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META-ANALYSIS

Effect of intraperitoneal local anesthetic on pain characteristics after laparoscopic cholecystectomy

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Author contributions: Choi GJ designed the study, conducted the study (selected study, extracted data), analysed and interpreted the data, wrote the manuscript; Kang H designed the study, conducted the study (extracted data), analysed and interpreted the data, wrote the manuscript; Baek CW conducted the study (helped to select study, assessed the risk of bias), provided critical revision of the manuscript; Jung YH conducted the study (helped to select study, assessed the risk of bias), provided critical revision of the manuscript; Kim DR conducted the study (selected study), analysed the data and wrote the manuscript; all authors approved the final manuscript.

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Abstract

AIM: To systematically evaluate the effect of intraperitoneal local anesthetic on pain characteristics after laparoscopic cholecystectomy (LC).

METHODS: We searched MEDLINE, EMBASE, and the Cochrane Library. Randomized controlled trials in English that compared the effect of intraperitoneal administration of local anesthetics on pain with that of placebo or nothing after elective LC under general anesthesia were included. The primary outcome variables analyzed were the combined scores of abdominal, visceral, parietal, and shoulder pain after LC at multiple time points. We also extracted pain scores at resting and dynamic states.

RESULTS: We included 39 studies of 3045 patients in total. The administration of intraperitoneal local anesthetic reduced pain intensity in a resting state after laparoscopic cholecystectomy: abdominal [standardized mean difference (SMD) = -0.741; 95%CI: -1.001 to -0.48, $P < 0.001$]; visceral (SMD = -0.249; 95%CI: -0.493 to -0.006, $P = 0.774$); and shoulder (SMD = -0.273; 95%CI: -0.464 to -0.082, $P = 0.097$). Application of intraperitoneal local anesthetic significantly reduced the incidence of shoulder pain (RR = 0.437; 95%CI: 0.299 to 0.639, $P < 0.001$). There was no favorable effect on resting parietal or dynamic abdominal pain.

CONCLUSION: Intraperitoneal local anesthetic as an analgesic adjuvant in patients undergoing laparoscopic cholecystectomy exhibited beneficial effects on postoperative abdominal, visceral, and shoulder pain in a resting state.

Key words: Local anesthetic; Laparoscopic cholecystectomy;

Intraperitoneal; Meta-analysis; Pain

Core tip: Pain after laparoscopic cholecystectomy is located at abdomen or shoulder, and abdominal pain includes visceral and parietal pain. This characteristic pain is mainly because of pneumoperitoneum, which leads to visceral and shoulder pain. Intraperitoneal local anesthetics thus can be a beneficial strategy given the origin of various type of pain after laparoscopic cholecystectomy, which is evaluated systematically focused on the analgesic efficacy on pain characteristics. Intraperitoneal local anesthetics in patients undergoing laparoscopic cholecystectomy has the evidence to reduce postoperative abdominal, visceral, and shoulder pain. Further less heterogeneous evidence is necessary to draw definite conclusion.

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INTRODUCTION

Laparoscopic cholecystectomy (LC) is a widely performed surgical procedure that achieves superior outcomes in postoperative pain, recovery time, cosmetic issues, and morbidity[1]. LC is associated with less postoperative pain than open cholecystectomy, but patients still experience significant pain. Pain after LC is characterized by body component, which is different from laparotomy[2]. This difference is roughly divided into abdominal and shoulder pain, according to location[3]. Abdominal pain consists of two components: visceral pain associated with tissue injury due to gallbladder dissection and the stretching of nerve endings in the peritoneal cavity; and parietal pain related to the incisional trauma at the port sites. Shoulder pain is referred by diaphragmatic stretching[4].

A number of studies reported various treatment modalities to relieve pain after LC. A therapeutic approach using intraperitoneal local anesthetic (IPLA) is remarkable because the beneficial effect of this strategy is closely linked to pain characteristics after LC, which primarily arises from pneumoperitoneum. The results of the available data on the efficacy of IPLA in LC are inconsistent. Therefore, a systematic review would be informative to create evidence for IPLA use in LC. Several systematic reviews from a variety of perspectives based on postoperative pain or safety issues were published[5-8]. However, there is no data on the effect of IPLA on pain characteristics after LC.

This review investigated the effect of IPLA on pain after LC through a systematic evaluation of the available literature. Pain characteristics, including visceral, parietal, and shoulder pain, were the primary focus of this meta-analysis. Pain at resting and dynamic states was also assessed, and the limitations of the data were reviewed.

MATERIALS AND METHODS

Literature search

A meta-analysis of studies investigating the effect of IPLA in LC was conducted according to the protocol recommended by the Cochrane Collaboration[9]. Two authors (Choi GJ and Kang H) independently performed database searches using EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials (CENTRAL) in April 2014 and updated in March 2015. The reference lists of the identified literature were also searched manually. Search terms were used based on the following combination of keywords: local anesthetics, lidocaine, lignocaine, ropivacaine, bupivacaine, levobupivacaine, procaine, intraperitoneal, intra-abdominal, laparoscopic cholecystectomy, and randomized trials.

Study selection

Randomized controlled trials (RCTs) in English that compared the effects of the intraperitoneal administration of local anesthetic (IPLA group) with placebo or no treatment (control group) on pain after elective LC under general anesthesia were included. Studies that combined IPLA with other interventions were included if there were comparable intervention and control groups in which the only difference was the use of IPLA. Studies with more than one IPLA or control group were included if there were comparable groups that met the inclusion criteria. Two authors (Choi GJ and Kim DR) independently selected eligible studies and reached a consensus on study inclusion or exclusion. Disagreements over study inclusion or exclusion were settled by discussions with the two senior authors (Baek CW and Jung YH).

Data extraction

When studies did not provide detailed pain characteristics, *i.e.*, visceral or parietal pain and resting or dynamic pain were not clarified, we considered abdominal pain and pain at the resting state. Pain from coughing, moving, or inspiration was regarded as dynamic abdominal pain. We treated the intraperitoneal administration of normal saline and nothing as the control group. We combined all of the IPLA or control groups if a given study had more than one IPLA or control group to avoid multiple counting of the same individuals[10]. We extracted data from partial groups that were eligible in a study with several groups if the groups

were comparable. Data from studies in which wound infiltration with local anesthetics was applied to both intervention and control groups, or not, in a single study with several groups greater than four were extracted to effectively yield two sub-studies of whether wound infiltration with local anesthetics was performed. Studies reporting pain severity on a visual analog scale (VAS) or numerical rating scale (NRS) were included. We selected the VAS if various scales including VAS were used. We considered the median pain evaluation value as the time point when pain evaluation times were presented as ranges. Means and standard deviations of pain scores for intervention and control groups were extracted from tables, graphs, or text. We attempted to contact the corresponding author to obtain data if the values were not reported. We calculated these values using the methods described in the Cochrane handbook when contact was unsuccessful[9].

Two authors (Choi GJ and Kang H) independently extracted the following data: name of the first author; year of publication; number of participants and their respective allocation; type of local anesthesia; pain characteristics evaluated (abdominal, visceral, parietal, or shoulder pain; pain at resting or dynamic states); time points of pain score evaluations; pain scores at each time point; and incidence of shoulder pain.

Risk of bias assessment

Two authors (Baek CW and Jung YH) independently assessed the quality of eligible studies using the Cochrane Collaboration's Tool for assessment of risk of bias[9]. Quality was evaluated based on the following seven potential sources of bias: random sequence generation; allocation concealment; blinding of the participants; blinding of the outcome assessors; incomplete outcome data; selective reporting; and other bias. The methodology of each trial was graded as 'high', 'low' or 'unclear' to reflect a high risk of bias, low risk of bias and uncertainty of bias, respectively.

Statistical analysis

The pooled risk ratio (RR) or standardized mean difference (SMD) and 95%CIs were calculated for each outcome. We used the χ^2 test for homogeneity and the I^2 test for heterogeneity. We regarded a level of 10% significance ($P < 0.100$) in the χ^2 statistic or an I^2 greater than 50% as considerable heterogeneity, and we used the Mantel-Haenszel random-effect model. Otherwise, we applied the Mantel-Haenszel fixed-effect model[9,11]. We performed subgroup analyses based on the type of local anesthetics and wound infiltration. We also conducted sensitivity analyses to evaluate the influence of a single study on the overall effect estimate by the exclusion of one study. Data measured at multiple time-points were dependent on each other, and multiple comparisons at each time point would increase the possibility of type I error. Therefore, we combined the outcomes of multiple time points and performed analyses using the pooled combined outcomes.

Publication bias was evaluated using a funnel plot and Egger's linear regression test. If the funnel plot was asymmetrical or the P value was < 0.100 by the Egger's test, we considered the presence of a publication bias and performed trim and fill analyses.

We performed all analyses using Comprehensive Meta-analysis software (version 3.0, Biostat, Englewood, NJ, United States).

RESULTS

Search results

A total of 998 records were identified using our electronic and manual search strategy. The titles and/or abstracts were screened, and 48 potentially eligible RCTs were retrieved. Full text assessments for eligibility excluded 9 studies. Finally, 39 studies were included in the present meta-analysis. Figure 1 presents the flow diagram of the literature selection process.

Study characteristics

A total of 3045 patients in 39 RCTs were included in this review: 1633 in the IPLA group and 1412 in the control group. Fourteen studies had more than one IPLA and/or control group based on following factors[12-25]: specification of study solution, such as volume, concentration, or type of local anesthetics; timing of when IPLA was administered in relation to gallbladder dissection; and combination of study solution and adrenaline. Five studies with several groups had only two eligible groups for comparison[26-30]. We produced two sub-studies from one study in which two independent investigations were performed[24]. There were four studies that yielded two sub-studies based on whether wound infiltration with local anesthetics was applied[18,19,31,32]. Dynamic abdominal pain was evaluated in the following states: moving[19,25]; coughing[15,19,24]; inspiration or deep breathing[15,24]; sitting up and valsalva[33]. Joris *et al*[34] reported no information on the standard deviations of IPLA group except for a range of standard errors. Therefore, we estimated standard deviations from the most conservative value of standard errors to minimize the possibility of type I error. Limited data were reported on visceral and parietal pains in one study[35] and the severity of abdominal and shoulder pain in another study[36]. Only data of the incidences of shoulder pain in both studies were included in present meta-analysis. Table 1 summarizes the study characteristics.

Results of meta-analysis

Resting abdominal pain was evaluated in 30 studies (2263 patients)[12-14,16,17,19-30,32,33,37-47]. There was a

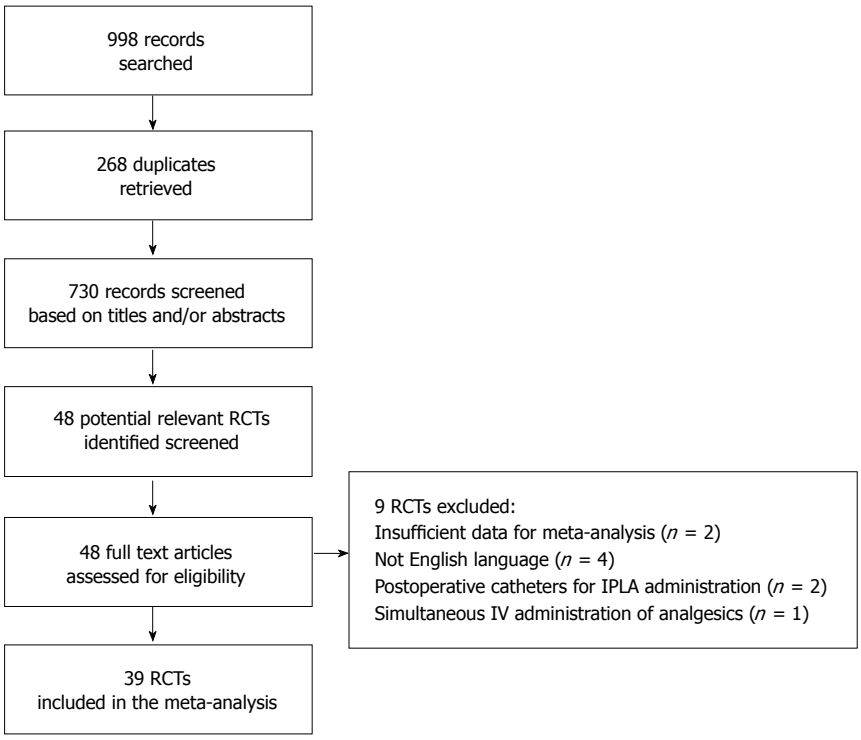


Figure 1 Flow diagram of studies identified and selected.

significant reduction in pain scores with the use of IPLA compared to the control group (SMD = -0.741; 95%CI: -1.001 to -0.48, $P < 0.001$; $I^2 = 87\%$; Figure 2A).

Dynamic abdominal pain was measured in five studies (335 patients)[15,19,24,25,33]. IPLA administration did not exhibit a significant decrease in pain scores compared to the control group (SMD = -0.320; 95%CI: -0.649 to 0.010, $P = 0.002$; $I^2 = 66\%$; Figure 2B). The exclusion of Raetzell *et al*[24] changed the result (SMD = -0.402; 95%CI: -0.777 to -0.028, $P = 0.001$; $I^2 = 70\%$).

Visceral and parietal pain scores at a resting state were examined in three studies (148 patients)[18,31,34]. There were no data for dynamic states. IPLA administration significantly reduced visceral pain scores compared to the control group (SMD = -0.249; 95%CI: -0.493 to -0.006, $P = 0.774$; $I^2 = 0\%$; Figure 2C), but there was no reduction in parietal pain score using IPLA (SMD = -0.305; 95%CI: -0.708 to 0.098, $P = 0.036$; $I^2 = 61\%$; Figure 2D).

Shoulder pain at a resting state was evaluated, including severity in eight studies (729 patients)[12,20,27-29, 31,34,48] and incidences in 14 studies (1092 patients)[15,17-19,35-38,41-43,46,49,50]. There were no data for dynamic states. IPLA administration significantly reduced shoulder pain severity (SMD = -0.273; 95%CI: -0.464 to -0.082, $P = 0.097$; $I^2 = 39\%$; Figure 2E) and incidence (RR = 0.437; 95%CI: 0.299 to 0.639, $P < 0.001$; $I^2 = 68\%$; Figure 2F).

Sensitivity analyses, except for one case in a dynamic abdominal pain and subgroup analyses, based on type of local anesthesia used did not alleviate substantial heterogeneity or change the significance of the result.

Publication bias

A funnel plot was used for every comparison, and all data displayed a symmetrical appearance. The results of Egger's test indicated that publication bias was unlikely for all outcomes: resting abdominal pain ($P = 0.076$); dynamic abdominal pain ($P = 0.416$); visceral pain ($P = 0.143$); parietal pain ($P = 0.508$); shoulder pain severity ($P = 0.683$); and incidence of shoulder pain ($P = 0.239$). We performed trim and fill analyses on the assumption that publication bias was evident for resting abdominal pain to evaluate the influence of publication bias. The result of resting abdominal pain remained significant (SMD = -0.914; 95%CI: -1.182 to -0.646), which suggests that publication bias was unlikely (Figure 3).

DISCUSSION

The results of our meta-analysis suggest that IPLA is effective for the control of resting abdominal, visceral, and shoulder pain. This effect may be explained by the mechanisms of pain development after LC and the action of IPLA, but these mechanisms are multifactorial and not clearly understood. Visceral pain may be initiated by tissue injury due to gallbladder removal from the liver bed and the stretching of nerve endings[4]. Pneumoperitoneum causes a stretching of the peritoneum and the diaphragmatic muscle

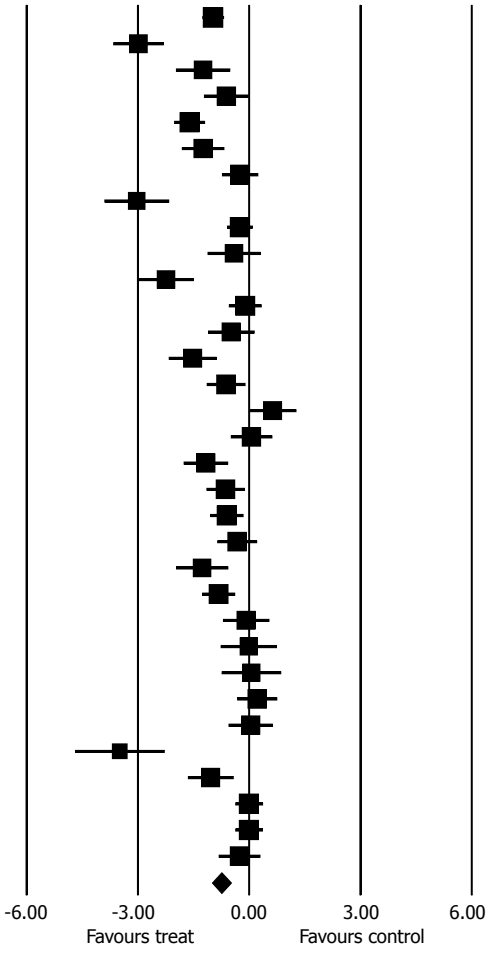
Table 1 Study characteristics

Study	Year	Patients (*n*) IPLA/control	Type of LA	Pain characteristics	Postoperative time point (h)
Chundrigar *et al*[39]	1993	28/30	B	Abdominal (R)	1, 2, 4, 8
Pasqualucci *et al*[21]	1994	28/14	B	Abdominal (R)	0, 4, 8, 12, 24
Rademaker *et al*[23]	1994	30/15	B, L	Abdominal(R)	0.5, 1, 2, 4
Joris *et al*[34]	1995	20/20	B	Visceral/Parietal (R) Shoulder (S)	1, 2, 4, 6, 8, 24, 48
Raetzell *et al* (1)[24]	1995	20/10	B	Abdominal (R, D)	4, 24, 48, 72
Raetzell *et al* (2)[24]	1995	12/12	B	Abdominal (R)	1, 2, 3, 4, 5, 6, 24
Scheinin *et al*[25]	1995	40/20	B	Abdominal (R, D)	24, 48, 72, 96, 120, 144, 168
Pasqualucci *et al*[22]	1996	82/27	B	Abdominal (R)	0, 4, 8, 12, 24
Szem *et al*[46]	1996	26/29	B	Abdominal (R) Shoulder (I)	3, 9, 15, 21
Mraović *et al*[45]	1997	40/40	R	Abdominal (R)	0.5, 4, 8, 12, 24
Cunniffe *et al*[49]	1998	55/50	B	Shoulder (I)	NA
Tsimoyiannis *et al*[29]	1998	50/50	B	Abdominal (R)	2, 6, 12, 24, 36, 48, 72
Elfberg *et al*[40]	2000	33/32	B	Abdominal (R)	2, 4, 8, 24, 48
Elhakim *et al*[41]	2000	25/25	L	Abdominal (R) Shoulder (I, S)	0, 1, 6, 12, 18, 24
Gharaibeh *et al*[50]	2000	37/38	B	Shoulder (I)	NA
Lee *et al*[18]	2001	80/68	B	Visceral/Parietal (R) Shoulder (I)	1, 3, 6, 9, 24, 48
Labaille *et al*[35]	2002	25/12	R	Visceral/Parietal (R, D) Shoulder (I)	0, 0.5, 1, 2, 4, 8, 12, 20
Maestroni *et al*[44]	2002	30/30	R	Abdominal (R)	0, 4, 8, 12, 24
Lepner *et al*[28]	2003	20/20	L	Abdominal (R) Shoulder (S)	1, 3, 6, 12, 18, 24
Ng *et al*[36]	2004	21/22	LB	Abdominal (R, D) Shoulder (I, S)	0, 1, 2, 3, 4
Jabbour-Khoury *et al*[27]	2005	20/20	B	Abdominal (R) Shoulder (S)	0, 1, 2, 6, 12, 24
Louizos *et al*[19]	2005	54/50	B	Abdominal (R, D) Shoulder (I, S)	0.5, 4, 8, 12, 24
Barczyński *et al*[14]	2006	60/60	B	Abdominal (R)	4, 8, 12, 24, 48
Karaaslan *et al*[16]	2006	50/15	B	Abdominal (R)	0, 4, 8, 12, 24
Alkhamesi *et al*[13]	2007	40/40	B	Abdominal (R)	0, 6, 12, 24
Garcia *et al*[33]	2007	19/13	B	Abdominal (R, D)	0, 2, 4, 8, 12, 24
Kucuk *et al*[17]	2007	60/20	B, R	Abdominal (R) Shoulder (I)	0, 1, 2, 4, 8, 12, 24
Ahmed *et al*[12]	2008	100/100	B, L	Abdominal (R)	0, 4, 8, 12, 24
Pappas-Gogos *et al*[20]	2008	40/20	R	Abdominal (R) Shoulder (S)	2, 4, 6, 12, 24, 48, 72
Alper *et al*[37]	2009	20/20	LB	Abdominal (R) Shoulder (I)	0, 0.5, 1, 2, 4, 6, 8, 12, 24
Golubović *et al*[26]	2009	30/30	B	Abdominal (R)	0.5, 1, 2, 4, 24
Zimmer *et al*[47]	2010	25/25	B	Abdominal (R) Shoulder (S)	1, 2, 24
El-Labban *et al*[42]	2011	63/63	LB	Abdominal (R) Shoulder (I)	0.5, 4, 8, 12, 24
Hilvering *et al*[43]	2011	39/39	LB	Abdominal (R) Shoulder (I)	0.5, 2, 4, 8, 24
Cha *et al*[31]	2012	40/40	R	Visceral/Parietal (R) Shoulder (S)	2, 4, 8, 12, 24, 48
Ingelmo *et al*[15]	2013	56/29	R	Abdominal (D) Shoulder (I)	4, 24, 48, 72
Alper *et al*[38]	2014	22/22	LB	Abdominal (R) Shoulder (I)	0, 0.5, 1, 2, 4, 6, 8, 12, 24
Niknam *et al*[48]	2014	84/85	R	Shoulder (S)	4, 72
Yang *et al*[30]	2014	22/24	L	Abdominal (R)	2, 4, 8, 12, 24, 48
Yeh *et al*[32]	2014	110/110	LB	Abdominal (R)	1, 6, 24

IPLA: Intraperitoneal local anesthetics; LA: Local anesthetics; R: Resting; D: Dynamic; I: Incidence; S: Severity; R: Ropivacaine; L: Lidocaine; B: Bupivacaine; LB: Levobupivacaine; NA: Not available.

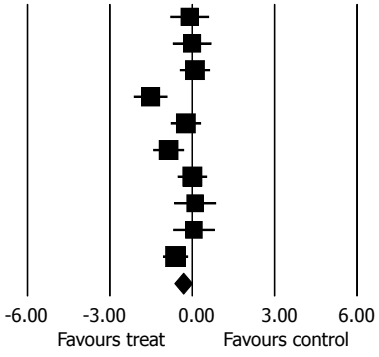
A

Study name	Subgroup within study	Time point	Std diff in means	Lower limit	Upper limit
Ahmed 2008[12]	Combined	Combined	-0.966	-1.261	-0.672
Alkhamesi 2006[13]	B	Combined	-2.980	-3.663	-2.296
Alper 2009[37]	LB	Combined	-1.238	-1.972	-0.503
Alper 2014[38]	LB	Combined	-0.608	-1.213	-0.004
Barczyński 2006[14]	B	Combined	-1.599	-2.019	-1.180
Chundriger 1993[39]	B	Combined	-1.238	-1.813	-0.664
Elfberg 2000[40]	B	Combined	-0.239	-0.728	0.251
Elhakim 2000[41]	LB	Combined	-3.027	-3.902	-2.151
El-Labban 2011[42]	LB	Combined	-0.242	-0.593	0.108
Garcia 2007[33]	B	Combined	-0.402	-1.115	0.311
Golubović 2009[26]	B	Combined	-2.233	-2.975	-1.491
Hilvering 2011[43]	LB	Combined	-0.100	-0.545	0.345
Jabbour-Khoury 2005[27]	B	Combined	-0.477	-1.110	0.156
Karaaslan 2006[16]	B	Combined	-1.517	-2.165	-0.870
Kucuk 2007[17]	Combined	Combined	-0.616	-1.138	-0.094
Lepner 2003[28]	L	Combined	0.638	-0.002	1.278
Louizos 2005 (1)[19]	LB	Combined	0.069	-0.491	0.630
Louizos 2005 (2)[19]	LB	Combined	-1.162	-1.762	-0.562
Maestroni 2002[44]	R	Combined	-0.630	-1.149	-0.112
Mraović 1997[45]	B	Combined	-0.597	-1.047	-0.146
Pappas-Gogos 2008[20]	R	Combined	-0.320	-0.860	0.220
Pasqualucci 1994[21]	B	Combined	-1.262	-1.966	-0.558
Pasqualucci 1996[22]	B	Combined	-0.818	-1.267	-0.369
Rademaker 1994[23]	Combined	Combined	-0.077	-0.707	0.553
Raetzell 1995 (1)[24]	B	Combined	-0.005	-0.764	0.755
Raetzell 1995 (2)[24]	B	Combined	0.065	-0.738	0.869
Scheinin 1995[25]	B	Combined	0.222	-0.317	0.761
Szem 1996[46]	B	Combined	0.047	-0.552	0.645
Tsimoyiannis 1998[29]	B	Combined	-3.482	-4.694	-2.270
Yang 2014[30]	L	Combined	-1.033	-1.652	-0.413
Yeh 2014 (1)[32]	LB	Combined	0.001	-0.374	0.376
Yeh 2014 (2)[32]	LB	Combined	0.000	-0.374	0.374
Zimmer 2010[47]	B	Combined	-0.255	-0.817	0.306
			-0.741	-1.001	-0.481



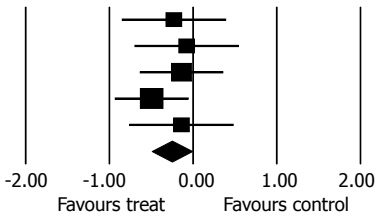
B

Study name	Subgroup within study	Time point	Std diff in means	Lower limit	Upper limit
Garcia 2007 (1)[33]	B	Combined	-0.090	-0.796	0.617
Garcia 2007 (2)[33]	B	Combined	0.000	-0.706	0.706
Louizos 2005 (1)-1[19]	LB	Combined	0.103	-0.448	0.655
Louizos 2005 (2)-1[19]	LB	Combined	-1.513	-2.127	-0.898
Louizos 2005 (1)-2[19]	LB	Combined	-0.228	-0.781	0.325
Louizos 2005 (2)-2[19]	LB	Combined	-0.854	-1.419	-0.289
Scheinin 1995[25]	B	Combined	0.011	-0.527	0.549
Raetzell 1995 (1)[24]	B	Combined	0.111	-0.653	0.875
Raetzell 1995 (2)[24]	B	Combined	0.068	-0.693	0.828
Ingelmo 2013[15]	R	Combined	-0.603	-1.062	-0.145
			-0.320	-0.649	0.010



C

Study name	Subgroup within study	Time point	Std diff in means	Lower limit	Upper limit
Cha 2012 (1)[31]	R	Combined	-0.227	-0.850	0.395
Cha 2012 (2)[31]	R	Combined	-0.075	-0.698	0.547
Lee 2001 (1)[18]	B	Combined	-0.138	-0.636	0.361
Lee 2001 (2)[18]	B	Combined	-0.493	-0.935	-0.051
Joris 1995[34]	B	Combined	-0.136	-0.760	0.487
			-0.249	-0.493	-0.006



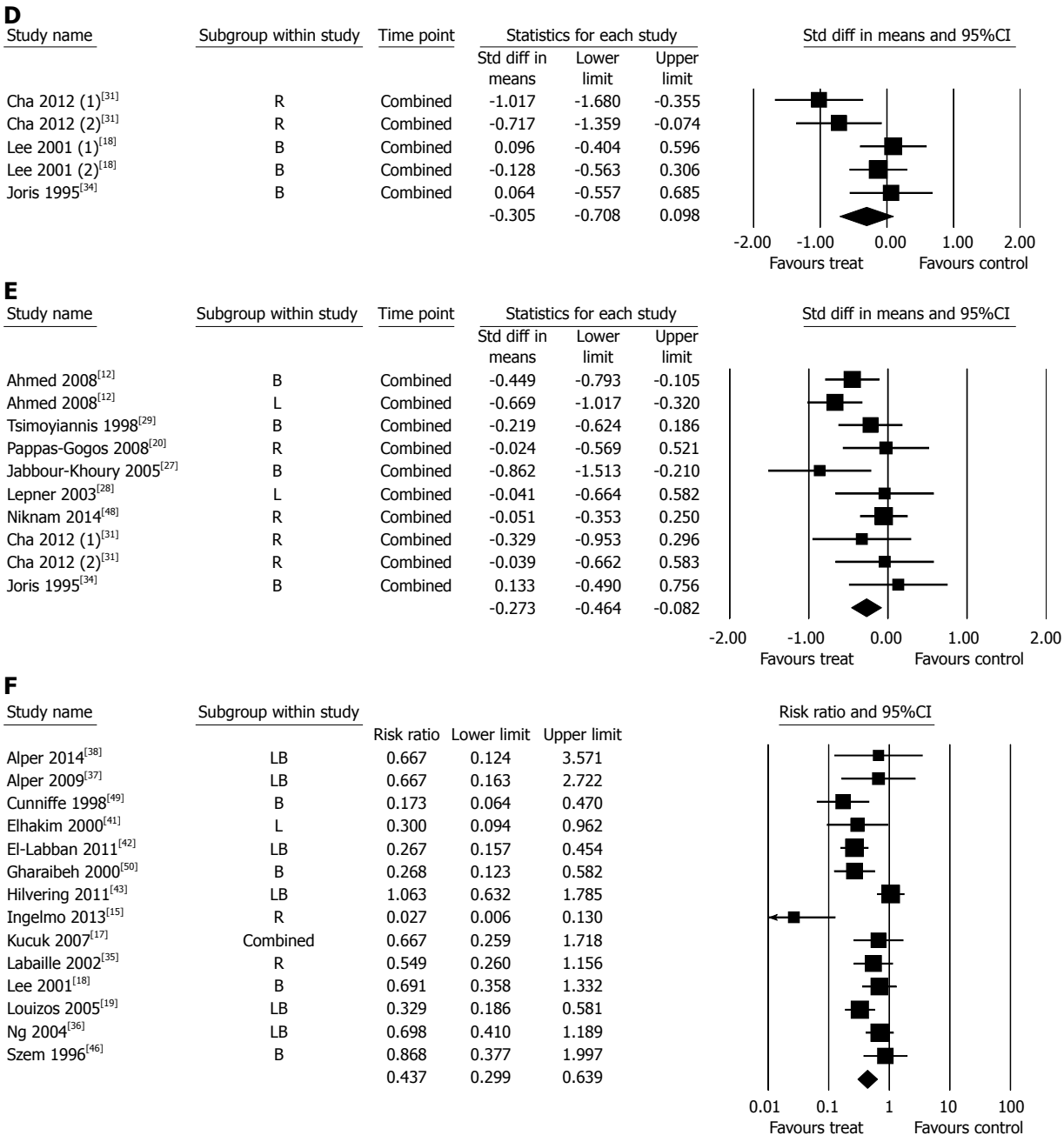


Figure 2 Forest plot of resting abdominal pain (A), dynamic abdominal pain (B), visceral pain (C), parietal pain (D), shoulder pain (severity) (E) and shoulder pain (incidence) (F).

fibers, which irritates phrenic nerve endings[2,4]. The phrenic nerve innervates the gallbladder and liver, and this nerve shares a common route with nerves that innervate the shoulder[51]. Dissolved carbon dioxide contributes to diaphragmatic irritation[52]. Therefore, the pain induced by pneumoperitoneum leads to referred pain in the shoulder. The topical application of local anesthetic to the viscera, *i.e.*, IPLA, exhibits an analgesic effect by blocking visceral nociception from the area of tissue damage and the peritoneum. The systemic absorption of local anesthetics through the peritoneal surface may also play a role in the analgesic effect by attenuating nociception[53].

Most studies included in present review evaluated abdominal pain, not visceral pain. Visceral pain made up a large portion of abdominal pain after LC compared to parietal or shoulder pain in several studies[18,34,35]. Therefore, we expected that the results of visceral and abdominal pain would exhibit a similar tendency. The administration of IPLA induced a significant reduction in visceral and abdominal pain at resting states after LC.

IPLA did not significantly reduce parietal pain in the present review. This result may be explained by the different origins of parietal and visceral pain. The analgesic effect of IPLA is favorable to visceral pain because IPLA is aimed at the injured viscera in the peritoneal cavity, not the abdominal wall. Parietal pain

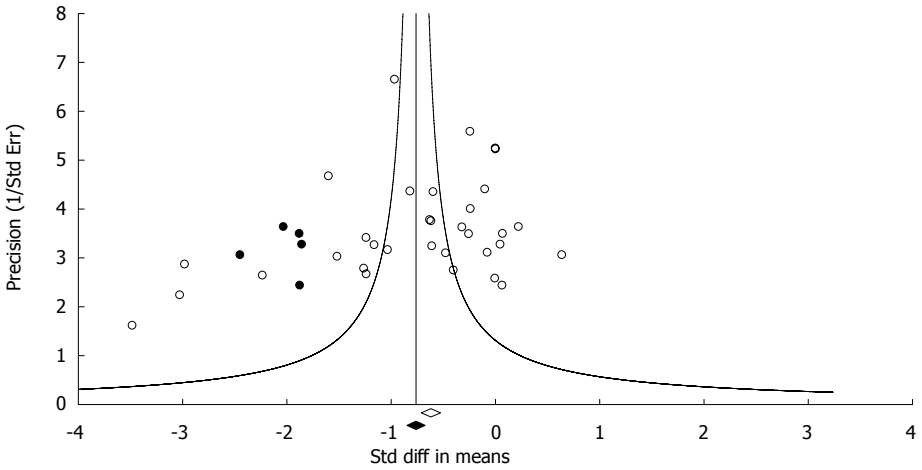


Figure 3 Funnel plot of publication bias of resting abdominal pain.

is a lesser component of the pain that is somatic origin and induced by the surgical incision in the abdominal wall for trocar insertion[2]. The origin of parietal pain supports the application of local anesthetics to trocar insertion sites, *i.e.*, wound infiltration with local anesthetics would be beneficial. Several studies investigated the effect of wound infiltration on pain after LC[54] and demonstrated favorable results in regard to pain control. Therefore, we performed subgroup analyses on wound infiltration. However, our meta-analysis demonstrated that parietal pain was not reduced in the wound infiltration subgroup, which is inconsistent with the results of previous studies.

Some of the included studies assessed abdominal pain in a dynamic state, such as moving, coughing, inspiration, or valsalva. Movement demands the contraction of primarily abdominal muscles, but coughing or deep inspiration is mediated by the movement of intraabdominal viscera[34]. Each type of movement suggests an aggravation of parietal and visceral pain. IPLA did not significantly alleviate dynamic abdominal pain in the present meta-analysis. Our results revealed that IPLA was effective on visceral pain in a resting state. Abdominal pain may be represented by visceral pain, which is worsened by coughing or inspiration. Therefore, we performed a subgroup analysis of studies that investigated abdominal pain during coughing or inspiration on the assumption that our results of the effect of IPLA on dynamic pain would be altered. However, subgroup analyses did not alter this result.

The present review is limited by the substantial heterogeneity between studies and the quality of included studies. There are many potential sources of clinical and methodological heterogeneity, such as dose, concentration, or volume of IPLA, the timing or site of IPLA administration, the volume and pressure of pneumoperitoneum, and the analgesic method during the postoperative period. We tried to conduct sensitivity and subgroup analyses for some of the possible factors, but we could not consider all of these factors in our analysis. Second, the quality of the included studies was limited. Notwithstanding this limitation, our study was the first meta-analysis to evaluate the effect of IPLA on pain characteristics after LC application using a rigorous methodology.

In conclusion, IPLA as an analgesic adjuvant in patients undergoing LC exhibited a favorable effect on postoperative abdominal, visceral, and shoulder pain during a resting state.

COMMENTS

Background

Laparoscopic cholecystectomy (LC) is widely performed because of the benefits associated with lower invasiveness, but patients still experience significant postoperative pain. Numerous studies demonstrated therapeutic strategies for pain after LC, including the administration of intraperitoneal local anesthetic (IPLA). There were three types of pain characteristics after LC: visceral, parietal, and shoulder pain. It would be beneficial for postoperative pain management to provide evidence of the effect of IPLA on pain after LC. Therefore, the authors systematically evaluated the effect of IPLA on pain characteristics after LC.

Research frontiers

Postoperative pain management is an important issue in LC. Recent recognition of different pain components suggests that strategies for pain therapy should focus on pain characteristics based on their origins. Currently, LC and pain characteristics are significantly promising subjects of research.

Innovations and breakthroughs

Several meta-analyses on LC were performed, but no studies systematically evaluated the effect of IPLA on pain components after LC. This study is the first report of a meta-analysis to investigate the effect of IPLA on pain characteristics after LC.

Applications

This meta-analysis provides evidence of the effect of IPLA on pain characteristics after LC and suggests a more effective therapeutic approach based on pain components after LC.

Terminology

Pain characteristics after LC are composed of visceral, parietal, and shoulder pain. Visceral and shoulder pain are associated with pneumoperitoneum during laparoscopic surgery. Parietal pain is linked to trocar incisions. The origins of these components are different, and distinct therapeutic approaches should

be distinguished. IPLA in the present study reduced visceral and shoulder pain after LC, which suggests that intraperitoneally administered local anesthetic exerts an analgesic effect on the viscera and peritoneum that are affected by surgery and pneumoperitoneum.

Peer-review

The authors of this meta-analysis present the application value of intraperitoneal local anesthetic on pain after LC. This article is valuable for clinical physicians.

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