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Full Length Research Paper

Efficacy and safety of flurbiprofen axetil on preemptive analgesia for Chinese surgical patients: A meta-analysis

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This study was performed to evaluate the efficacy and safety of flurbiprofen axetil (FA) on preemptive analgesia for Chinese surgical patients. Medicinal databases and review articles were screened with prespecified criteria for randomized controlled trials that reported the effects of adverse reactions to FA and other analgesics for preemptive analgesia. The qualities of included studies were critically evaluated. A total of 848 articles were found and 17 articles were finally included. Heterogeneity test: Analysis of visual analog scale (VAS) at 4 h after operation (Qstatistic = 97.37, P < 0.00001, I^2 = 87%), analysis of VAS at 8 h after operation (Qstatistic = 128.95, P < 0.00001, I^2 = 90%), analysis of VAS at 12 h after operation (Qstatistic = 20511.23, P = 0.13, I^2 = 100%), analysis of VAS at 24 h after operation (Qstatistic = 188.15, P < 0.00001, I^2 = 91%), and safety analysis (Q statistic = 17.61, P = 0.05, I^2 = 38%). The results of meta-analysis showed that compared with the control group, FA was more effective in VAS at 4 h after operation (mean difference (MD) = -1.23, 95% confidence interval (CI): -1.54 to -0.92), 12 h after operation (MD = -4.42, 95%CI: -10.06 to 1.23), and 24 h after operation (MD = -0.87, 95%CI: -1.24 to -0.51). There were no significances between FA treatment and control group in VAS at 8 h after operation. Moreover, FA was safer than the control group (OR = 0.70, 95%CI: 0.49 to 0.99). Funnel-plot displayed some unsymmetrical figures, indicating that there were publication biases in each analysis. The evidence currently available shows that FA was effective and safe on preemptive analgesia for Chinese surgical patients.

Key words: Flurbiprofen axetil, preemptive analgesia, systemic review, meta-analysis.

INTRODUCTION

Flurbiprofen axetil (FA) is a member of the phenylalkanoic acid derivative family of nonsteroidal anti-inflammatory drugs (NSAIDs), and it exerts potent function of anti-inflammation and antinociception after intravenous (iv) injection (Buritova and Besson, 1998; Roszkowski et al., 1997). It has been reported that FA, an injectable prodrug of flurbiprofen, when administered intravenously could reduce the pain on injection of propofol (Fujii and Shiga, 2006, 2009). Recently, some studies also reported that FA could reduce postoperative pains (Lin, 2010; Mikawa et al., 1997; Nakayama et al., 2001; Nishiike et al., 2007; Takada et al., 2007; Wang et al., 2008, 2009). However, the conclusions of which are not credible, because of small sample size and lacks of systemic evaluation of methodologic quality.

In order to demonstrate its efficacy and safety, we make a systemic review about clinical random control trials (RCTs) focused on FA in preemptive analgesia for Chinese surgical patients.

METHODOLOGY

Search sources and strategy

The search strategy was made according to working handbook 4.2.7 from the Cochrane collaboration (Sackett et al., 2002). We systematically searched Medline (1991 to November, 2011), EMbase (1991 to November, 2011), CBMdisc (1991 to November,

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2011), and CNKI (1994 to November, 2011) for randomized trials examining the efficacy and safety of FA on preemptive analgesia for Chinese surgical patients. In addition, we conducted a manual search of abstracts from selected conferences and also searched by hand the bibliographies of all relevant trials. The following search criterion was used: ("preemptive analgesia" or "analgesia") and ("flurbiprofen axetil" or "flurbiprofen"), and language was limited to English or Chinese.

Study selection

Two reviewers independently conducted the literature search and extraction of relevant articles. The title and abstract of potentially relevant studies were screened for appropriateness before retrieval of the full articles. The following selection criterions were used to identify published studies for inclusion in this meta-analysis: (a) study design: RCTs; (b) population: Chinese surgical patients; (c) intervention: FA versus other active analgesics, such as tramadol and fentanyl; (d) outcome variable: VAS at 4 h after operation, VAS at 8 h after operation, VAS at 12 h after operation, VAS at 24 h after operation and adverse reaction rate.

Data extraction

From each study, the following information was abstracted: author, year of publication, study design, characteristics of the population, simple size, treatment proposal, types of surgical operation, VAS at 4 h after operation, VAS at 8 h after operation, VAS at 12 h after operation, VAS at 24 h after operation and adverse reaction rate.

Assessment of study quality

The quality of the included studies was assessed based on a well-established, validated scale developed by Jadad et al. (1996). A Jadad score was calculated using the following 7 items: (1) Was the study described as a random trial? (2) Was the randomization scheme described and appropriate? (3) Was the study described as double-blind? (4) Was the method of double blinding appropriate? That is, were both the patient and the assessor appropriately blinded? (5) Was there a description of dropouts and withdrawals? (6) Deduct one point if the method used to generate the sequence of randomization was described and was inappropriate. (7) Deduct one point if the study was described as double blind, but the method of blinding was inappropriate.

The first five items were indications of good quality, and each was counted as one point towards an overall quality score. The final two items indicated poor quality, and a point was subtracted for each if its criteria were met. The range of possible scores was 0 to 5 (0 being weakest and 5 being strongest). Any study with a Jadad score < 3/5 was considered to be of poor quality, and excluded.

Statistical analysis

For dichotomous outcomes, we calculated a pooled mean difference (MD), odds ratio (OR) and 95% confidence interval (CI). The MDs and ORs of different RCTs were combined by using the random effects model as previous described (Der et al., 1986), if true, between-study heterogeneity exists or else use Mantel and Haenszel fixed-effects model instead (Mantel et al., 1959). Intertrial statistical heterogeneity was explored using the Cochran Q test with calculated I^2, indicating the percentage of the total variability in effect estimates among trials, that is, due to heterogeneity rather than to chance (Higgins et al., 2003). I^2 values of 50% or more indicate a substantial level of heterogeneity. We evaluated the presence of publication bias by means of visual inspection of the funnel plot (whether it was symmetrical or not). All P values were two-sided with statistical significance set at an α level of 0.05. We followed the "quality of reporting meta-analysis guidelines" for reporting and discussing these meta-analytical results (Moher et al., 1999). All the statistical analysis was carried out by the Cochrane collaboration's RevMan 5.0 software.

RESULTS

Study characteristics

There were 848 articles relevant to the search term and 17 articles (Chen et al., 2011, 2008; Ding et al., 2007; Fan, 2009; He et al., 2008; Li and Xie 2007; Li and Lin 2010, Li et al, 2009; Luo et al., 2009; Song et al., 2010; Sun et al., 2007; Wang et al., 2007, 2008; Xie et al., 2006; Zeng et al., 2008; Zhao et al., 2009) involving 848 Chinese surgical patients (FA treatment group: 425 patients; control group: 423 patients) were included in this meta-analysis finally. Ages and sex ratio were similar in each group, respectively. The flow chart for the selection of RCTs to be included in our analysis is as shown in Figure 1. The characteristics of the included trials are showed in Table 1.

Methodologic quality assessment

All the trials included in this meta-analysis mentioned the term "random", but the detail method was illuminated in 1 article only. There were 17 trials that mentioned the term "double blind", but only 7 articles explained the detail method. All the 17 trials described the data of the patients who withdrew during the treatment. According to the Jadad score, 10 articles and 7 articles were regarded as high quality literature and low quality literature, respectively (Table 1).

Heterogeneity test

We choose fixed-effect model to make meta-analysis, because there was no significant heterogeneities in safety analysis (Q statistic = 17.61, P = 0.05, I^2 = 38%). Because of heterogeneity, random-effect model was used to make analysis for VAS at 4 h after operation (Qstatistic = 97.37, P < 0.00001, I^2 = 87%), VAS at 8 h after operation (Qstatistic = 128.95, P < 0.00001, I^2 = 90%), VAS at 12 h after operation (Qstatistic = 20511.23, P = 0.13, I^2 = 100%), and VAS at 24 h after operation (Qstatistic = 188.15, P < 0.00001, I^2 = 91%).

Meta-analysis of VAS at 4 h after operation

FA treatment group and control group were recorded in

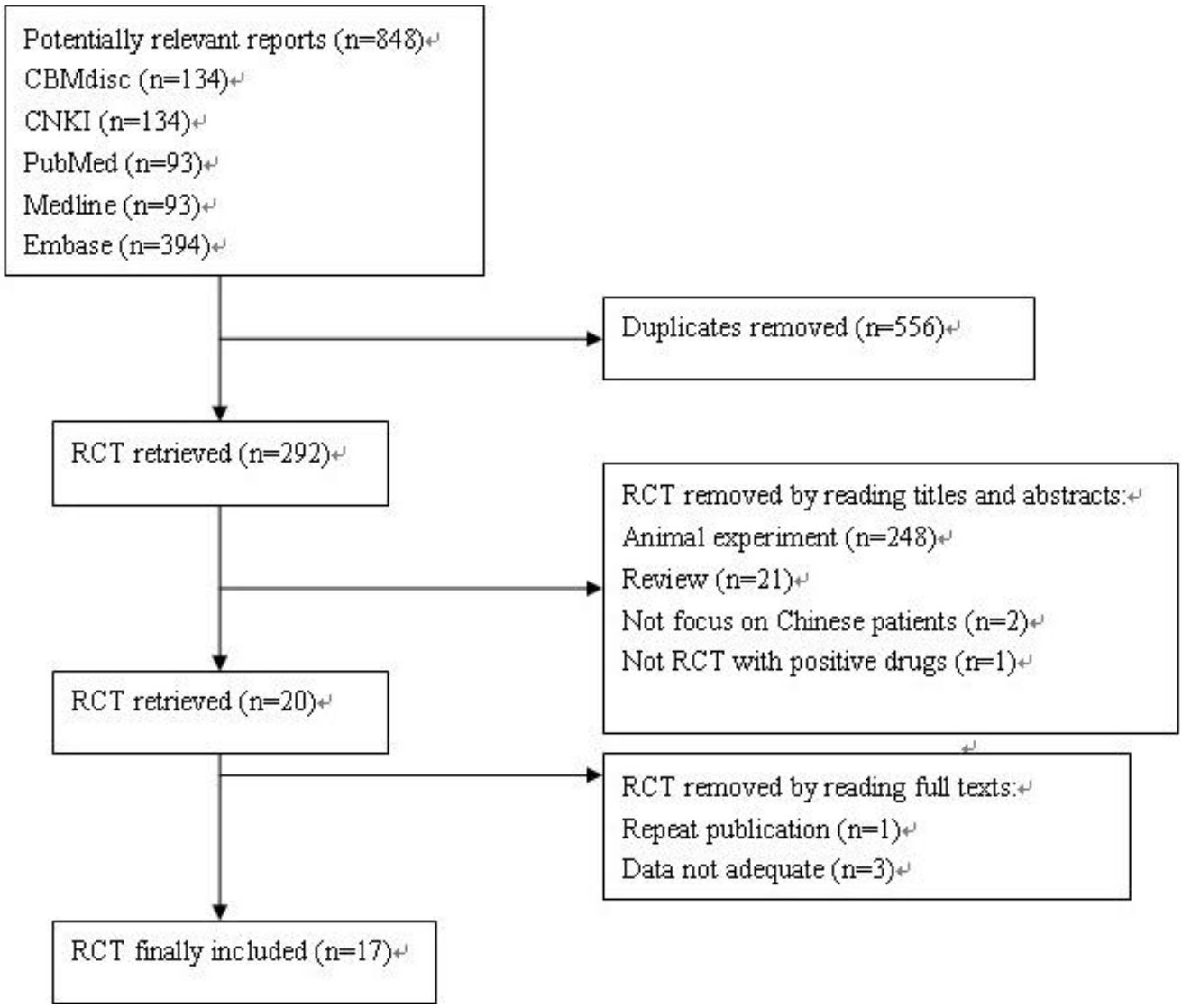

Figure 1. Chat for the search result and trials screen.

the 14 trials finally included. Active analgesics involved in this analysis were tramadol or fentanyl. The results of meta-analysis (MD = -1.23, 95%CI: -1.54 to -0.92) confessed that VAS at 4 h after operation in FA treatment group is less than in control group of Chinese surgical patients (Figure 2).

Meta-analysis of VAS at 8 h after operation

FA treatment group and control group were recorded in the 14 trials finally included. Active analgesics involved in this analysis were tramadol or fentanyl. The results of meta-analysis (MD = -1.13, 95%CI: -1.54 to -0.73) confessed that VAS at 8 h after operation in FA treatment group is less than in control group of Chinese surgical patients (Figure 3).

Meta-analysis of VAS at 12 h after operation

FA treatment group and control group were recorded in the 12 trials finally included. Active analgesics involved in this analysis were tramadol or fentanyl. The results of meta-analysis (MD = -4.42, 95%CI: -10.06 to 1.23) confessed that VAS at 4 h after operation in FA treatment group is less than in control group of Chinese surgical patients (Figure 4).

Meta-analysis of VAS at 24 h after operation

FA treatment and control groups were recorded in all the

Table 1. Characteristics of the 17 randomized clinical studies included in this meta-analysis.

Author	Jaded score	Treatment protocol (T/C)	Sample size (T/C)	VAS at 4 h after operation	VAS at 8 h after operation	VAS at 12 h after operation	VAS at 24 h after operation	Adverse reaction rate (%)
Chen et al. (2008)	3	T: FA(pre)+GA C:GA	T: 40 C: 40	NA	NA	1.10±0.90 2.60±0.90	1.00±0.90 2.00±0.90	20.00 32.50
Chen et al. (2011)	3	T: FA(pre) C:FA (pro)	T: 20 C: 20	1.20±0.20 1.80±0.50	2.10±0.70 3.40±0.80	2.90±0.50 4.2±0.70	3.10±0.70 4.60±0.90	NA
Ding et al. (2007)	3	T: FA(pre)+GA C: GA	T: 32 C: 32	1.10±1.00 2.40±1.90	1.10±1.50 1.50±1.90	NA	0.90±1.20 1.20±1.60	31.25 50.00
Fan et al. (2009)	2	T: FA(pre)+GA C: GA	T: 24 C: 24	2.05±0.77 2.83±0.74	2.27±0.81 3.01±0.85	2.23±0.51 1.88±0.69	1.15±0.35 1.25 0.25	NA
He et al. (2008)	3	T: FA(pre)+GA C: GA	T: 15 C: 15	1.20±0.90 2.70±1.00	2.70±1.30 3.90±1.30	3.00±1.30 3.10±1.50	1.70±1.50 1.80±1.40	53.30 60.00
Li and Xie (2007)	2	T: FA(pre)+GA C: GA	T: 20 C: 20	NA	NA	NA	4.8±0.8 6.8±0.9	15 10
Li et al. (2009)	3	T: FA(pre)+GA C: GA	T: 10 C: 10	2.50±1.52 3.83±0.75	2.33±1.37 4.17±1.6	2.00±1.41 3.67±0.51	2.50±1.52 5.17±1.52	NA
Li and Lin (2010)	3	T: FA(pre)+GA C: GA	T: 30 C: 30	3.30±0.80 4.50±1.30	2.80±1.00 3.80±1.10	2.20±1.00 3.40±0.90	2.00±1.00 2.30±0.70	10.00 40.00
Luo et al. (2009)	2	T: FA(pre)+GA C: GA	T: 20 C: 20	3.66±0.18 4.36±0.64	3.47±0.24 3.84±0.17	3.11±0.17 3.42±0.10	2.82±0.32 3.14±0.56	70.00 40.00
Song et al. (2010)	2	T: FA(pre)+GA C: GA	T: 30 C: 30	1.60±1.40 2.50±1.60	1.30±1.40 1.90±1.40	NA	0.80±1.40 1.30±0.90	20.00 46.70
Sun et al. (2007)	4	T: FA(pre)+GA C: GA	T: 30 C: 30	2.00±0.80 4.80±1.10	1.90±0.70 4.10±0.80	1.70±0.80 3.80±1.10	0.90±0.50 2.70±1.10	3.33 6.67
Wang et al. (2007)	3	T: FA(pre)+GA C: GA	T: 23 C: 21	2.00±0.74 2.76±0.77	2.34±0.71 3.05±0.59	NA	2.48±0.59 2.90±0.62	10.30 10.50
Wang et al. (2008)	2	T: FA(pre)+GA C: GA	T: 21 C: 21	1.85±0.71 3.50±1.81	1.71±0.67 3.30±1.51	NA	1.46±0.58 1.48±0.53	NA
Xie et al. (2006)	2	T: FA(pre)+GA C: GA	T: 40 C: 40	NA	NA	3.05±2.93 8.11±2.47	3.67±1.72 6.22±1.73	NA
Zeng et al., (2008)	3	T: FA(pre)+GA C: GA	T: 25 C: 25	3.10±0.80 4.60±1.10	2.00±0.90 4.00±1.20	1.90±0.70 3.50±1.40	1.00±0.50 2.30±1.10	24.00 16.00
Zeng and Li (2008)	2	T: FA(pre)+GA C: GA	T: 20 C: 20	2.50±0.90 3.40±1.20	3.20±1.10 3.40±1.30	3.60±1.40 3.80±1.30	2.70±0.90 2.60±1.10	NA
Zhao et al. (2009)	3	T: FA(pre)+GA C: GA	T: 25 C: 25	2.50±1.20 4.30±1.50	2.70±1.40 4.70±1.30	2.20±1.40 3.10±1.30	2.20±1.50 2.50±1.60	16.00 20.00

FA: Flurbiprofen axetil; FA(pre): flurbiprofen axetil of preemptive analgesia; FA(pro): flurbiprofen axetil of preemptive analgesia; GA: general anesthesia.

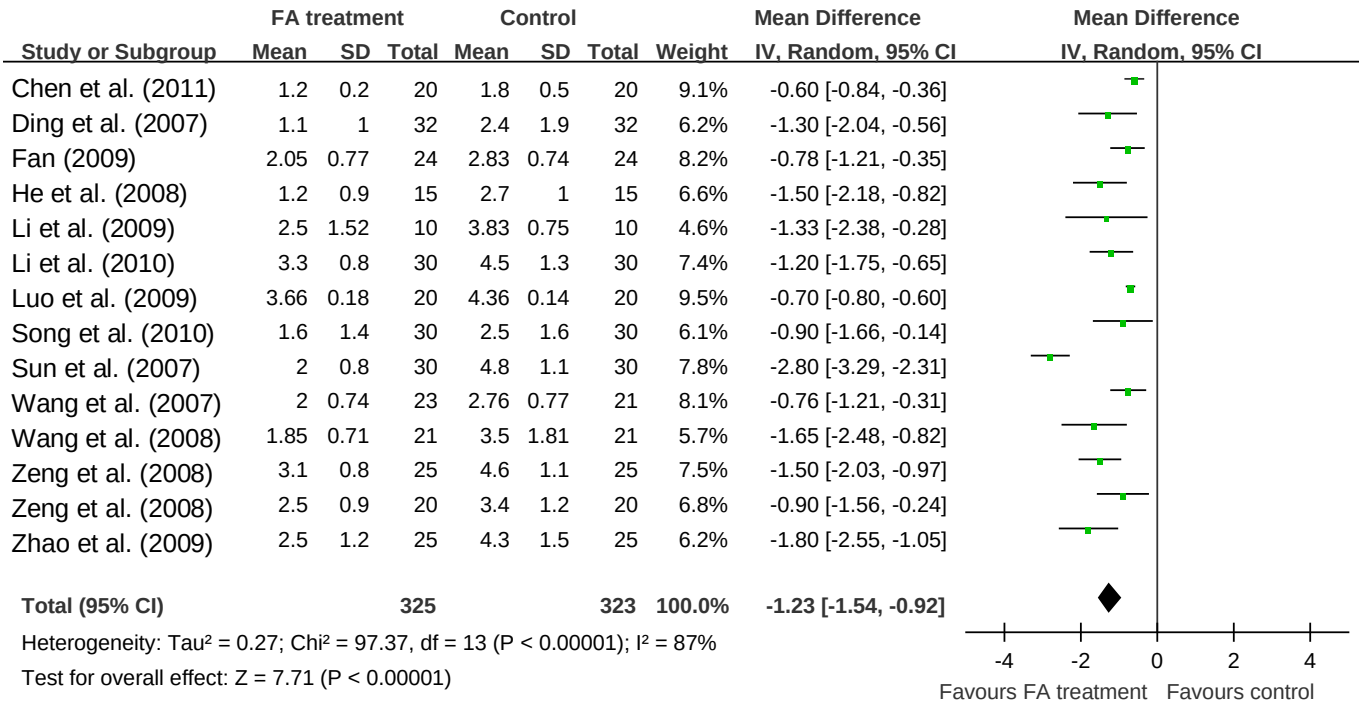

Figure 2. VAS at 4 h after operation between the FA treatment group and the control group.

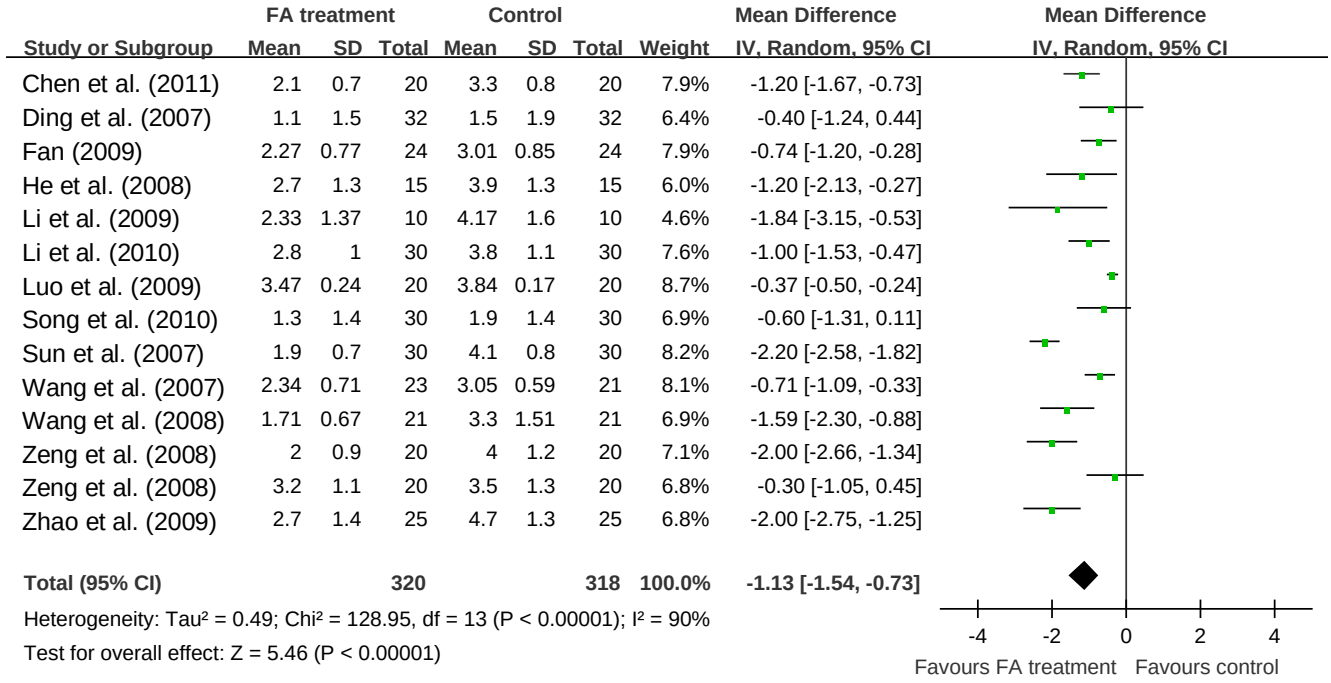

Figure 3. VAS at 8 h after operation between the FA treatment group and the control group.

17 trials finally included. Active analgesics involved in this analysis were tramadol or fentanyl. The results of meta-analysis (MD = -0.87, 95%CI: -1.24 to -0.51) confessed that VAS at 24 h after operation in FA treatment group is less than in control group of Chinese surgical patients (Figure 5).

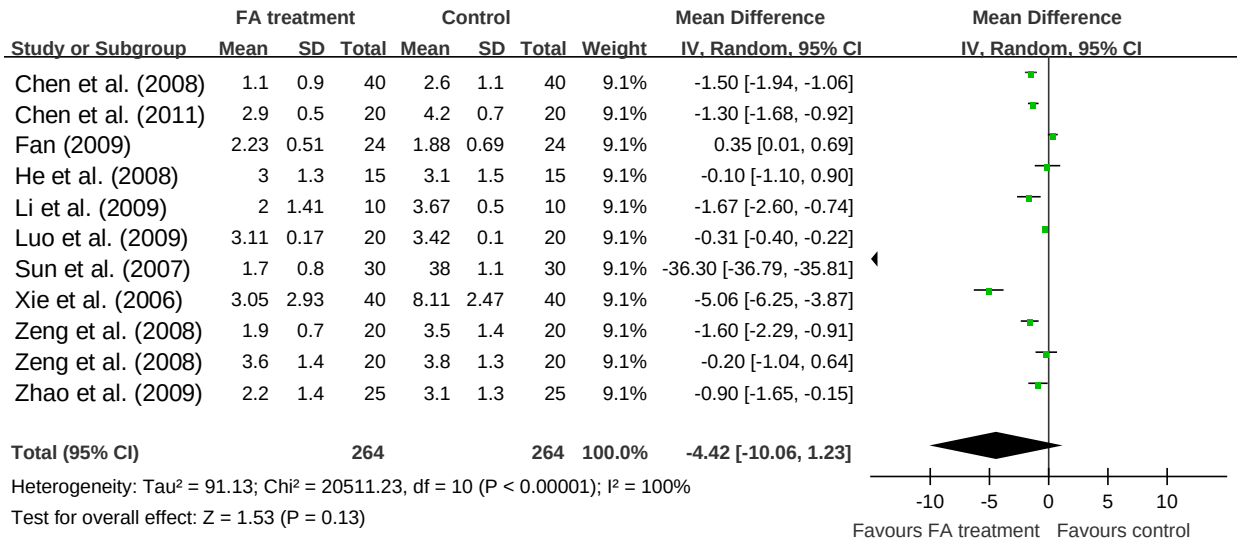

Figure 4. VAS at 12 h after operation between the FA treatment group and the control group.

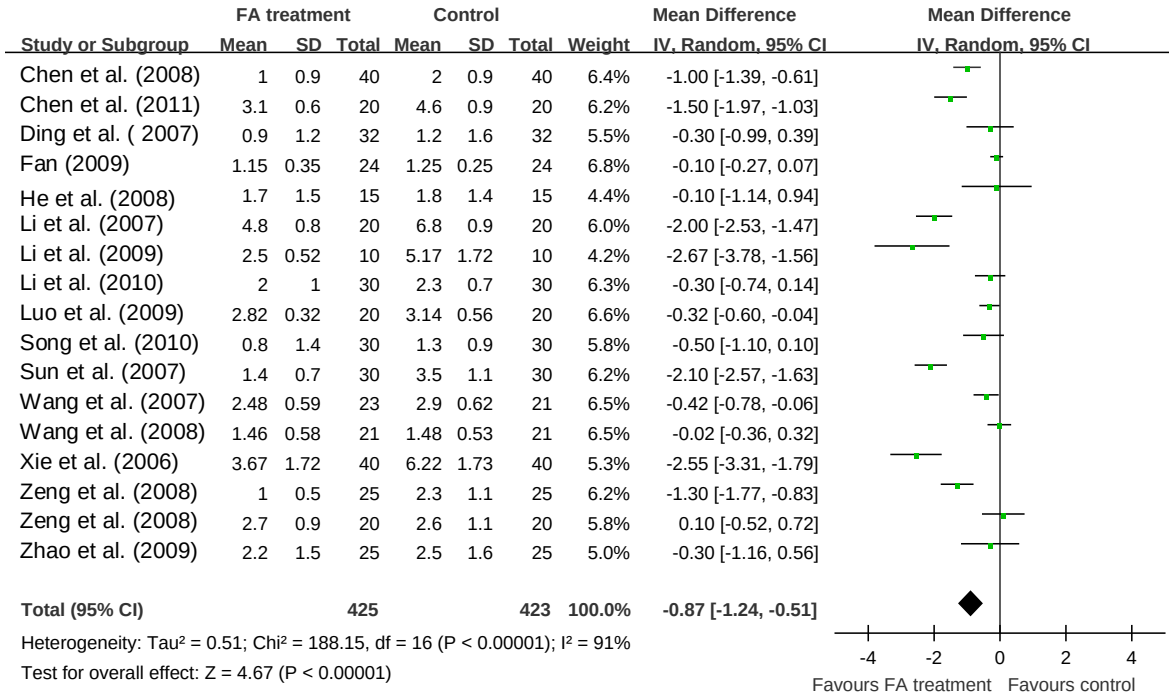

Figure 5. VAS at 24 h after operation between the FA treatment group and the control group.

Meta-analysis of safety

Adverse reaction rates of both FA and control group were recorded in the 12 trials finally included. The results of meta-analysis (OR = 0.70 95%CI: 0.49 to 0.99) confessed that FA is safer than the control group in Chinese surgical patients (Figure 6).

Publication bias

An analysis of publication bias was conducted. The funnel plots, to assess publication bias, are as shown in Figure 7. The shape of the funnel plots show some unasymmetries in all studies included in the meta-analysis. There exist some publication biases since the

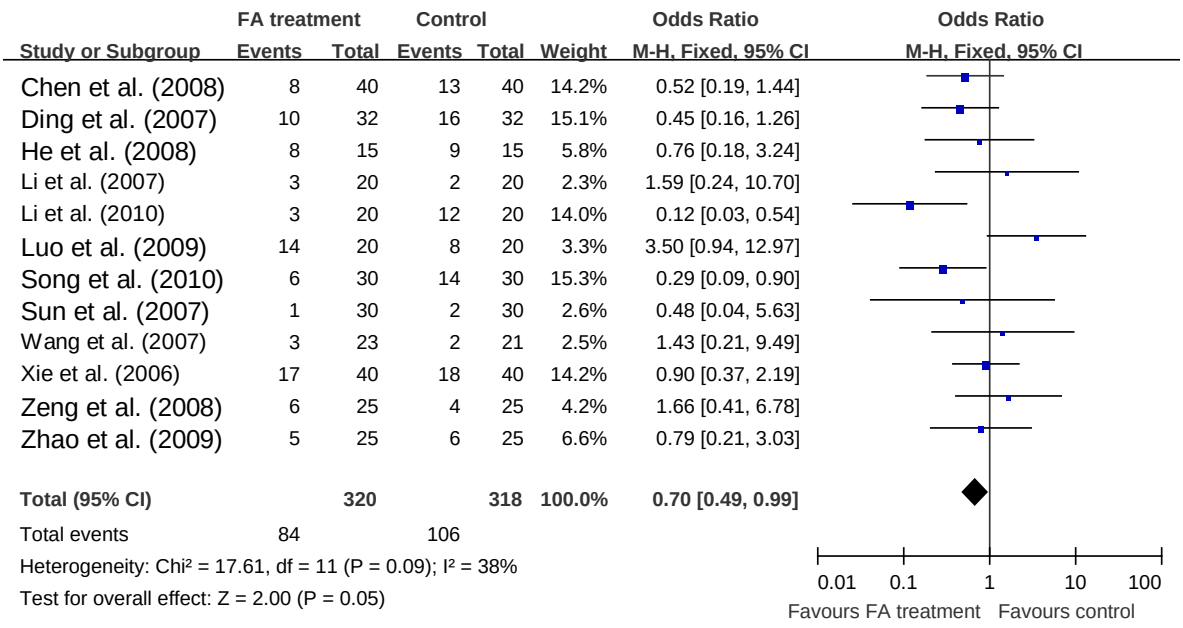

Figure 6. Adverse reactions rate between the FA treatment group and the control group.

funnel plots were unsymmetrical based on a visual analysis (Figure 7).

DISCUSSION

FA is prepared by esterification of flurbiprofen which makes the compound lipophilic and soluble in soybean oil within an intralipid based emulsion formulation for less irritation after iv injection (Simon and Benita, 1998). Flurbiprofen acts through inhibiting the cyclooxygenase reversibly, resulting in corresponding anti-inflammatory effect and causing the peripheral inhibition of prostaglandin (PG) synthesis (Basselin et al., 2007). In addition, flurbiprofen could also inhibit the migration of leukocytes into sites of inflammation and prevent the formation of thromboxane A2 by the platelets (Bolla et al., 2004; Van Ryan-McKenna and Buchanan, 1989). Thus, the anti-inflammatory and antinociceptive effects of flurbiprofen on postoperative pain was recommended for preemptive administration to suppress the synthesis of prostaglandin prophylactically at the area of the surgical injuries, which in return relieve the pain from the surgical wound (Nakayama et al., 2001).

A total of 17 literatures were finally included in this systemic review. All these articles, including a sample size of 848 totally were RCTs. Jadad score in 10 out of the 17 articles were more than three points. All the trials included in this meta-analysis mentioned the term "random", but the detail method was illuminated in 1 article only. Obviously, the included trials were lack of well-designed randomizations. A well-designed randomized controlled trial requires a thorough understanding of randomization, so that better results could be achieved. Randomization includes three important steps, namely, sequence generation, allocation concealment, and randomization implementation. Sequence generation is a method used to generate the random allocation sequence, including details of any restriction. Allocation concealment is to implement the random allocation sequence. Randomization implementtation is to generate the allocation sequence. Well-men designed randomized controlled trials are required to evaluate FA treatment versus routine treatment in Chinese surgical patients. It was suggested that we should be careful for randomization.

Moreover, there exist some publication biases in each analysis. The publication biases might be relevant to some methodological insufficiencies: (1) Randomization method may not be rigorous because the specific program of randomization was inferred in only one literature. (2) Selection bias may exist, for allocation concealment was not described in all of these articles included. (3) Selection bias, measuring bias, and implementation bias may exist because some studies did not describe whether blind method was used or not.

The results of this systemic review showed that FA was more effective than control group on preemptive analgesia for Chinese surgical patients. Thus, we can conclude that FA has stronger analgesic effect when compared with other active analgesics. The adverse reactions (ADRs), mainly gastrointestinal symptoms of FA referred to in this study were less likely to happen. The results of this systemic review showed that FA has less

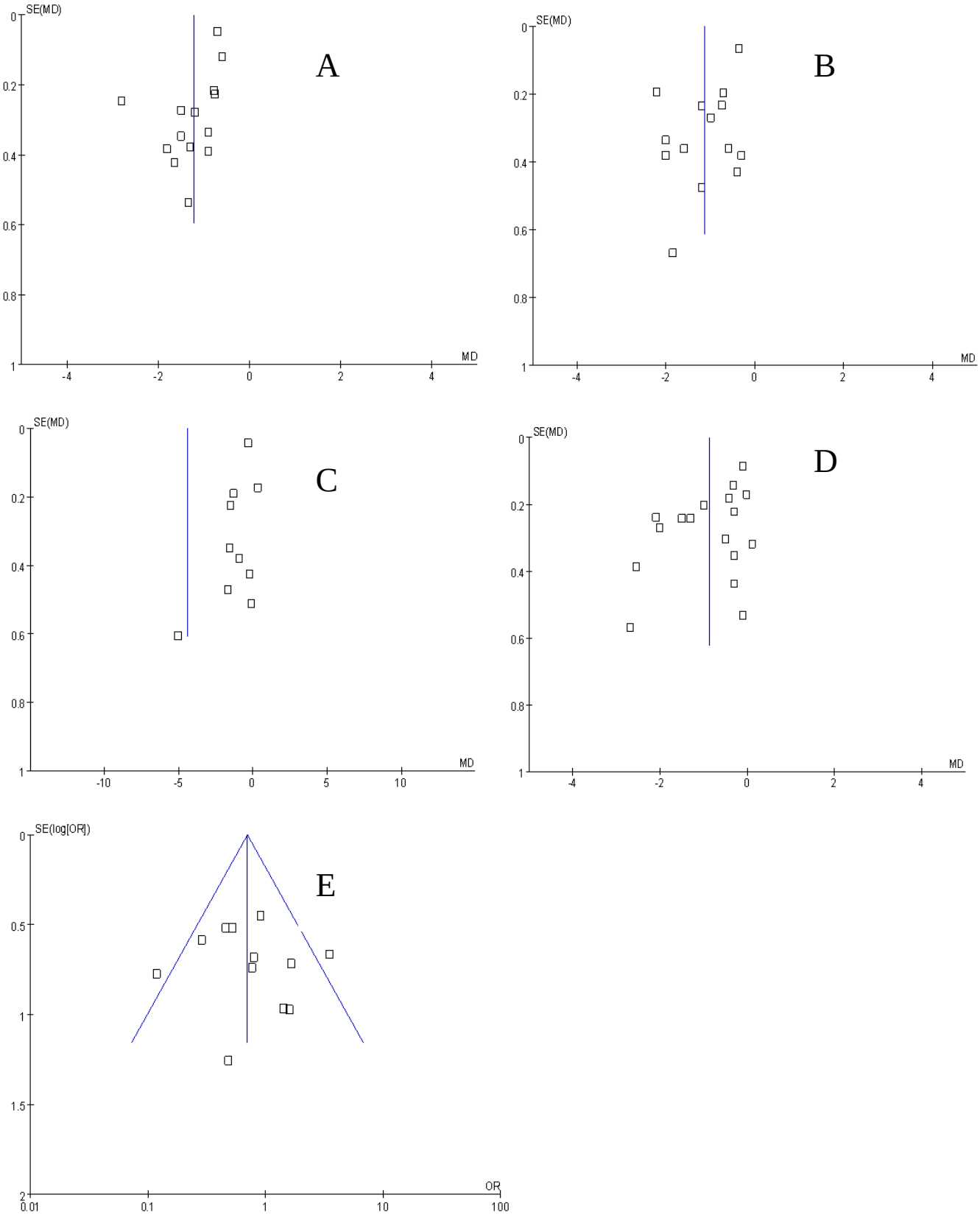

Figure 7. Funnel plots of sputum negative conversion tuberculosis cavity changes focus absorption and adverse effect. A: Funnel plot for VAS at 4 h after operation; B: Funnel plot for VAS at 8 h after operation; C: Funnel plot for VAS at 12 h after operation; D: Funnel plot for VAS at 24 h after operation; E: Funnel plot for ADRs rate.

ADRs than the control group in Chinese surgical patients. Therefore, we could conclude that FA was safer than other active analgesics.

Conclusion

In summary, our systemic review initially demonstrated the analgesic effects of FA in Chinese surgical patients, such as decreasing pain induced by various surgical operations. However, all the clinical trials involved were of small samples without blind methods, their results may show some uncertainties. We urgently hope the high-quality, double-blinded, and multi-centered RCTs will be carried out in the future to further confirm its efficacy and safety.

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REFERENCES

Basselin M, Villacreses NE, Lee HJ, Bell JM, Rapoport SI (2007). Flurbiprofen, a cyclooxygenase inhibitor, reduces the brain arachidonic acid signal in response to the cholinergic muscarinic agonist, are coline, in awake rats. Neurochem. Res. 32:1857-1867.

Bolla M, You D, Loufrani L, Levy BI, Levy-Toledano S, Habib A (2004). Cyclooxygenase involvement in thromboxanedependent contraction in rat mesenteric resistance arteries. Hypertens 43:1264-1269.

Buritova J, Besson JM (1998). Peripheral and/or central effects of racemic - S (+)- and R (-) -flurbiprofen on inflammatory nociceptive processes: ac-Fos protein study in the rat spina cord. Brit. J. Pharmacol. 125:87-101.

Chen XY, Cao HZ, Sun ZH (2011). Clinical effects of flurbiprofen axetil on preemptive analgesia during radical operation of thyroid cancer. Modern Oncolo. 19(3):565-566.

Chen Z, Li L, Ou YW (2008). Flurbiprofen used for preemptive analgesia in patients undergo gynecological laparoscopic surgery. J. China-Japan Friendship Hosp. 22(2):95-97.

Ding YH, Gu CY, Lou Y (2007). Application of pre- emptive analgesia with flurbiprofen axetil in patients undergoing laparoscopic cholecystectomy. Clin. Med. l27(11):29-31.

Fan ML (2009). Preemptive analgesia effects of flurbiprofen axetil injection in patients undergoing gastrectomy operation. Chin. J. Ethnomed. Ethnopharm. 18(7):23.

Fujii Y, Shiga Y (2005). Flurbiprofen axetil preceded by venous occlusion in the prevention of pain on propofol injection in the hand: A prospective, randomized, double-blind, vehicle-controlled, dose-finding study in Japanese adult surgical patients. Clin. Ther. 27(8):588-593.

Fujii Y, Shiga Y (2009). Pretreatment with flurbiprofen axetil, flurbiprofen axetil preceded by venous occlusion, and a mixture of flurbiprofen axetil and propofol in reducing pain on Injection of propofo in adult Japanese surgical patients: A prospective, randomized, double-blind, placebo-controlled study. Clin. Ther. 31(4):721-727.

He GW, Zhou ZC, Yuan SY (2008). Effect of preemptive analgesia with flurbiprofen axetil on serum gastrin in patients undergoing the lower extremity fracture surgery. Cent. Chin. Med. J. 32(1):35-37.

Li AB, Xie H (2007). Flurbiprofen used as preemptive analgesia of patients with laparoscopic cholecystectomy. Pract. Clin. Med. 8(12):55-57.

Li ZP, Lin YF (2010). Antinociceptive effects of flurbiprofen axetil on patients received upper abdominal surgery: the role of preemptive analgesia. Qinghai Med. Pharm. J. 40(4):6-8.

Li YH, Han M, Ma HC (2009). Preemptive analgesia effects of flurbiprofen axetil on respiratory function in patients undergoing thoracotomy. J. Jilin Univ. (Medicine Edition) 35(3):515-518.

Lin Q (2010). Preemptive analgesia with flurbiprofen axetil or tramadol before gynecologic hysteroscopic surgery: a comparison of outcome. Fujian Med. J. 32(5):123-125.

Luo H, Li J, Huang ZL (2009). Postoperative analgesic effects of flurbiprofen axetil applied on patients with arthroscopic surgery of knee. Prac. Med. J. 25(10):1666-1667.

Mikawa K, Nishina K, Maekawa N, Shiga M, Obara H (1997). Dose-response of flurbiprofen on postoperative pain and emesis after paediatric strabismus surgery. Can. J. Anaesth., 44: 95-98.

Nakayama M, Ichinose H, Yamamoto S (2001). Perioperative intravenous flurbiprofen reduces postoperative pain after abdominal hysterectomy. Can. J. Anesth., 48: 234-237.

Nishiike S, Kato T, Nagai M (2007). Preoperative flurbiprofen for pain prevention after tonsillectomy in adults. J. Clin. Anesth., 19: 596-600.

Roszkowski MT, Swift JQ, Hargreaves KM (1997). Effect of NSAID administration on tissue levels of immunoreactive prostaglandin E2, leukotriene B4, and (S)-flurbiprofen following extraction of impacted third molars. Pain 73:339-345.

Simon, Benita (1998). Submicron emulsions in drug targeting and delivery. CRC Press. pp. 135.

Song WJ, Zhai XD, Dong JL (2010). Postoperative analgesic effects of flurbiprofen axetil injection applied on patients with naigated knee arthroplasty. Hebei Med. J., 32(20): 2877-2878.

Sun ZT, Han XP, Miao LJ (2007). Preemptive analgesia for postoperative pain relief of flurbiprofen axeti injection on children. Chin. J. Pain. Med. 13(4):213-217.

Takada M, Fukusaki M, Terao Y, Yamashita K, Inadomi C (2007). Preadministration of flurbiprofen suppresses prostaglandin production and postoperative pain in orthopedic patients undergoing tourniquet inflation. J. Clin. Anesth. 19:97-100.

Xie YH, Fang C, Zhou L (2006). Flurbiprofen used for preemptive analgesia of patients wi th abdomi nal cholecystectomy. Anhui Med. Pharmaceut. J., 10(8): 571-572.

Van Ryan-McKenna J, Buchanan MR (1989). Relative effects of flurbiprofen on platelet 12-hydroxy-eicosatetraenoic acid and thromboxane A2 production: influence on collagen-induced platelet aggregation and adhesion. Prostaglandins Leukot. Essent. Fatty Acids 36:171-174.

Wang FZ, Shen XF, Xu SQ (2008). Preemptive combined preventive delivery of flurbiprofen axetil produced effective analgesia after lumpectomy. Acute Pain 10:65-71.

Wang FZ, Shen XF, Guo XR (2009). Analgesic effectiveness of flurbiprofen axetil after uterine curettage on abortion: A randomized controlled trial. Acute Pain 11:43-50.

Wang Q, Wang ZC, Liu HQ (2007). Postoperative analgesic effects of flurbiprofen axetil applied preoperatively on patients with spinal cord injury. Chin. J. Rehabil. Theory Pract. 13(11):1019-1020.

Zeng RF, Ni YF, Wang JG (2008). Postoperative analgesic effects of flurbiprofen axetil on postoperative analgesia in patient undergoing surgery of vocal cord under suspension laryngoscope. Clin. Med. 28(9):68-69.

Zeng ZD, Li HM (2008). Postoperative analgesic effects of flurbiprofen axetil on postoperative analgesia in patient undergoing laparoscopic cholecystectomy. Chin. J. Med. Guide 10(5):723-724.

Zhao B, Xia XQ, Luo HL (2009). Postoperative analgesic effects of flurbiprofen axetil applied on patients with laparoscopic cholecystectomy. Anhui Med. J. 30(9):1114-1115.