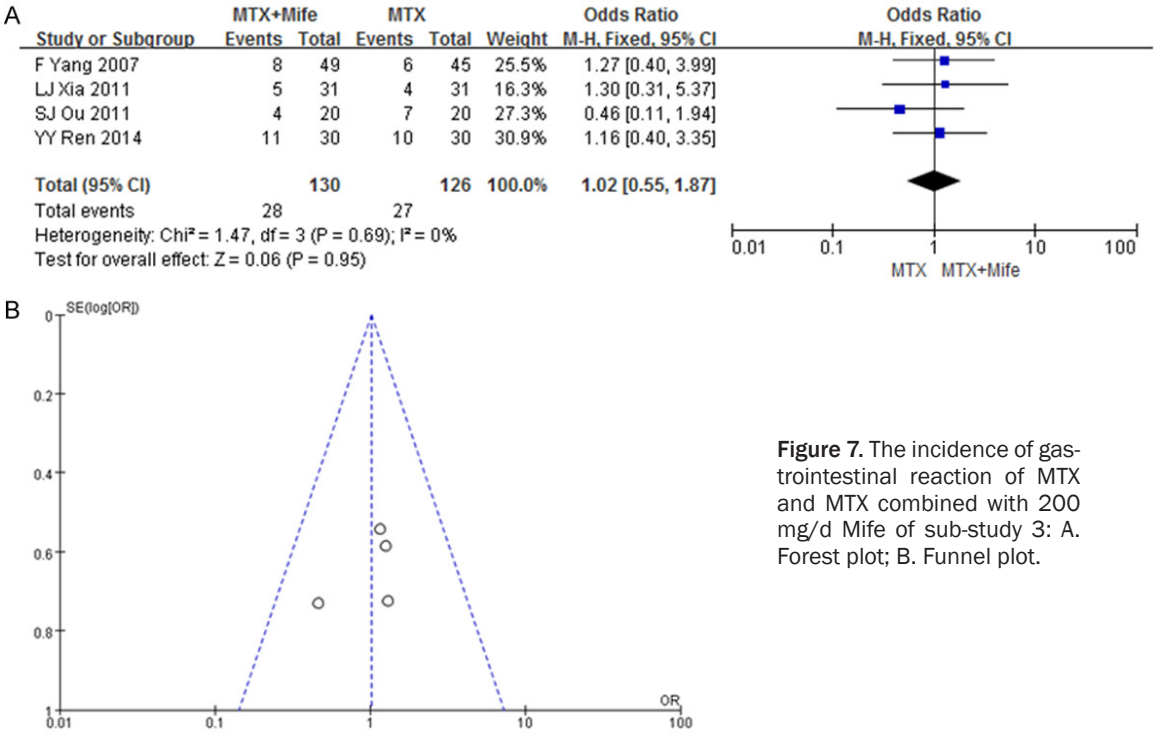

Figure 7. The incidence of gastrointestinal reaction of MTX and MTX combined with 200 mg/d Mife of sub-study 3: A. Forest plot; B. Funnel plot.

pregnancy was much higher than MTX alone (sub-study 1, OR=3.66, 95% CI 2.56-5.23, P<0.00001; sub-study 2, OR=3.66, 95% CI 2.56-5.23, P<0.0001; sub-study 3, OR=3.71, 95% CI 2.49-5.52, P<0.00001), which is consistent with the results of included studies. This

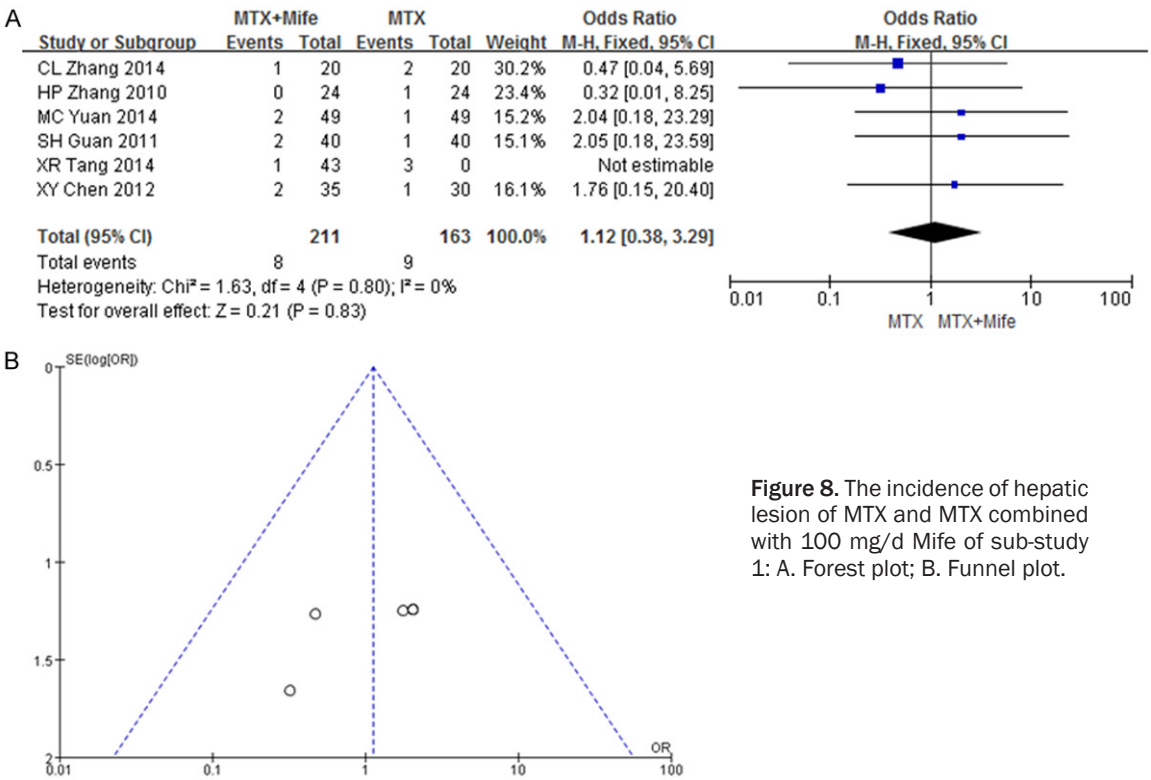

Figure 8. The incidence of hepatic lesion of MTX and MTX combined with 100 mg/d Mife of sub-study 1: A. Forest plot; B. Funnel plot.

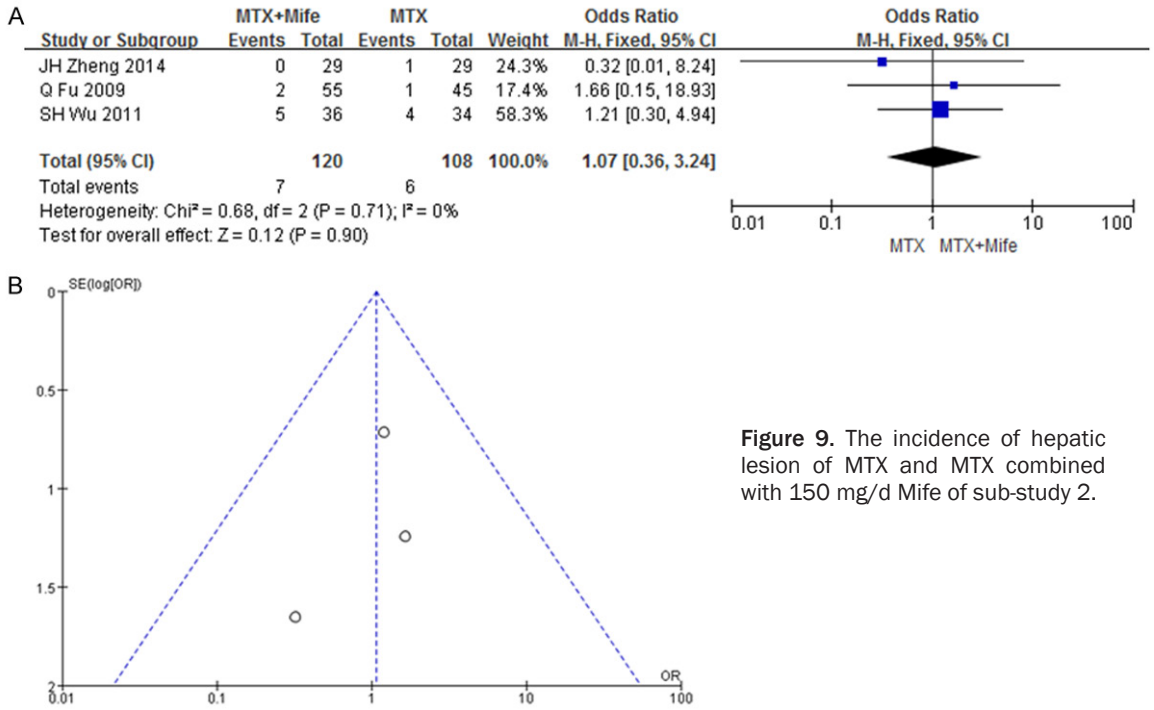

Figure 9. The incidence of hepatic lesion of MTX and MTX combined with 150 mg/d Mife of sub-study 2.

indicated that the combination treatment is better than treating with MTX alone; among them, the combined value of sub-study 2 is larger than sub-study 1, and the combined value of sub-study 3 is the highest. To some extent, we can explain that under the same dose of MTX, the higher dose of mifepristone, the higher the cure rate is.

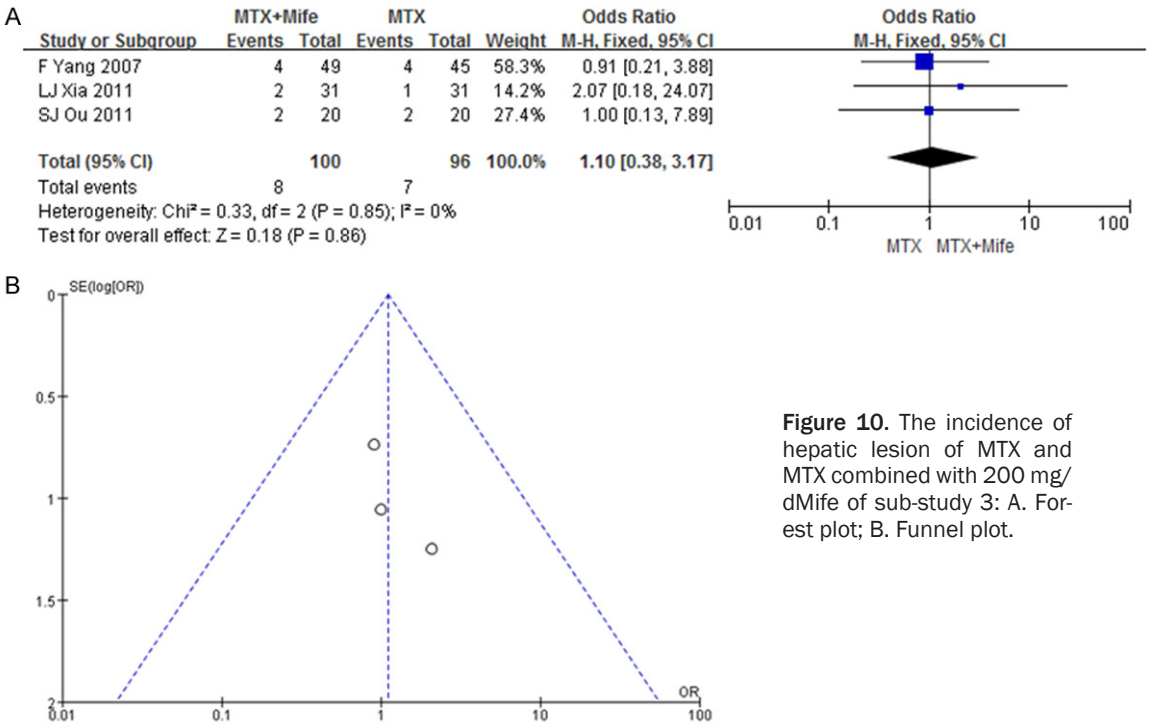

Figure 10. The incidence of hepatic lesion of MTX and MTX combined with 200 mg/dMife of sub-study 3: A. Forest plot; B. Funnel plot.

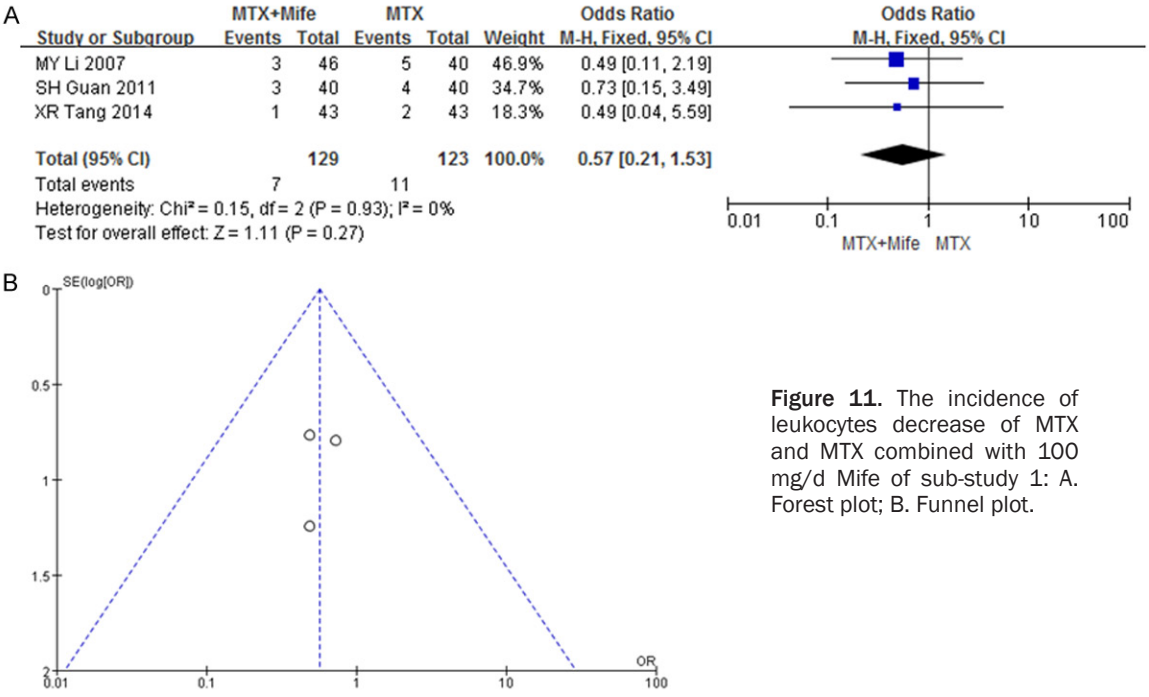

Figure 11. The incidence of leukocytes decrease of MTX and MTX combined with 100 mg/d Mife of sub-study 1: A. Forest plot; B. Funnel plot.

All included studies reported gastrointestinal adverse reactions. The combined results of this study showed that there was no significant difference of gastrointestinal reactions between treatment group and control group (sub-study 1, OR=1.15, 95% CI 0.68-1.94, P=0.60; sub-study 2, OR=0.69, 95% CI 0.40-1.19, P=0.18; sub-study 3, OR=1.02, 95% CI 0.55-1.87, P=0.95). This indicates that the impact on digestive system of MTX and the combined treatment is similar. The combined treatment can not only improve the cure rates, shorten

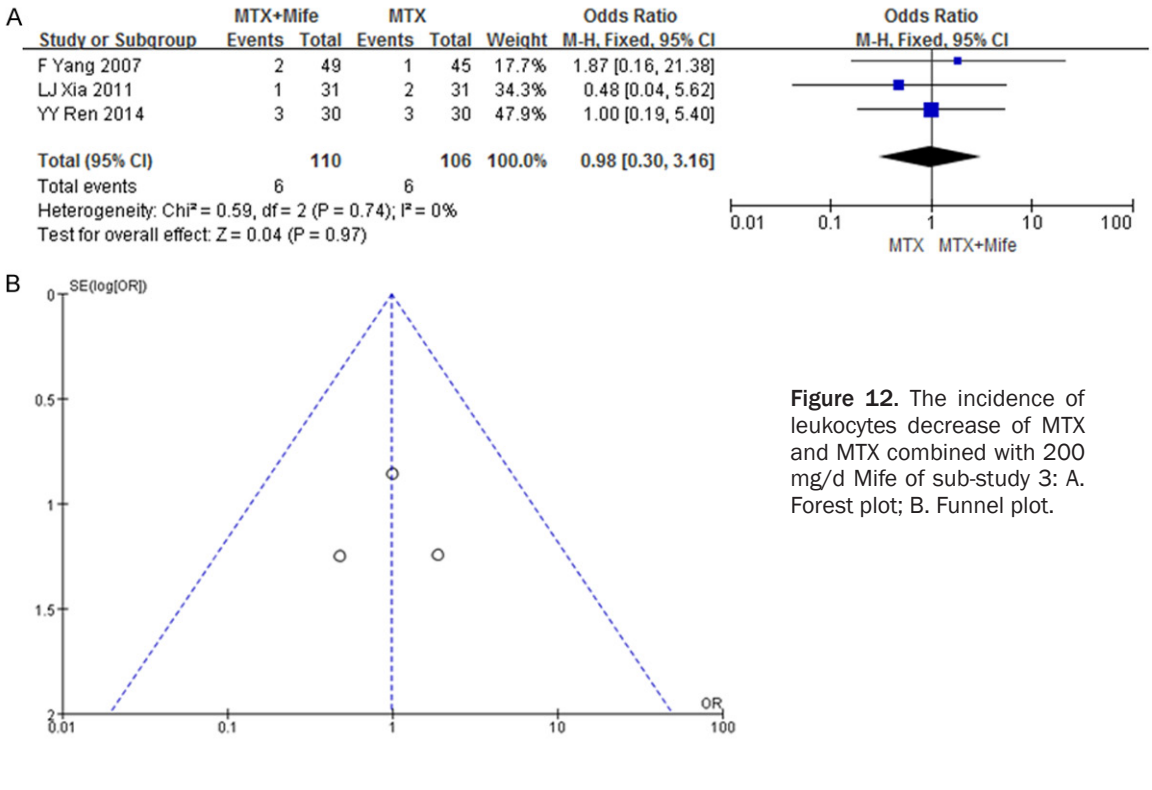

Figure 12. The incidence of leukocytes decrease of MTX and MTX combined with 200 mg/d Mife of sub-study 3: A. Forest plot; B. Funnel plot.

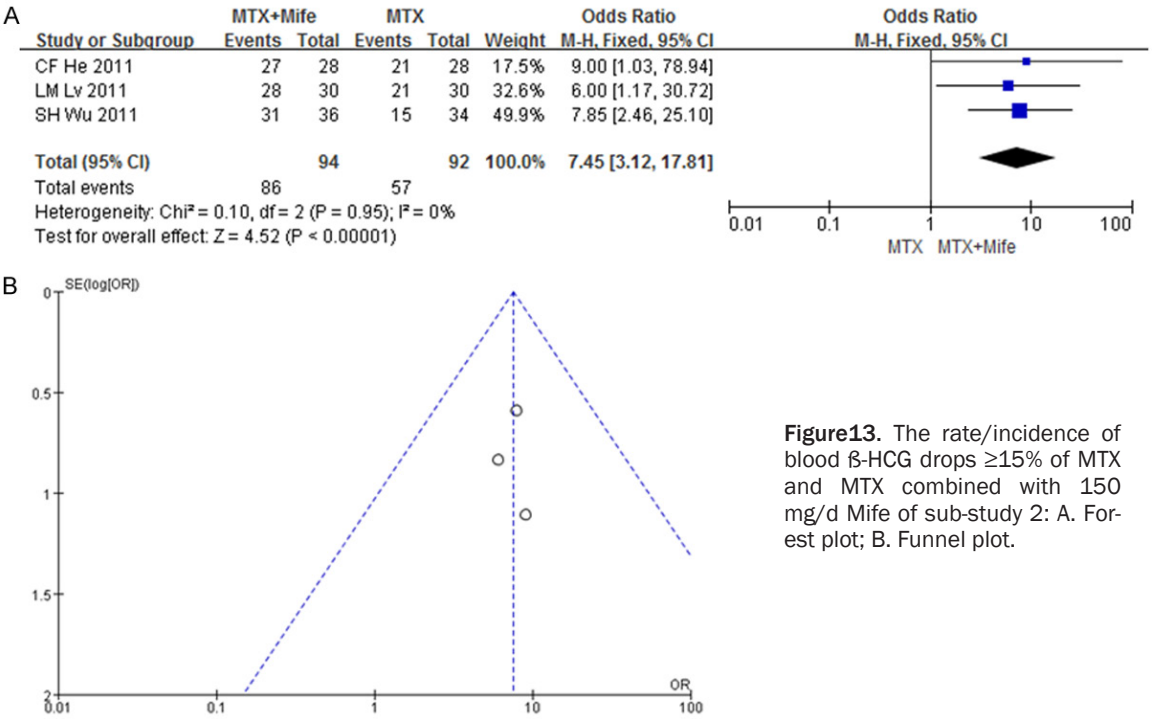

Figure13. The rate/incidence of blood ß-HCG drops ≥15% of MTX and MTX combined with 150 mg/d Mife of sub-study 2: A. Forest plot; B. Funnel plot.

the healing time but also do not increase the adverse effects. Besides, the increasing dose of mifepristone do not increase the gastrointestinal adverse reactions. Therefore, the combined treatment is worth to be widely applied.

Some of the included studies reported the cases of hepatic lesion, and the case numbers of the treatment group and control group was similar. The combined analysis of this study reached the same results that there was no sig-

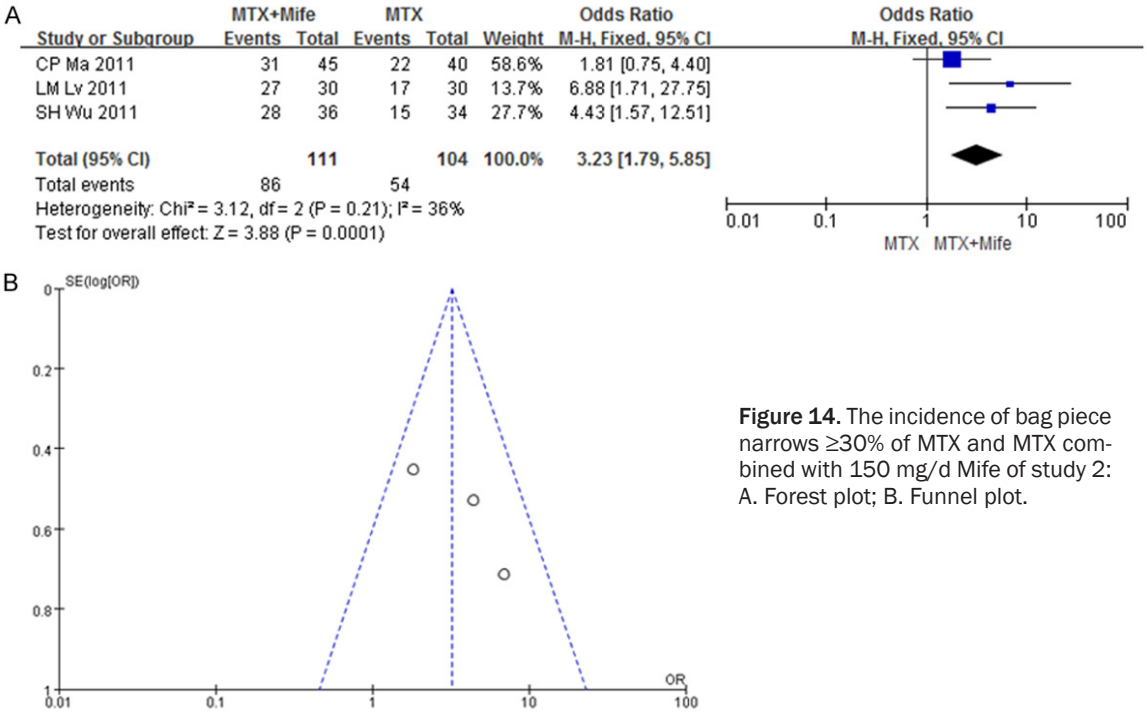

Figure 14. The incidence of bag piece narrows ≥30% of MTX and MTX combined with 150 mg/d Mife of study 2: A. Forest plot; B. Funnel plot.

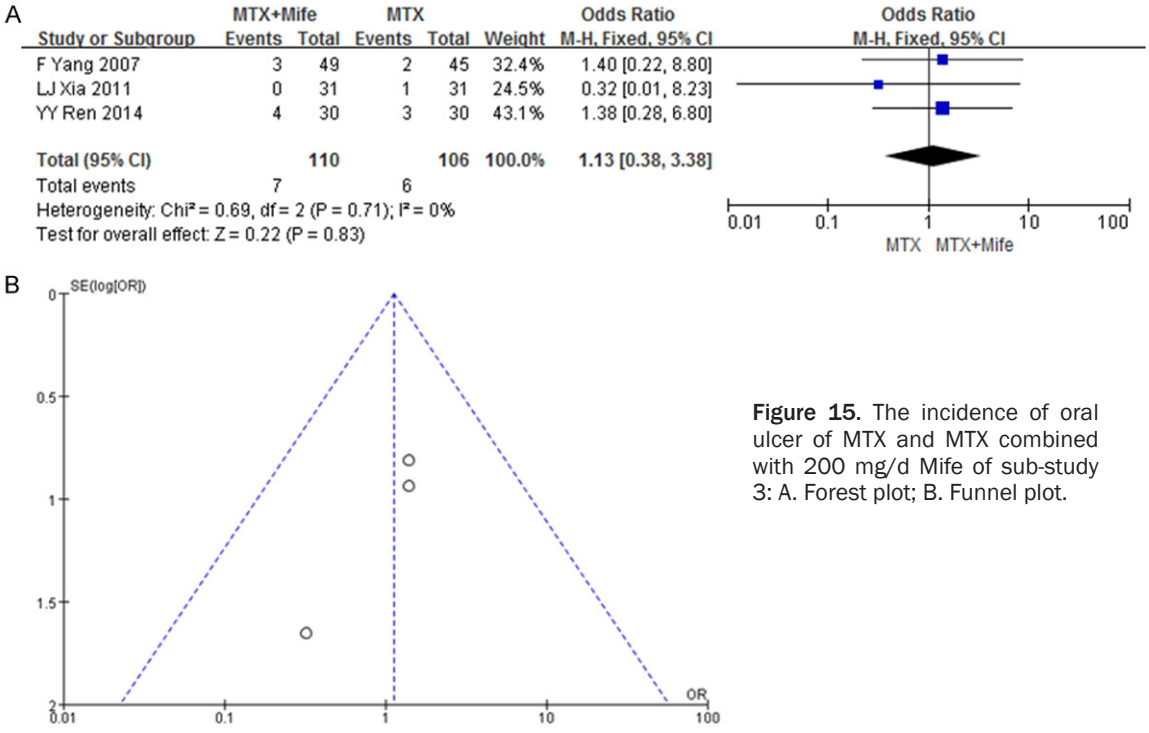

Figure 15. The incidence of oral ulcer of MTX and MTX combined with 200 mg/d Mife of sub-study 3: A. Forest plot; B. Funnel plot.

nificant difference between MTX treatment and MTX combined mifepristone treatment on hepatic lesion. Meanwhile, with the increasing dose of mifepristone, the incidence of hepatic lesion does not increase. So that, the combination therapy is a relatively safe and effective treatment methods.

Studies have found that the cure rates of conservative treatment of ectopic pregnancy was

significantly associated with the content of blood ß-HCG and the size of bag piece, the lower the blood levels of ß-HCG and the faster the bag piece narrowed, the higher the cure rates was. So the level of blood ß-HCG and the size of the bag piece are important indicators to assess the therapeutic effect. Some of the included studies reported the cases of blood ß-HCG decline/drop ≥15% and bag piece narrows ≥30%. The combined results showed that the blood ß-HCG decline/drop ≥15% and bag piece narrows ≥30% of treatment group and control group were significantly different, indicating that the combined treatment of ectopic pregnancy has a higher cure rates, shorter treatment time and more reliable treatment effect.

In the past, most of the studies on MTX in combination with mifepristone treatment of ectopic pregnancy were single research, lacked of evidence-based evidence and there were some controversy on the dosage of mifepristone. Compared with previous studies, literatures included in this study were randomized controlled trials (RCT). There was no significant difference between the general information of patients, the dosages and other aspects of the studies. Compared with the existing systematic reviews, this study not only analyzed the cure rates of MTX treatment and combined treatment, but also analyzed the side effects and the treatment-related indicators. We also quantitatively assessed the dosage of mifepristone. It is confirmed that the cure rates of the combined treatment was much higher than MTX treatment, and also quantitatively indicating that the side effects did not rise as the cure rates improving while increasing the dose of mifepristone. The combined results of this study provided references to the clinical use of the combined treatment.

In summary, MTX in combination with mifepristone of ectopic pregnancy have lots of advantages. Such as high cure rates, good efficacy, short time of blood ß-HCG level and bag piece narrows to normal. While being treated with the combination of MTX and mifepristone, the incidence of the gastrointestinal adverse reactions, hepatic lesion and other adverse reactions did not rise. This study may provide a powerful evidence of evidence-based medicine for the combination therapy of MTX and mifepristone.

Disclosure of conflict of interest

None.

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