Intrathecal Morphine Versus Transversus Abdominis Plane Block for Caesarean Delivery: a Systematic Review and Meta-analysis

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Abstract

Background: In recent years, the number of cesarean deliveries is on the rise. Although intrathecal morphine (ITM) can relieve pain and is widely applied in cesarean deliveries, it is also associated with many side effects. As a new analgesic technology, transversus abdominis plane (TAP) block has also begun to play a certain role after cesarean delivery, with fewer adverse effects. This article mainly compares the analgesic and adverse effect of ITM and TAP block in cesarean delivery.

Methods: We systematically searched PubMed, Cochrane library, Embase and Web of Science, for randomized controlled trials before October 5, 2020 to compare ITM and TAP block. Our main result is the pain score at rest 24 hours after cesarean delivery, and the secondary result is the pain score at movement 24 hours after operation, postoperative nausea and vomiting (PONV), itching, and morphine consumption. We conducted a subgroup analysis based on economic development.

Result: Six articles with 563 sample sizes were included. The results showed there was no significant difference between ITM and TAP block in the pain score at rest 24 hours after surgery (95% CI: -1.33 to 0.40; P=0.29). After subgroup analysis based on economic development, Parturients in the ITM group have lower rest pain score than those in the TAP group (95% CI: -1.27 to -0.28; P=0.002) in the developed area. There was no significant difference in the 24h moving pain score (95% CI:-1.47 to 0.29;P=0.19）and incidence of pruritus (95% CI:0.87 to 8.85;P=0.08). The ITM group showed less morphine consumption when compared with the TAP group (95% CI:-13.12 to -2.95;P=0.002）. The incidence of PONV was lower in the TAP group as compared to the ITM group (95% CI:1.92 to 4.87; P<0.00001).

Conclusion: We found that Parturients in the ITM and TAP block groups had similar analgesic effects. However, after subgroup analysis, in developed countries, Parturients in the ITM group has better analgesic effects than those in the TAP block group with less morphine consumption. Differently, TAP block had low side effects such as nausea, vomiting. Therefore, if patients cannot use ITM for analgesia after cesarean delivery, or patients have high risk of PONV, then TAP is still a valuable analgesia option.

Registration number: Registered on Prospero with the registration number of CRD42020210135

Introduction:

In recent years, because of social and psychological reasons, the rate of cesarean delivery has increased year by year(1). Postoperative pain will not only bring psychological torture to patients, but also have a certain degree of impact on the recovery of patients after surgery and wound recovery (2, 3). For parturients after cesarean delivery, on the one hand, the lack of analgesia will affect the mother's postpartum recovery, breast-feeding, and baby development, on the other hand, it will also increase the risk of postpartum depression(4, 5). Recently, it has been reported that about 500,000 women in Europe suffer from acute postoperative pain every year(3). Therefore, it is essential to get effective analgesic methods for parturients after cesarean delivery is surging.

Intrathecal morphine (ITM) for analgesia is considered to be the "gold standard" for analgesia after cesarean delivery. ITM can make it easier for hydrophilic morphine to reach the cerebrospinal fluid and act on the central nervous faster(6). Therefore, the use of ITM can provide a better analgesic effect after cesarean delivery compared with the technique of systemic opioid analgesia(7, 8). Although ITM has obvious analgesic advantages, its side effects such as nausea, vomiting, itching, and even respiratory depression have restricted its further application(9, 10).

With the rapid development of ultrasound technology, transversus abdominis plane (TAP) block is more and more popular in local anesthesia technology. Local anesthetics were mainly injected into the superficial layer of TAP and deep layer of internal oblique muscle, thus blocking the anterior abdominal wall afferent nerve of T6-L1(11). Recent studies indicated, that TAP block may play a vital role as an effective pain block of somatic surface pain induced by incision, which is much more obvious than the visceral pain caused by the traditional transverse incision (12, 13).

There are some meta-analyses on patient-controlled intravenous analgesia, quadratus lumborum block, and intrathecal morphine injection in the literature. However, most of these studies discussed the analgesic effect of TAP combined with ITM, some researchers believe that in the case of postoperative analgesia with ITM, the addition of TAP cannot further alleviate the pain. and only one meta-analysis compared the analgesic effect of TAP and ITM after cesarean delivery(14). In this meta-analysis, the results showed that ITM had a better analgesic effect than TAP at rest 24 hours after surgery. However, the evidence was not convincing since only two RCTs were included. To bridge the gap, we updated this and included more RCTs, hoping to summarize and compare the results of analgesic effect and side effects of ITM and TAP after cesarean delivery.

Methods:

This systematic review and meta-analysis are reported according to PRISMA recommendation and has been registered on Prospero (number: CRD420210135)(15). The two researchers (YTR and HXM) searched PubMed, Cochrane Library and EMBASE from inception to October 9, 2020, without limit on language and region.

A comprehensive search strategy was employed using relevant search terms selected from Medical Subject Headings, Embase Subject Headings, and Entry Terms. The databases were explored using a search algorithm with Boolean operators: "(transversus abdominis plane block OR transversus abdominis block OR abdominal Muscle block OR TAP) AND (Spinal Injections OR Intrathecal Injections OR Intraspinal Injection OR ITM) AND (cesarean section OR cesarean delivery OR abdominal deliveries OR C Section OR postcesarean section)."

Study selection

The determination of inclusion and exclusion criteria preceded our meta-analysis. Inclusion criteria were as follows:1. Adult female; 2. ASA ≤ 3; 3. Spinal anesthesia; 4. Cesarean section/delivery; 5. Pfannenstiel incision. Our exclusion was as follows: 1. Observational or retrospective study; 2. BMI ≥ 40; 3. History of drug allergy and opioid tolerance. The two researchers (YTR and HXM) read the titles and abstracts, and selected documents that meet the inclusion for full-text reading. If there are differences, the third researcher (WRR) evaluated them. The authors then performed additional literature searches of the clinical trials registry (www.clinicaltrials.gov).

Data extraction

The two researchers(YTR and HXM) independently extracted the following data（Table 1）: 1. The number of participants, 2. Age, 3. Weight, 4. The analgesic methods of the control group and the intervention group, 5. Drugs, 6. Methods of anesthesia, 7. Extra medications, 8. Pain score, 9. Corresponding side effects (nausea, vomiting, itching). Discrepancies were resolved by consensus or, if necessary, by discussion with a third author (WRR).

Data is extracted for synthesis either directly from the paper, extrapolate from graphs using Plot digitizer (http://www.plotdigitizer.sourceforge.net) or, if this is not possible, the corresponding authors are contacted for the needed data. We extract continuous results as the mean and standard deviation. If there is no direct data in the original text, we will extract the data from the graph. If the median is displayed, then we will use Hozo and other formulas to convert the median and range to mean and standard deviation (16).

Quality of the reviewed trials was assessed independently by two of the authors (YTR and HXM) using the Cochrane Risk of Bias tool.

Outcome

We set the pain score at rest 24 hours after the operation as the primary outcome and converted the evaluation criteria of 0-100 points to 0-10 points for analysis. If the data in the original article reported both the visceral score and the somatic score, the higher pain score was selected for data analysis. Among the main outcome, we conducted a subgroup analysis based on economic development. The pain score at movement 24 hours after the operation, nausea and vomiting, the incidence of itching, and the consumption of morphine were set as the secondary outcome.

Postoperative morphine requirement was compared between groups. Other forms of opiate analgesia were converted to intravenous morphine equivalents as follows: oral tramadol (1 : 20), parenteral fentanyl (10 : 1), and intravenous oxycodone (1 : 1)(17, 18).

Data analysis

For continuous variables, we use 95% confidence interval and mean difference to present them. For dichotomous variables, the odds ratio (OR) value was used to delicate them. We used I^2 to evaluate the heterogeneity of the literature, and I^2 values > 50% was suggested significant heterogeneity between studies (19). For continuous data, we determined the mean differences (MD). The heterogeneity should be explored by appropriate subgroup analyses. All statistical analysis was performed in ReviewManager5.3.

Risk of bias assessment

Two authors(YTR and HXM) independently assessed the methodological quality of each study using the Cochrane Collaboration Risk of Bias tool for RCTs(20). This tool includes assessment of the risks of random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. The risk of bias was classified as high, low or unclear. Disagreement between the two reviewers regarding the overall risk of bias assessment were resolved through discussion and consensus.

Result:

The systematic database search identified 369 reports. After removing duplicate studies, we screened 338 records. 30 full-text publications were assessed for eligibility after title and abstract reviewing. We excluded 24 studies because the participants, interventions or outcomes did not meet our inclusion criteria or because the study was not an RCT. We selected and included a final 6 RCTs for the final analysis(21-26). A flow chart of the study selection process was presented in Fig. 1.

Study characteristics

Table 1 Characteristics of included studies

Author,year	Total Sample	Methods	Age	Weight	Sample	Drug	Anesthesia	Additional drug
Kwkiriza,2019	n=130	ITM	24.7 (5.6)	65.2 (11.9)	n=65	Morphine 0.1mg	Spinal anesthesia with bupivacaine 10mg	Diclofenac 50 mg and paracetamol 1 g every 8 hours
		TAP	24.8 (4.8)	63.9 (12.5)	n=65	Bupivacaine75mg		
Kanazi, 2010	n=57	ITM	33 (6)	82(13)	n=28	Morphine 0.2mg	Spinal anesthesia with bupivacaine 12.75mg	Rectal diclofenac 100 mg every 12 hours and intravenous acetaminophen 1 g every 6 hours
		TAP	30 (5)	78(16)	n=29	Bupivacaine75mg		
McMorrow, 201	n=40	ITM	33 (4)	70 (13)	n=20	Morphine 0.1mg	Spinal anesthesia with bupivacaine 11-12.5mg and 10ug fentanyl	Rectal diclofenac 100 mg every 18 hours and oral acetaminophen 1 g every 6 hours
		TAP	33 (5)	72 (14)	n=20	Bupivacaine75mg		
Dereu, 2019	n=181	ITM	34 [31 to 38]	74 [67 to 83]	n=89	Morphine 0.1mg	Spinal anesthesia with bupivacaine 10mg and fentanyl 25ug and epinephrine 100ug	Paracetamol orally 1 g every 6 hours and ibuprofen 600 mg every 8 hours
		TAP	34 [30.75 to 37	74.5 [67 to 82.25	n=92	Bupivacaine 150mg and clonidine 75ug		
Loane, 2012	n=66	ITM	35(3)	81(13)	n=33	Morphine 0.1mg	Spinal anesthesia with bupivacaine 11.25 mg and fentanyl 10 ug	Naproxen orally or rectal 500 mg every 12 hours and acetaminophen 1 g every 6 hours
		TAP	34(5)	78(12)	n=33	Ropivacaine 3mg/kg, no more than 200mg		
Jarraya, 2016	n=86	ITM	33.24(5.7)	75.63(11.7)	n=43	Morphine 0.1mg	Spinal anesthesia with bupivacaine 10mg and fentanyl 2.5ug	Paracetamol orally 1 g of every 6 hours and ketoprofen 100 mg and tramadol 100 mg every 12 hours
		TAP	32.83(6.1)	76.63(10.4)	n=43	Ropivacaine 60mg		

The number represents the mean (standard deviation) or median (interquartile range) ITM, intrathecal morphine; TAP, transversus abdominis plane block;

Table 1 summarizes the characteristics and outcomes of the 6 RCTs included according to the search criteria. There were 5 studies(22-26) and 1 study (21) conducted in the developed country and developing country, respectively. We conducted a subgroup analysis for this. All included studies were published before October 2020. The sample size of these studies ranged from 40 to 180.In the 6 RCTs, most of the studies used 10–12.75 mg bupivacaine with or without opioid for spinal anesthesia, and one(24) of them additionally added epinephrine for spinal anesthesia. All studies in the ITM group used morphine at 0.1-0.2 mg. Four studies(21-24) in the TAP group used bupivacaine for local blockade, while the other two trials(25, 26) used ropivacaine. One(24) study in the TAP group also added clonidine 75ug.

Quality assessment

Risk of bias of all the RCTs is presented in Fig. 2. According to the Cochrane Risk of Bias tool，we got four trails(21, 22, 24, 25) at high level in terms of risk of bias. Three of them(22, 24, 25) were at a high risk of attribution, and two of them(21, 25) had a high risk of other bias, and one of them(21) was at a high risk of selection bias. Four studies(21, 22, 26) were at unclear risk of bias owing to selection bias, detection bias, attribution bias, or reporting bias.

Primary outcome

Pain scores at rest 24 hours after operation

A five studies of 474 patients reported pain scores at rest 24 hours after surgery(21-25). Compared with the TAP group, there was no significant difference in the pain score of the ITM group (MD: -0.47; 95% CI

-1.33 to 0.40; I^2=79%; P=0.29) (Fig. 3). According to the economic situation, a subgroup analysis showed that in developed countries(22-25), the pain score of the ITM group was lower than that of the TAP group, indicating that ITM brought better analgesic effects (MD: -0.77; 95% CI -1.27 to -0.28; I^2=0%; P=0.002). There was only one study (with a small sample size)(21) in developing country, thus it was not analyzed.

Secondary outcome

Pain scores at movement 24 hours

Five studies including 474 patients provided pain scores at moving 24 hours after surgery(21-25). There was no significant difference between the pain score of ITM and the TAP group (MD: -0.59; 95% CI -1.47 to 0.29; I^2=83%; P=0.19) (Fig. 4). Through subgroup analysis, it is found that although in the developed countries(22-25), the pain score of ITM is lower than that of the TAP group (MD: -0.94; 95% CI -1.80 to -0.07; I^2=62%; P=0.03), but after grouping, there is still research heterogeneity. After discussion, we concluded that there is a higher risk of attrition bias in one study(24), which may be the cause of the heterogeneity.

PONV 24 hours

The incidence of nausea and vomiting was recorded in five articles, of which 519 were reported (Fig.5) (21, 22, 24-26). Among these trials, Statistically difference in nausea and/or vomiting was found when ITM compared to TAP (odds ratio: 3.06; 95% CI: 1.92 to 4.87; P􏰀0.00001; Fig. 5) with mild heterogeneity (I2 = 26%).

Morphine consumption

A total of 287 people reported the consumption of morphine 24 hours after operation (Fig. 6)(23-25). There was a difference in morphine consumption between ITM and TAP (MD:-8.04; 95􏰀 CI:-13.12 to -2.95; I^2=66􏰀; P=0.002), which indicated that compared with the consumption of morphine in TAP, intrathecal morphine analgesia had a certain reduction in postoperative morphine demand. There is also a certain degree of heterogeneity among the included studies, but because there are few included studies, it is difficult to conduct subgroup analysis.

Itching 24 hours

A total of 560 samples from 6 literatures recorded pruritus 24h after surgery (Fig. 7)(21-26). Among these trials, no statistically difference in Itching was found when ITM was administered compared to TAP (odds ratio: 2.78, 95% CI: 0.87 to 8.85; P =0.08;) (Fig. 7) with high heterogeneity (I^2 = 76%). In one study, patients were asked to express the degree of pruritus subjectively, and there was no objective record and evaluation of whether pruritus occurred(23), so it may be a source of heterogeneity.

Discussion:

This systematic review and meta-analysis included the results of six RCTs to compare the analgesic effects of ITM and TAP after cesarean delivery. The results showed that there was no significant difference in pain scores between ITM and TAP groups. However, there was a high heterogeneity among the included literature. A subgroup analysis was conducted according to the economic regions and found that the analgesic effect of ITM was better than TAP at rest and movement in developed countries. In addition, the consumption of morphine in ITM group was less than that in TAP group. Although there was no significant difference in the incidence of postoperative pruritus between ITM group and TAP group, we should pay attention to the higher incidence of nausea and vomiting in ITM group compared with TAP group.

There has been no meta-analysis that individually and systematically compares the analgesic effects of ITM and TAP after cesarean delivery yet. Among the existing analgesic methods after cesarean delivery, ITM is undoubtedly the first choice of anesthesiologists(27). Although morphine can bring relatively superior analgesic effects, its adverse reactions (nausea and vomiting, respiratory depression, etc.) have limited its application(9). Because of the low clearance rate of opioids in newborns, higher dosage of utilization would lead to increasing chance of accumulation in the newborn's brain (28).Therefore, researchers are trying to explore the optimal analgesic method. In recent years, with the rapid development of ultrasound technology, ultrasound-guided transversus plane abdominis block has attracted attention. The traditional pfannenstiel cesarean delivery incision is located in the classic area of the abdomen, which is usually used as the injection site of lateral approach anesthesia, which also provides a theoretical basis for us to use TAP for analgesia after cesarean delivery(29).

Previously, one meta-analysis had been conducted to compare ITM and TAP for multimodal analgesia after cesarean delivery(14). However, this study focused on the analgesic effects of the combined utilization of TAP and ITM. In this meta-analysis, it was found that in parturients received ITM, TAP had little blocking effect and could only reduce the early postoperative movement pain score. In Mishriky's meta-analysis, although the comparison of the analgesic effects between ITM and TAP was mentioned, the authors did not perform further analysis and conclusions because of the small sample size of the included literature and excessive bias. In our meta-analysis, we included enough literature, evaluated the quality of the literature, compared the effects of ITM and TAP for post-cesarean analgesia through various outcome, and analyzed the heterogeneity.

In present meta-analysis, it was found that the analgesic effect of ITM was significantly better than that of TAP in developed areas after grouping based on economic development, while there was no significant difference in pain scores between TAP group and ITM group in economically backward areas. After repeated reading of the included literature, we determined that the heterogeneity of the results mainly came from kwikiriza's RCT(21), and summarized the possible reasons for the heterogeneity as follows: 1. The sample source of this article is different from other literatures. Kwikiriza's RCT comes from Uganda, a poor area in Africa. In the region, postoperative care and resources are very limited, and some basic care in the ward even needs to be provided by the patients' family and friends. In the case of nursing staff scarcity, patients cannot get postoperative analgesics in time, and postoperative follow-up for patients cannot be completed on time. 2. Most of the parturients in this area come from self-sufficient agricultural areas. To some degree of education, the willingness to relieve pain and to express pain are different from other groups of people. In their culture, pain is considered common. Unless the researchers repeatedly asked, they will not take the initiative to report mild pain, which also brings bias to the study.

In our meta-analysis, it was found that parturients in the ITM group had better analgesic effects, and had less postoperative demand for morphine, however, they had more postoperative adverse reactions. Although the incidence of postoperative pruritus in the ITM group and the TAP group was not statistically significant, the incidence of postoperative nausea and vomiting in the TAP group was much lower than that of the ITM group. This is also the advantage of the TAP technology. How to apply the advantages of TAP to multimodal analgesia may be an important direction of our future research.

This review has some limitations. First of all, the included literature is small and the number of samples is insufficient. With the increase of relevant research, our understanding of ITM and TAP will continue to be expanded. In addition, there is a study from a developing area, and its outcome have a higher risk of bias. Secondly, pregnant women with a previous history of cesarean delivery are not excluded. The multipara had used ITM or TAP for postoperative analgesia after the previous cesarean delivery. If the randomized treatment in this study is inconsistent with the pattern previously used in parturient, they may have doubts about the analgesic effect, thus breaking the blindness. Third, the dose and concentration of local anesthetics used in the study were different, and corresponding drugs were also used after surgery, such as paracetamol, dexamethasone and so on. Although both groups used these postoperative drugs, it also increased the complexity of the study. Finally, there is no detailed information about the technique used in transversus abdominis block. Transverse abdominis plane block is completed under ultrasound or landmark positioning. However, these different methods may produce different blocking effects, this may be the focus of future study.

Conclusion:

In conclusion, our meta-analysis shows that ITM can bring better analgesic effects to parturents after cesarean delivery, and the postoperative demand for morphine is less compared to TAP in developed countries. In addition, the incidence of itching was comparable between groups, while a higher incidence of nausea and vomiting were presented in ITM group. Thus, it was advised TAP as a valuable analgesia option for patients who cannot use intrathecal morphine for analgesia after cesarean delivery, or patients who have high risk of nausea and vomiting.

Further study should be focused on post-cesarean analgesia in developing countries. According to reports, most deliveries in the world are performed in these places(30). However, in these areas, due to the lack of personnel and economy, it is difficult to achieve good care and superior anesthesia technology. How to perform postpartum analgesia under the conditions of lack of resources may be the focus of our future study, and more randomized controlled trials are needed.

Abbreviations:

OR: odds ratio; CI: confidence interval; MD: mean difference; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCTs: randomized controlled trials; MeSH: Medical Subject Heading; ITM: intrathecal morphine; TAP: transversus abdominis plane; PONV: postoperative nausea and vomiting

Declarations:

Ethics approval and consent to participate:

Not applicable

Consent for publication:

Not applicable

Availability of data and materials:

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests

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Authors' contributions:

Tao-ran Yang made substantial contributions to conception and design of the study; Tao-ran Yang, Xue-mei He and Ru-rong Wang searched literature, extracted data from the collected literature and analyzed the data; Tao-ran Yang wrote the manuscript; Xue-han Li and Ru-rong Wang revised the manuscript; All authors approved the final version of the manuscript

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Figures

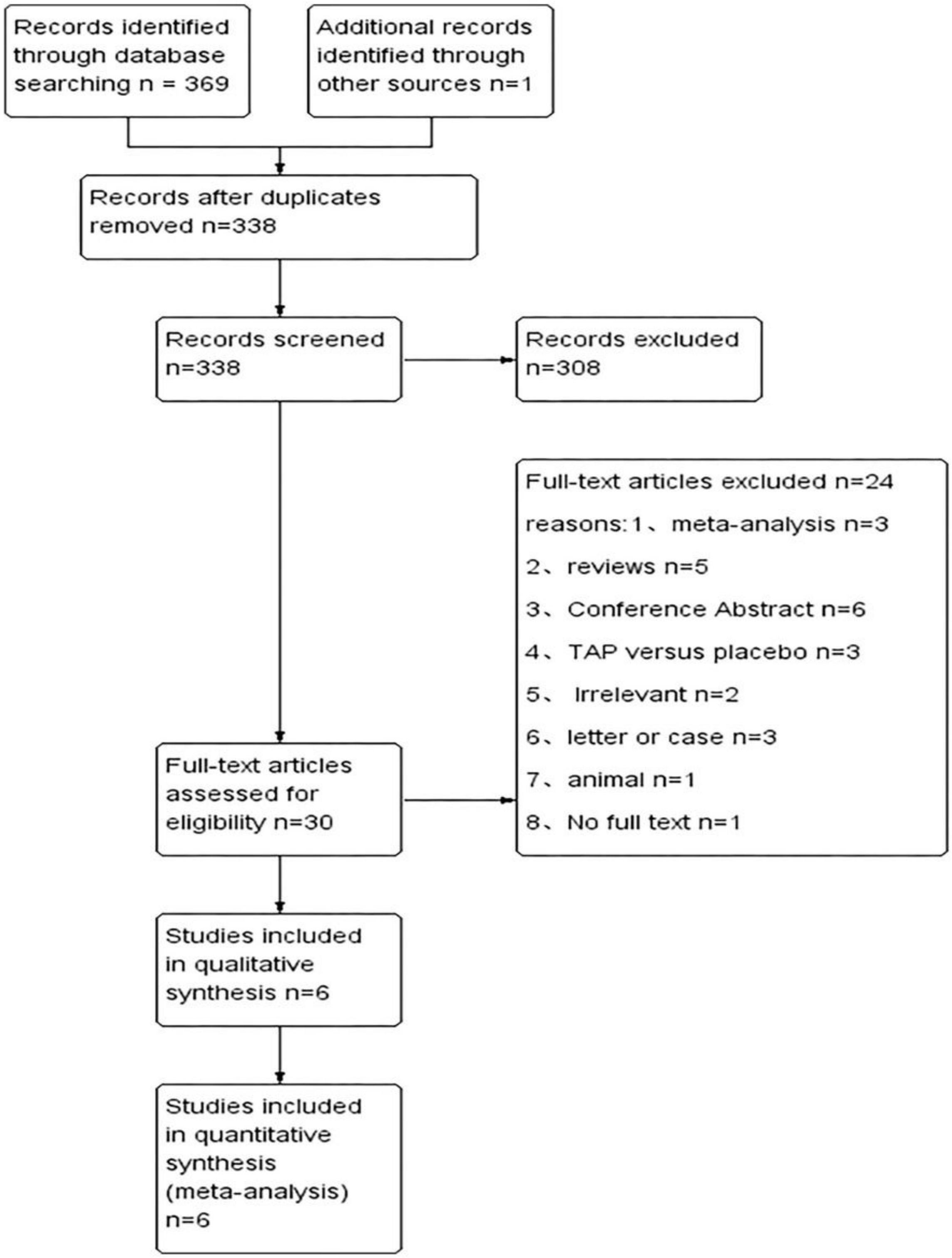

Figure 1

Flow chart showing selection of articles for review

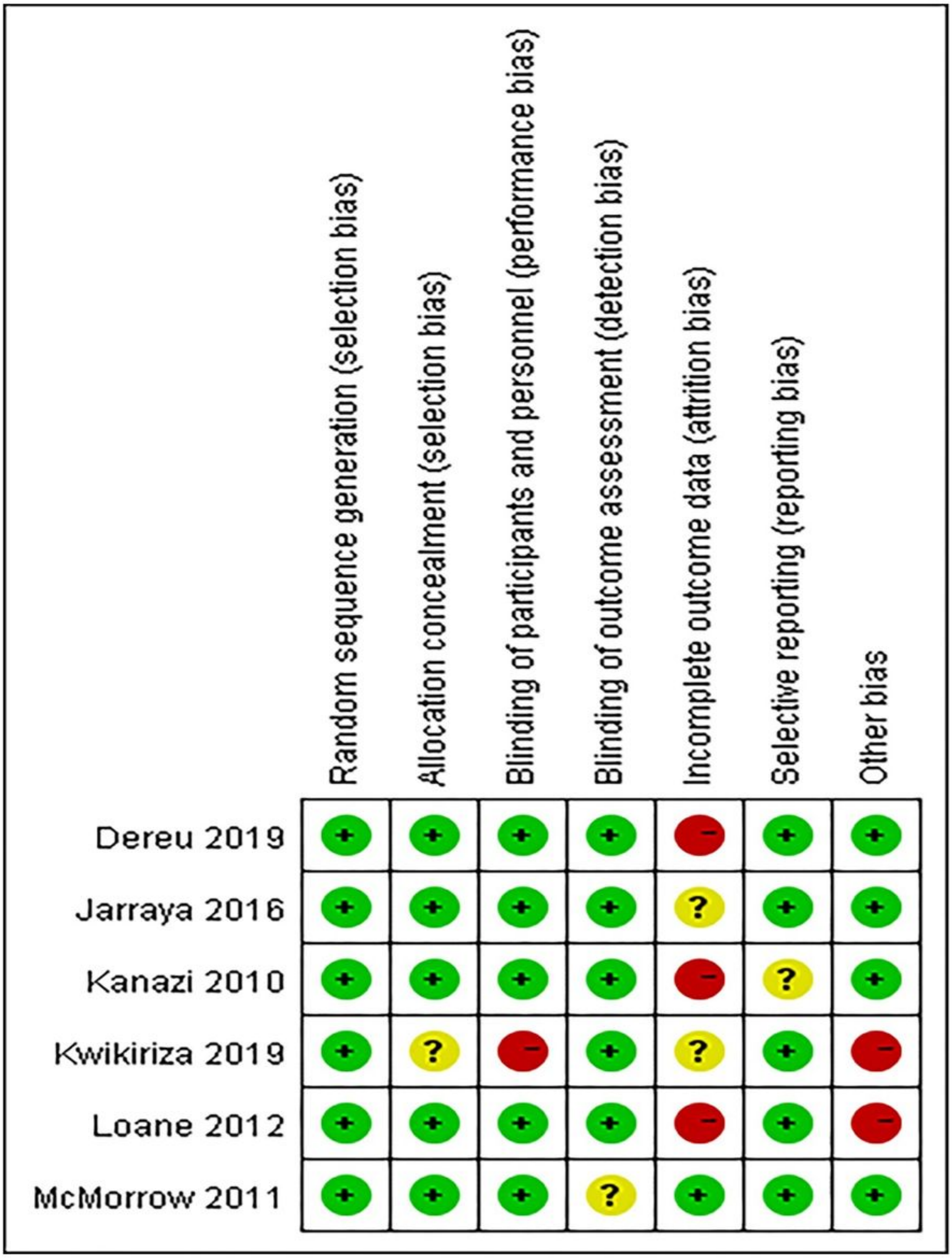

Figure 2

Quality assessment of included trials. Legends: Green circle=low risk of bias; red circle=high risk of bias; yellow circle=unclear risk of bias

Study or Subgroup	ITM Mean	ITM SD	ITM Total	TAP Mean	TAP SD	TAP Total	Weight	Mean Difference IV, Random, 95% CI
3.2.1 Developed country								
Dereu 2019	1.65	2.26	89	2.35	2.26	92	24.1%	-0.70 [-1.36, -0.04]
Kanazi 2010	3.29	3.12	28	3.5	2.34	29	15.8%	-0.21 [-1.65, 1.23]
Loane 2012	1.64	2.32	33	2.36	2.32	33	19.0%	-0.72 [-1.84, 0.40]
McMorrow 2011	1.07	0.8	20	2.96	3.35	20	15.1%	-1.89 [-3.40, -0.38]
Subtotal (95% CI)			**170**			**174**	**74.0%**	**-0.77 [-1.27, -0.28]**
Heterogeneity: Tau² = 0.00; Chi² = 2.75, df = 3 (P = 0.43); I² = 0%								
Test for overall effect: Z = 3.05 (P = 0.002)								
3.2.2 Developing country								
Kwikiriza 2019	2.9	1.31	65	2.3	1.31	65	26.0%	0.60 [0.15, 1.05]
Subtotal (95% CI)			**65**			**65**	**26.0%**	**0.60 [0.15, 1.05]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.61 (P = 0.009)								
Total (95% CI)			**235**			**239**	**100.0%**	**-0.47 [-1.33, 0.40]**
Heterogeneity: Tau² = 0.70; Chi² = 18.84, df = 4 (P = 0.0008); I² = 79%								
Test for overall effect: Z = 1.06 (P = 0.29)								
Test for subgroup differences: Chi² = 16.09, df = 1 (P < 0.0001), I² = 93.8%								

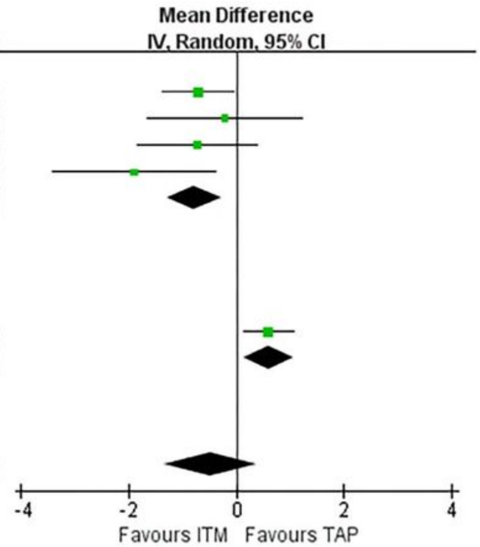

Figure 3

Forest plot showing pain scores at rest 24h after surgery according to the economic situation

Study or Subgroup	ITM Mean	ITM SD	ITM Total	TAP Mean	TAP SD	TAP Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 Developed country								
Dereu 2019	5	1.51	86	5.35	2.26	90	24.3%	-0.35 [-0.92, 0.22]
Kanazi 2010	4.18	2.73	28	4.29	3.12	29	14.9%	-0.11 [-1.63, 1.41]
Loane 2012	3.64	2.32	33	5	1.55	33	20.5%	-1.36 [-2.31, -0.41]
McMorrow 2011	2.34	1.84	20	4.64	3.03	20	14.6%	-2.30 [-3.85, -0.75]
Subtotal (95% CI)			**167**			**172**	**74.5%**	**-0.94 [-1.80, -0.07]**
Heterogeneity: Tau² = 0.46; Chi² = 7.97, df = 3 (P = 0.05); I² = 62%								
Test for overall effect: Z = 2.13 (P = 0.03)								
3.1.2 Developing country								
Kwikiriza 2019	3.9	1.21	65	3.4	1.2	65	25.5%	0.50 [0.09, 0.91]
Subtotal (95% CI)			**65**			**65**	**25.5%**	**0.50 [0.09, 0.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.37 (P = 0.02)								
Total (95% CI)			**232**			**237**	**100.0%**	**-0.59 [-1.47, 0.29]**
Heterogeneity: Tau² = 0.74; Chi² = 23.18, df = 4 (P = 0.0001); I² = 83%								
Test for overall effect: Z = 1.32 (P = 0.19)								
Test for subgroup differences: Chi² = 8.67, df = 1 (P = 0.003), I² = 88.5%								

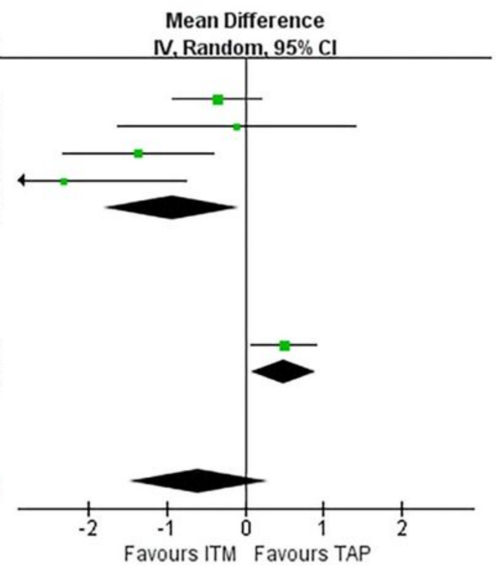

Figure 4

Forest plot showing pain scores at movement 24h after surgery according to the economic situation

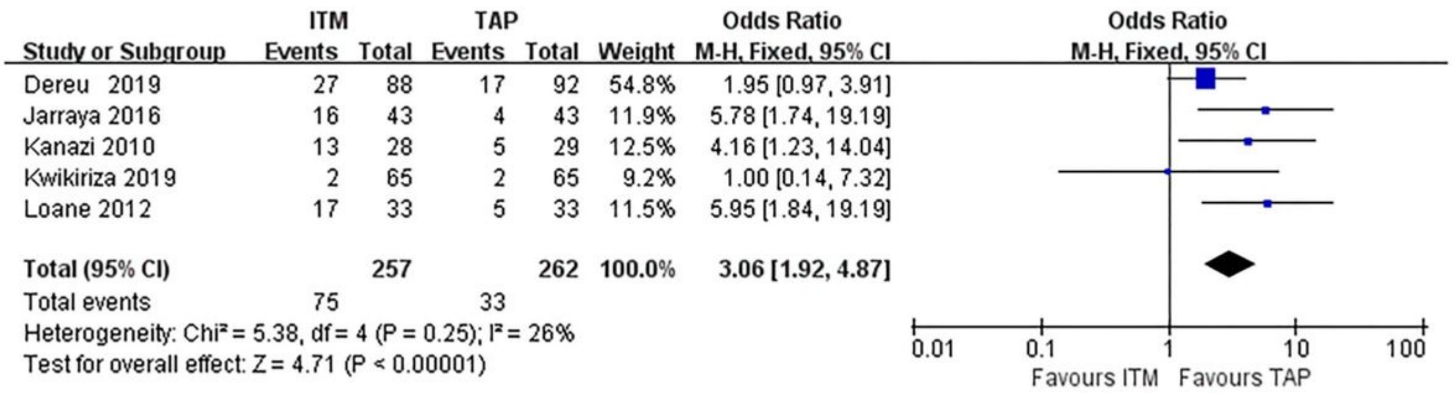

Figure 5

Forest plot showing the incidence of nausea and vomiting after surgery

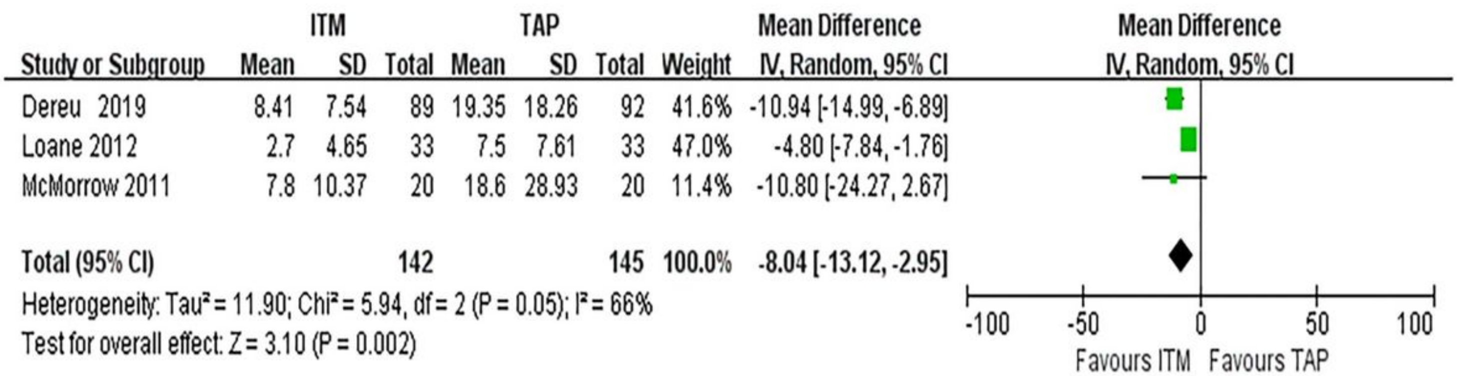

Figure 6

Forest plot showing the consumption of morphine 24 hours after surgery

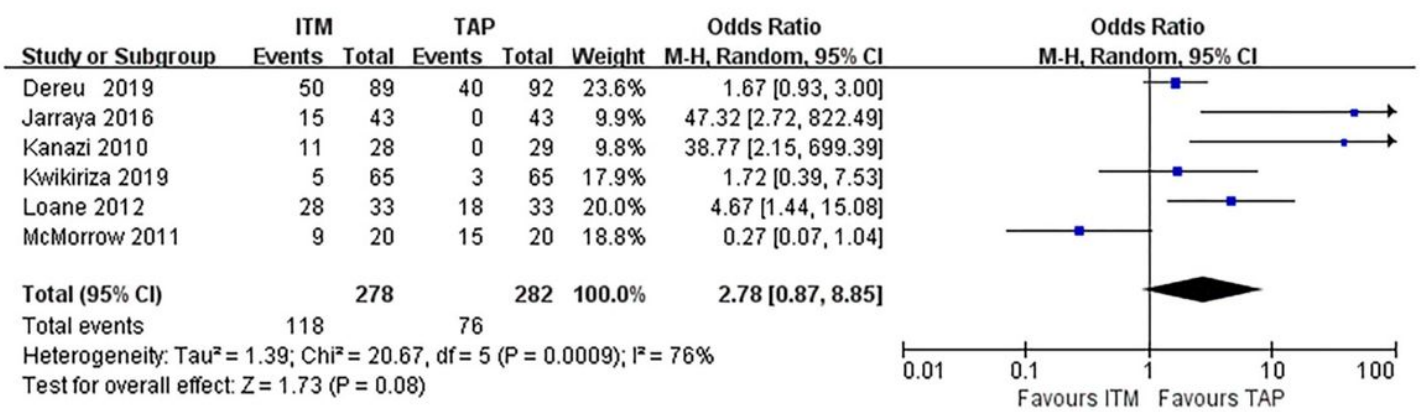

Figure 7

Forest plot showing the incidence of itching after surgery