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Ultrasound-Guided Transversus Abdominis Plane Block Compared with Wound Infiltration for Postoperative Analgesia Following Laparoscopic Cholecystectomy: a Systematic Review and Meta-analysis

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너무나도 부족한 제가 교수님들 곁에서 함께 일하고 배우면서 대학원 과정을 수료하고, 새로운 지식을 얻어갈 수 있음이 저에게는 큰 행운입니다. 이번 논문에서 메타분석이라는 낯설지만 또한 흥미로운 분야에 대한 새로운 배움을 많이 얻었습니다. 이 경험을 기반으로 더 많은 선진 지식들을 흡수하여 환자들에게 어떤 것이 가장 좋을지를 고민하고 연구하는 마취통증의학과 의사가 되도록 하겠습니다.

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사랑합니다.

2022년 2월

배 진 홍

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1. Introduction

Laparoscopic cholecystectomy (LC) is the gold standard method to treat gallstone disease. However, many patients frequently suffer from postoperative pain including visceral, somatic, and shoulder pain and various modalities have been tried for pain relief (1-3).

The ultrasound-guided interfascial plane blocks gradually became a trend. It is a part of multimodal analgesia methods that help to reduce the amount of used opioids during postoperative recovery by alleviate acute pain after surgical procedures. Consequentially decreased use of opioid reduce the side effects of opioid, helping the patient to recover after surgery.

The transversus abdominis plane (TAP) block, one of them, has been increasingly used for providing somatic anesthesia to anterolateral abdominal wall. It is more effective for controlling pain at the lower abdominal surgery (4) and the subcostal approach, which is one of the TAP block methods has been recently recognized that more effective for upper abdominal surgery, including cholecystectomy. (5). This method blocks the anterior rami of thoracolumbar nerves from T6 to T9 which supply the upper anterolateral abdominal wall muscles and skin. Wound infiltration (WI) is local anesthetics (LA) infiltration of the trocar sites and it is another effective method of providing analgesia after LC (6,7). Several meta-analyses have shown that both TAP block and WI are more effective compared to placebo in pain relief after LC. (8,9). And recent meta-analyses reported that the TAP block had a superior analgesic effect than WI in patients who underwent LC (10). However, in that study, various kind of TAP block techniques involving classical lateral approach, subcostal approach, and laparoscopy guided technic

were included.

Therefore, we investigated whether subcostal TAP had superior analgesic effect compared to WI in patients who underwent LC through systematic review and meta-analysis of randomized controlled trials (RCTs).

2. Material and Methods

2.1 Protocol and Registration

The authors performed the systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline(11). The predefined protocol was registered in the International Prospective Register of Systematic Reviews (CRD42021254121).

2.2 Eligibility Criteria

All RCTs comparing subcostal TAP block and port site infiltration about pain after LC surgery were searched. Paper selection was not excluded based on publication year, publication location, and language used. Nonrandomized studies, case reports, letters to editors, review articles, and animal studies were not included in the literature search. The total amount of opioid used over 24 h was designated as the primary outcome. The pain scores at 2, 6, 12 h and 24 h after surgery and the occurrence of postoperative nausea and vomiting (PONV) were designated as the secondary result. We used random-effects model to estimate mean differences (MD) and odds ratio (OR).

2.3 Sources and Search

In order to avoid omission of literature, two authors (P.J.H. and B.J.H.) separately searched the literature (PubMed, EMBASE and CENTRAL). To compare the analgesic effect of subcostal TAP block and WI after LC, the search terms consisted of Medical Subject Headings terms and keywords, including “transversus abdominis plane” and “TAP”. Each result was combined by the Boolean operator “AND” or “OR”. Search terms in real material searches are shown in Table 1. The search was performed until August 2021.

2.4 Study Selection, Data Collection Process, and Data Items

After two authors (P.J.H. and B.J.H.) reviewed the title and abstract of each paper, then papers not related to this study were excluded. Subsequently, the full texts of the articles were retrieved and reviewed to include studies that met the aim of this study. After reading the entire contents of all papers, articles that met the goals of this study were selected and included in the study. In conclusion, the selected studies and contents are summarized in a spreadsheet. Among the data of each paper, the first author, year of publication, study size, local anesthetic usage, PCA use, pain score, and occurrence of PONV were extracted. GetData Graph Digitizer 2.26 (http://www.getdata-graph-digitizer.com) was used to digitize and extract the data from the graph. Any differences between each author (P.J.H. and B.J.H.) were discussed and corrected.

2.5. Risk of Bias in Individual Studies

Two independent authors (P.J.H. and B.J.H.) evaluated the quality of included articles by measuring risk of bias for RCT using the Cochrane Collaboration's tool (12). Random sequence generation, allocation concealment, blinding of participants, blinding of outcome assessors, incomplete outcome data, selective reporting, and other bias were evaluated. Each bias was graded as low, unclear, or high. The corresponding authors (P.J.H. and B.J.H.) were consulted to make a consensus for any disagreements.

2.6. Summary Measures and Synthesis of Results

Review Manager 5.3 (Nordic Cochrane Center, Cochrane Collaboration, Copenhagen, Denmark) was used for statistical analyses. Mean difference (MD) and 95% confidence intervals (CI) were calculated for continuous variables. For the data expressed as the median and range (minimum to maximum or interquartile range), the mean and standard deviation were calculated by Wan's formula (13). Odds ratio (OR) and 95% CI were calculated for dichotomous variables. A continuity correction of 0.5 was applied to zero total event RCTs, which means that no patients in both groups experienced the outcome event (14). When high heterogeneity is expected, the analysis was performed by applying a random-effects model. In case the number of combined studies was lower than 10, the Hartung - Knapp - Sidik - Jonkman method was used in the random-effects analysis to minimize the error rate (15). Forest plot shows the results of the meta-analysis. The

degree of heterogeneity among the included articles was expressed by calculating the I^2 statistic. It was interpreted as no (0 - 25%), low (25 - 50%), moderate (50 - 75%), or high (75 - 100%). Other types of opioid was converted to ans equivalent amount of morphine doses (iv morphine 10 mg = oral morphine 30 mg = iv fentanyl 100 μg = iv pethidine 75 mg = iv tramadol 100 mg = iv nalbuphine 10 mg = oral hydrocodone 30 mg = oral codeine 165 mg). Pain scores described in numeric rating scale, 11-point verbal or visual scale were converted to a 0 - 10 analogue scale and statistical evaluation were performed.

3. Results

3.1. Identification of studies

A total 334 articles were retrieved through literature search. After removing 117 duplicated manuscripts, 217 studies remained. Subsequently, after reviewing the title and abstract, 206 articles were excluded, and 11 papers remained. After reading the full text of 11 papers, 5 studies were excluded, and the final 6 studies were selected. A final 6 studies involving 314 patients were included in the final analysis (Figure 1). The 314 patients were equally assigned to the TAP group and the WI group, 157 each. Characteristics of each RCTs are summarized in Table 2 (16-21).

3.2. Risk of Bias

The risk of bias of each articles are reported in Figure 2. The main contributor to high risk of bias was the performance process with five trials. In those studies, both the practitioners and the patients know what procedure was performed because the researcher directly selects either tap or WI.

3.3. Primary outcome

3.3.1. Cumulative 24-hour opioid consumption

Six RCTs reported cumulative postoperative opioid consumption in 314

patients. As a result, the cumulative consumption of opioids was significantly lower in the TAP block gruop than in the WI gruop. (MD -6.66, 95% CI −9.40 to −3.91, $p < 0.001$) (Figure 3). A high level of heterogeneity was found among the studies (I^2 = 95%, $p < 0.001$).

3.4. Secondary outcomes

3.4.1. Pain scores after surgery

The pain score at 2 h was reported in 6 RCTs, including 314 patients and 6, 12, 24 h pain scores were reported in 5 RCTs, including 271 patients. The pain scores at 4 different time points after surgery are reported in table 3. At all time points, notably lower pain scores were reported by patients receiving TAP blocks compared with those receiving WI treatment and heterogeneity was moderate to high.

3.4.2. PONV

Four RCTs, including 228 patients, reported the incidence of PONV, and the incidence was similar between the two groups (OR 0.58, 95% CI 0.23 to 1.44, $p > 0.05$) (Figure 4). A low level of heterogeneity was found among the studies.

Table 1A. Search Strategy for Each Database

MEDLINE 1. (((laparoscop* [Title/Abstract]) OR (coelioscop* [Title/Abstract])) OR (celioscop* [Title/Abstract])) OR (peritoneoscop* [Title/Abstract]) 2. cholecystectom* [Title/Abstract] 3. cholecystectomy, laparoscopic[MeSH] 4. (1 and 2) or 3 5. (transvers* [Title/Abstract]) AND (abdom* [Title/Abstract]) 6. subcostal[Title/Abstract] 7. TAP[Title/Abstract] 8. (((block*[Title/Abstract]) OR (analg*[Title/Abstract])) OR (an*esthe*[Title/Abstract])) OR (inject*[Title/Abstract]) 9. (5 or 6 or 7) and 8 10. 4 and 9 11. 10 AND (groups[tiab] OR trial[TIAB] OR randomly[TIAB] OR "drug therapy"[SH] OR placebo[TIAB] OR randomized[TIAB] OR "controlled clinical trial"[PT] OR "randomized controlled trial"[PT]) NOT (animals[MH] NOT (humans[MH] AND animals[MH]))
EMBASE 1. 'laparoscopic cholecystectomy'/exp 2. (((laparoscop*: ab,ti) OR (coelioscop*:ab,ti)) OR (celioscop*:ab,ti)) OR (peritoneoscop*: ab,ti) 3. cholecystectom*: ab,ti 4. 1 or (2 and 3) 5. (transvers*: ab,ti) AND (abdom*: ab,ti)

Table 1B. Search Strategy for Each Database (continued)

6. subcostal: ab,ti
7. TAP: ab,ti
8. (((block*: ab,ti) OR (analg*: ab,ti)) OR (an*esthe*: ab,ti)) OR (inject*: ab,ti)
9. (5 or 6 or 7) and 8
10. 4 and 9
11. groups: ti,ab
12. trial: ti,ab
13. (random$ or placebo$): ti,ab
14. controlled clinical trial$: ti,ab
15. (compare or compared or comparison): ti
16. (open NEXT/2 label): ti,ab
17. ((double or single or doubly or singly) NEXT/2 (blind or blinded or blindly)): ti,ab
18. 'double blind procedure'
19. (parallel group*): ti,ab
20. (crossover or cross over): ti,ab
21. ((assign$ or match or matched or allocation) NEXT/5 (alternate or group* or intervention* or patient* or subject* or participant*)): ti,ab
22. (assigned or allocated):ti,ab
23. (controlled NEXT/7 (study or design or trial)): ti,ab
24. OR/11-23
25. 10 and 24

Table 1C. Search Strategy for Each Database (continued)

Cochrane

1. (((laparoscop*: ti,ab,kw) OR (coelioscop*: ti,ab,kw)) OR (celioscop*: ti,ab,kw)) OR (peritoneoscop*: ti,ab,kw)
2. cholecystectom*: ti,ab,kw
3. cholecystectomy, laparoscopic[MeSH]
4. (1 and 2) or 3
5. (transvers*:ti,ab,kw) AND (abdom*:ti,ab,kw)
6. subcostal:ti,ab,kw
7. TAP:ti,ab,kw
8. (((block*:ti,ab,kw) OR (analg*:ti,ab,kw)) OR (an*esthe*:ti,ab,kw)) OR (inject*:ti,ab,kw)
9. (5 or 6 or 7) and 8
10. 4 and 9

Table 2. Characteristics of the Studies Included in the Systemic Reviews and Meta-analysis

Study	Group	Treatment	Postoperative analgesia
Arık 2020	Unilateral sTAP (n=24) WI (n=24) Control (n=24)	20mL 0.25% bupivacaine	i.v. paracetamol, tramadol at the end of surgery i.v. PCA of tramadol without basal infusion i.v. rescue dexketoprofen
Baral 2019	Bilateral sTAP (n=30) WI (n=30)	20mL 0.25% bupivacaine	i.v. paracetamol q 6 h i.v. rescue pethidine
Ibrahim 2020	Bilateral sTAP (n=21) WI (n=21) ESP(n=21)	40ml 0.25% bupivacaine	i.v. paracetamol q 6 h i.v. PCA of morphine without basal infusion
Ramkiran 2018	Unilateral sTAP (n=21) WI (n=20) TAP+RSB (n=20)	20ml 0.25% bupivacaine	i.v. rescue tramadol 50mg
Suseela 2018	Bilateral sTAP (n=40) WI (n=40)	40ml 0.25% bupivacaine	i.v. paracetamol q 8 h i.v. rescue tramadol and diclofenac
Tolchard 2012	Unilateral sTAP (n=21) WI (n=22)	1mg/kg 0.25% bupivacaine	i.v. fentanyl, i.v. diclo fenac, i.v. paracetamol, rescue i.m. morphine, rescue oral codeine

ESP: erector spinae plane block; PCA: patient controlled analgesia; RSB: rectus sheasth block; sTAP: subcostal transversus abodominis plane block; WI: wound infiltration.

Table 3. Secondary Pain-related Outcome

Outcome	Studies	Participants	Mean difference [95% CI]	I^2 (%)	p value
Pain score at 2h	6	314	-0.70 [-1.28, -0.12]	87	<0.05
Pain score at 6h	5	271	-0.89 [-1.52, -0.25]	73	<0.01
Pain score at 12h	5	271	-0.99 [-1.54, -0.44]	69	<0.001
Pain score at 24h	5	271	-0.73 [-1.16, -0.29]	60	<0.001

CI: confidence intervals.

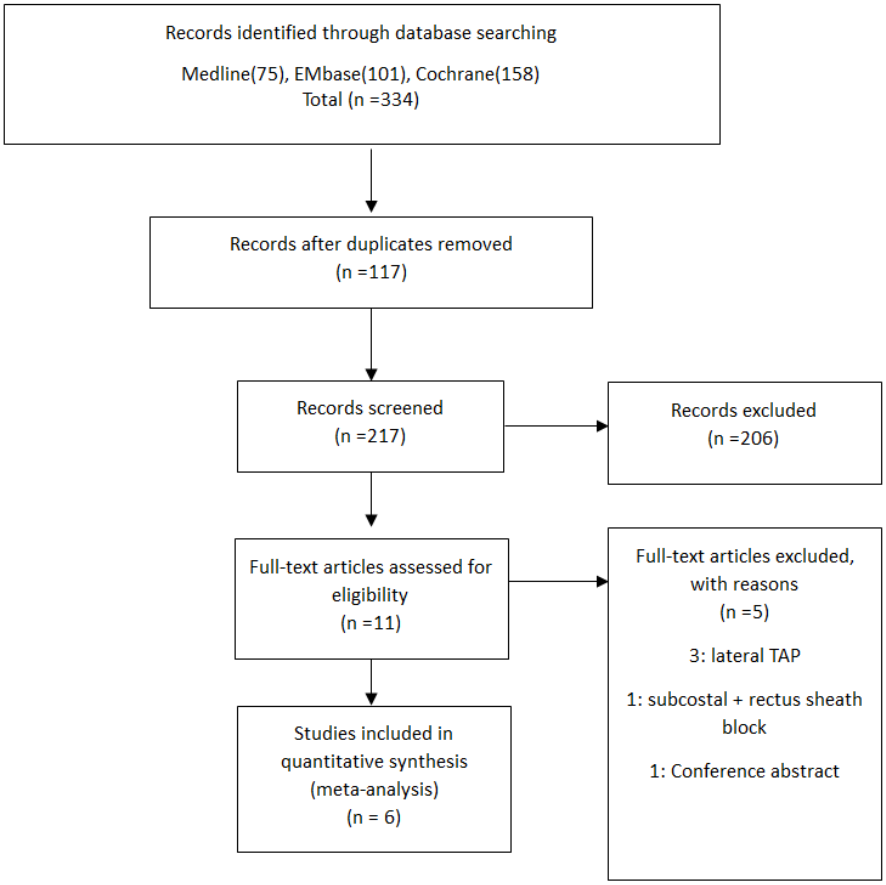

Figure 1. Flow chart of database search and study selection.
TAP: transversus abodominis plane block

Figure 2. Cochrane collaboration risk of bias summary: evaluation of bias risk items for each included study. Green circle: low risk of bias; red circle: high risk of bias; yellow circle: unclear risk of bias.

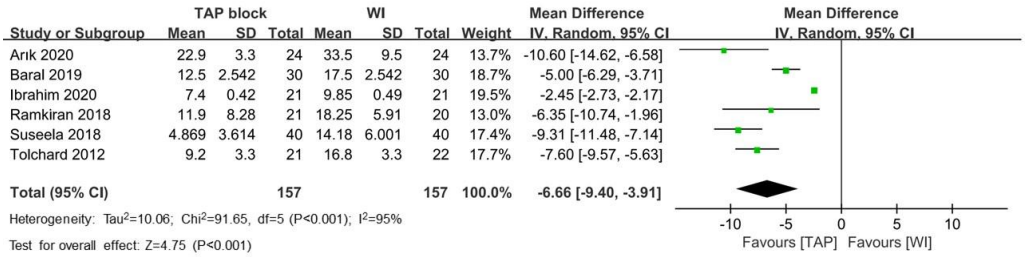

Figure 3. Forest plot for postoperative opioid consumption. Opioid consumption was significantly lower in the subcostal TAP block group than in the WI group. CI: confidence interval; SD: standard deviation; TAP: transversus abdominis plane; WI: wound infiltration.

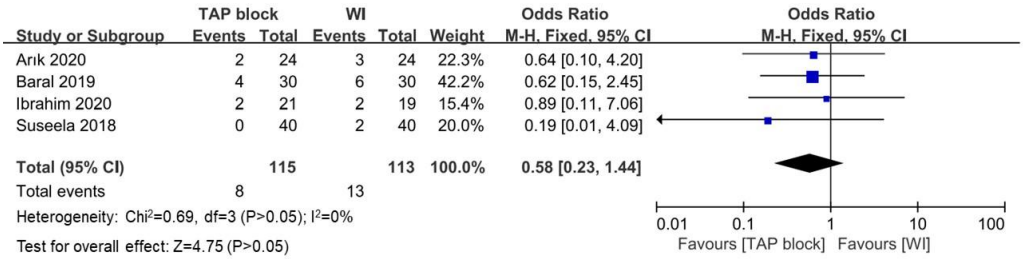

Figure 4. Forest plot for postoperative nausea and vomiting. Postoperative nausea and vomiting was comparable between the subcostal TAP block group and the WI group. CI: confidence interval; TAP: transversus abdominis plane; WI: wound infiltration.

4. Discussion

This meta-analysis demonstrate that ultrasound-guided subcostal TAP blocks lead to reduce postoperative 24 h opioid consumption for patients undergoing LC compared to WI. Pain scores up to 24 h were also significantly lowered in a subcostal TAP blocks group. However, there was no significant reduction in PONV compared to WI.

This study shows that subcostal TAP block reduced opioid consumption after LC compared to WI. This is in good agreement with the results of previous analyzes of other meta-analyses (9,10). Multimodal analgesia is focused on reducing the use of opioids because the higher the consumption of opioids, the higher the chance of experiencing opioid-related side effects, which leads to increased hospitalization mortality, prolonged hospitalization, and 30-day readmission rates (22,23). Previous studies demonstrated that both subcostal TAP block and WI reduced 24 h opioid consumption compared to placebo group (8,9). Therefore, subcostal TAP block is effective component of multimodal analgesia in patient undergoing LC compared to WI.

This meta-analysis showed that subcostal TAP block reduced pain scores more than WI up to postoperative 24 h. In laparoscopic cholecystectomy, pain is either due to visceral pain (caused by the trauma of gallbladder resection) or cutaneous, muscular pain (caused by the skin and muscle incision at trocar sites) (24). Visceral pain originates from: (1) irritation of insufflated CO_2 gas that forms carbonic acid, (2) diaphragmatic muscle fiber stretching, and (3) residual pockets of gas in the abdominal cavity (1,25). Both subcostal TAP block and WI are somatosensory nerve block and could not cover visceral pain from

laparoscopic cholecystectomy. All of studies included used intravenous paracetamol or NSAID as a multimodal analgesia which may have covered the visceral components of pain.

This study found no significant differences in the incidence of PONV. Opioids use is a major factor in increasing PONV. In this study, the subcostal TAP group reduced the opioid usage compared to WI, but there was no difference in the incidence of PONV. Most studies have used paracetamol or NSAIDs rather than opioids as the first choice for postoperative pain control. This may have influenced the results with no difference in PONV between the two groups. In addition, the analgesics usage in WI group was probably reduced compared to the placebo group. Therefore, the incidence of PONV was comparable between subcostal TAP block and WI in this study.

The result of this study showed moderate to high level of heterogeneity except for PONV. Different dose usage of local anesthetics (10 ml vs. 20 ml), and diversity of range of block (unilateral vs. bilateral) and technique of WI and post-operative analgesia regimen can be considered as the cause of the high heterogeneity. In addition, subcostal TAP block can be divided into upper subcostal vs. lower subcostal approach. Although large volumes of LA were used for TAP block, difference of subcostal block technique may also affect the heterogeneity of this study.

We found several weaknesses in this meta-analysis. First, in all RTCs dermatomal sensory test result of the block was not included. The unknown effective range of block and the success or not of TAP may have influenced the results of our study. Second, although the doses of different types of opioids were converted to morphine-equivalent doses, it is not known how the effects of different types of opioids affected the results of current study. Third, blinding of performance was not

adequately performed in many studies. Except for one study, one of the two blocks was implemented, therefore, there is a possibility that it may influence performance of clinicians. Finally, we selected subcostal approach among the various TAP block technique. Recent meta-analysis collected RCTs for all kinds of TAP block (10). However, they did not perform the subgroup analysis for various techniques. Although TAP block is interfascial block, coverage of sensory block area could be different on each technique. Further analysis for all kinds of TAP blocks will be needed.

This study revealed that subcostal TAP block has better analgesic effects than wound infiltration in patients undergoing LC. It is suggested that clinicians might consider the subcostal TAP block as a component of multimodal analgesia.

5. Summary

This systematic review and meta-analysis of RCTs study was conducted to determine whether subcostal TAP block provides better analgesia compared with WI after LC. 6 studies including 314 patients were analyzed. 157 patients in each TAP group and WI group were compared for the cumulative consumption of 24-hour opioid. Pain scores at 2, 6, 12, 24 h after surgery were compared. Incidence of postoperative nausea and vomiting of 115 patients in TAP group and 113 patients in WI group were compared. This study revealed that subcostal TAP block has superior analgesic effects than wound infiltration in patients undergoing LC.

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Ultrasound-guided Transversus Abdominis Plane Block Compared with Wound Infiltration for Postoperative Analgesia Following Laparoscopic Cholecystectomy: a Systematic Review and Meta-analysis

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(Abstract)

Laparoscopic cholecystectomy (LC) is the gold standard method to treat gallstone disease, but still it produces significant postoperative pain. Ultrasound-guided transversus abdominis plane (TAP) blocks has been increasingly used for providing somatic anesthesia to anterolateral abdominal wall. Recent meta-analyses reported that the TAP block had a superior analgesic effect than WI in patients who underwent LC. And the subcostal TAP block has been recently recognized that more effective for upper abdominal surgery, including cholecystectomy. We analysed all RCTs comparing subcostal TAP block vs WI for analgesia in adult patients undergoing LC. The total amount of opioid used over 24 h was designated as the primary outcome. The pain scores at 2, 6, 12 h and 24 h after surgery and the occurrence of postoperative nausea and vomiting (PONV) were designated as the secondary result. Postoperative 24 hours opioid consumption was significantly lower in the subcostal TAP group than in the WI. The subcostal TAP group also showed significantly lower pain scores. Incidence of PONV did not significantly differ between the two groups. This study revealed that

subcostal TAP block has better analgesic effects than wound infiltration in patients undergoing LC.

복강경 담낭절제술에서 초음파유도 배가로근면 차단과 절개창 국소마취제 점적 투여의 술 후 통증 비교: 체계적 문헌 고찰과 메타분석

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(초록)

복강경 담낭절제술은 외과적 담낭 질환에서 가장 흔히 행해지는 수술적 치료이지만 여전히 수술 후 상당한 통증을 유발한다. 국소마취제를 사용한 초음파유도 배가로근면 차단과 수술 절개창 국소마취제 점적 투여는 수술 후 통증의 강도와 마약성 진통제의 사용을 줄일 수 있다고 밝혀져 있다. 배가로근면 차단은 체성통증의 치료에는 효과적이나 내장통증의 경감에 덜 효과적인 것으로 알려져 있고, 배가로근면 차단과 수술 절개창 국소마취제 점적 투여가 여러 통증의 치료에 사용되었을 때 상대적인 효용에 대해서는 아직 잘 연구되어 있지 않다. 이번 연구에서는 복강경 담낭절제술을 받은 성인 환자의 수술 후 통증에 대하여 늑골하 배가로근면차단과 수술 절개창 국소마취제 점적의 효용에 대하여 비교하는 모든 무작위 배정 임상 연구를 메타분석하였다. 1차 결과는 수술 후 24시간동안 사용된 아편유사제의 양으로 정의하였고 2차 결과는 수술 후 통증 점수와 수술 후 구역구토의

발생 유무로 하였다. 수술 후 아편유사제의 사용량은 수술 절개창 국소마취제 점적 시행 그룹보다 늑골하 배가로근면차단 시행 그룹에서 유의하게 낮았다. 통증점수도 수술 절개창 국소마취제 점적 시행 그룹에 비해 늑골하 배가로근면차단 시행 그룹이 유의하게 낮았으며 수술후 구역구토의 발생에서는 두 그룹에서 유의한 차이를 보이지 않았다. 본 연구를 통하여 복강경 담낭절제술을 받는 환자에서 늑골하 배가로근면차단을 시행하였을 때 수술 절개창 국소마취제 점적을 시행했을 때 보다 진통효과가 더 나은 것으로 나타났다.