Systematic review and meta analysis for pain reduction after laparoscopic gastric procedures

Article *in* British Journal of Surgery · January 2011

Impact Factor: 5.54 · DOI: 10.1002/bjs.7293 · Source: PubMed

4 authors, including:

Tarik Sammour
University of Texas MD Anderson Cancer Ce…
139 PUBLICATIONS **1,194** CITATIONS
SEE PROFILE

Sanket Srinivasa
65 PUBLICATIONS **600** CITATIONS
SEE PROFILE

Andrew G Hill
University of Auckland
277 PUBLICATIONS **3,350** CITATIONS
SEE PROFILE

Meta-analysis

Systematic review and meta-analysis of intraperitoneal local anaesthetic for pain reduction after laparoscopic gastric procedures

A. Kahokehr, T. Sammour, S. Srinivasa and A. G. Hill

Department of Surgery, Faculty of Medicine and Health Sciences, University of Auckland, Auckland, New Zealand
Correspondence to: Dr A. Kahokehr, South Auckland Clinical School, University of Auckland, Private Bag 93311, Otahuhu, Auckland, New Zealand (e-mail: arman.kahokehr@gmail.com)

Background: **With the advent of minimally invasive gastric surgery, visceral nociception has become an important area of investigation as a potential cause of postoperative pain. A systematic review and meta-analysis was carried out to investigate the clinical effects of intraperitoneal local anaesthetic (IPLA) in laparoscopic gastric procedures.**

Methods: **Comprehensive searches were conducted independently without language restriction. Studies were identified from the following databases from inception to February 2010: Cochrane Central Register of Controlled Trials, the Cochrane Library, MEDLINE, PubMed, Embase and CINAHL. Relevant meeting abstracts and reference lists were searched manually. Appropriate methodology according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was adhered to.**

Results: **Five randomized controlled trials in laparoscopic gastric procedures were identified for review. There was no significant heterogeneity between the trials ($\chi^2 = 10{\cdot}27$, 10 d.f., $P = 0{\cdot}42$, $I^2 = 3$ per cent). Based on meta-analysis of trials, there appeared to be reduced abdominal pain intensity (overall mean difference in pain score −1·64, 95 per cent confidence interval (c.i.) −2·09 to −1·19; $P < 0{\cdot}001$), incidence of shoulder tip pain (overall odds ratio 0·15, 95 per cent c.i. 0·05 to 0·44; $P < 0{\cdot}001$) and opioid use (overall mean difference −3·23, −4·81 to −1·66; $P < 0{\cdot}001$).**

Conclusion: **There is evidence in favour of IPLA in laparoscopic gastric procedures for reduction of abdominal pain intensity, incidence of shoulder pain and postoperative opioid consumption.**

Paper accepted 24 August 2010
Published online 26 October 2010 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.7293

Introduction

Pain after visceral surgery is thought to be multifactorial[1]. With the advent of minimally invasive techniques, including single-port laparoscopy and transluminal endoscopic surgery, there is potential to create minimal incisions on the abdominal wall or to bypass the abdominal wall altogether for visceral access and resection[2,3]. Although greatly reducing the need for analgesia, these advances in technique still result in visceral dissection and nociception after disruption of the peritoneum and resection of viscera.

Visceral pain is distinct from somatic pain[4]. Visceral signalling occurs through the enteric nervous system, which is complex and partly independent of the central nervous system with a vast network of distinct, and functionally diverse, neuronal subtypes[5]. Viscera such as the stomach and covering peritoneum convey unpleasant sensations and autonomic reactions to injury through afferents in the vagus nerve[6]. These so-called 'silent nociceptors' are activated by intraperitoneal inflammation and injury[4], giving rise to both painful and non-painful sensations that influence feeding and illness behaviours[7].

The ease of use and safety of local anaesthetics is well recognized, and collectively they serve as one of the most important classes of drug in perioperative care. The main advantage of local anaesthetic agents is that they do not have the adverse effects of systemically administered opioids, such as postoperative sedation, nausea, gastrointestinal paralysis and respiratory suppression, and act directly on the tissue to which they are applied. Local anaesthetics are commonly administered

in abdominal surgery by skin infiltration or epidurally, blocking somatic afferents and providing significant benefits in reducing postoperative abdominal wall pain, and hence improving recovery[8].

It is also possible to instil local anaesthetic solutions into the peritoneal cavity, thereby blocking visceral afferent signalling, and potentially modifying visceral nociception and downstream illness responses. Local anaesthetics applied to the peritoneal cavity have been used as 'field blocks' since as early as 1950[9–11]. Tubal ligation has been performed effectively and safely under abdominal wall and intraperitoneal local anaesthetic (IPLA) alone[12]. Peripheral techniques using local anaesthetic also seem to be gaining popularity[8]. However, the practice of IPLA administration is not routine in modern-day laparoscopic gastric procedures.

The aim of this review was systematically to evaluate the literature on the use of IPLA *versus* control in double-blinded randomized studies of adult patients undergoing laparoscopic gastric procedures, with pain outcomes as clinical measures of the effectiveness of the reduction in visceral nociception.

Methods

All aspects of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement were followed[13].

Search strategy

A comprehensive database search was carried out independently by the first two authors. The following databases were searched from inception to February 2010: MEDLINE, CINAHL, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL/CCTR), the Cochrane Library and Embase. The search terms (including truncations) were: 'local anaesth$', 'local anesth$', 'nerve conduct$', 'ropivicaine', 'bupivacaine', 'lidocaine', lignocaine', 'procaine', 'intra-abdominal$', 'intraperitoneal', 'visceral', 'laparosc$', 'gastric', 'stomach', 'bypass', 'peritoneum', 'coeliosco$' and 'surgery'. Language limitations were not applied.

Additional articles or abstracts were retrieved by means of hyperlinks and by manually scrutinizing the reference lists of relevant publications. Animal trials were excluded. Relevant academic meeting proceedings were also searched. Publications in languages other than English were translated into English with the help of academics at the Faculty of Medical and Health Sciences, University of Auckland. Authors were contacted for additional data when required. If no response was received after 4 weeks, a second attempt was made to obtain data.

Study selection

Publications were selected for review if they investigated, in a double-blinded randomized study, the effects of IPLA (treatment) *versus* placebo (control) on pain outcomes in adults undergoing laparoscopic gastric procedures. For studies that used IPLA both before and after dissection, only predissection results were included in the meta-analysis owing to the pre-emptive nature of the intervention. Exclusion criteria included open surgery, concomitant use of preperitoneal or abdominal wall (incisional/port-site) local anaesthetic, and concomitant use of intramuscular or intravenous analgesia unless IPLA use was being investigated alone as part of a multimodal regimen with a placebo-controlled comparison group. Two authors examined all retrieved articles independently; any disagreement over inclusion or exclusion was discussed with a third author and a consensus reached. The methodological quality of randomized clinical trials was assessed using the Jadad criteria[14].

Data extraction

Data abstraction was performed independently by two authors using electronic forms. The primary outcomes used for meta-analysis were abdominal pain scores measured on a visual analogue scale (0–100 mm or 0–10 cm) and incidence of shoulder tip pain. Quantitative data synthesis was performed and information was entered into tables based on postoperative pain at 6, 12 and 24 h after surgery. The median score was used as an estimate of the mean where the latter was not reported. Standard deviations were obtained from the author if not published, or calculated based on the methods described in the Cochrane handbook[15]. If data were still insufficient after the above efforts, the study was excluded because of missing information. Individual study bias including funding source was assessed at the study level. Mean difference was used to report pain intensity and odds ratio for incidence of shoulder tip pain, both with 95 per cent confidence intervals.

Total opioid analgesia requirement for the admission were extracted where possible and converted into morphine equivalence[16,17]. Non-steroidal analgesia use was not converted into morphine equivalence and not included in the meta-analysis. The summary measure was reported as difference in means.

Statistical analysis

Meta-analysis was performed using Review Manager version 5.0 (The Nordic Cochrane Centre, Copenhagen, Denmark). A fixed-effects model was used unless there was concern regarding a small study effect, in which case a comparison was made between fixed- and random-effects models[18]. Results of the meta-analysis were assessed by graphical presentations of mean difference or odds ratio according to the outcome and 95 per cent confidence intervals represented on forest plots. $P < 0{\cdot}050$ considered statistically significant.

Heterogeneity between studies was assessed by three methods. First, publication bias was tested using the funnel plot graphical exploration method[18]. Second, a χ^2 test for statistical heterogeneity was performed, with $P < 0{\cdot}100$ being considered statistically significant. Finally, I^2 statistics were used to assess clinical heterogeneity[19]. If statistical heterogeneity was identified, sensitivity analysis was performed to detect small study effects by comparison of the fixed- and random-effects estimates of the intervention[18]. In the event of moderate or high clinical heterogeneity (defined as I^2 at least 50 per cent), methodological subgroup analysis was performed[19] in which trials with a Jadad score of 4 and 5 rated were grouped together as 'high-quality' studies and all other trials grouped as 'low-quality' trials to investigate the cause further. Study weight was by sample size.

Results

Five studies were suitable for meta-analysis. These were in fundoplication[20,21], Roux-en-Y bypass[22,23] and gastric banding[24].

Study characteristics

The PRISMA[13] flow diagram for systematic reviews is presented in *Fig. 1*. The characteristics of all five trials included in this review[20–24], and one trial excluded[25], are summarized in *Table 1*. Exclusion of the latter trial was because of concomitant use of intramuscular analgesia in the placebo (control) group but not in the IPLA group. The local anaesthetic agents in the included studies were bupivacaine[20,22–24] and lidocaine[21]. A low-dose infuser was used by one trial to deliver IPLA[24]. Mode and technique of delivery are summarized in *Table 1*.

Safety

There were no reports of any adverse events following IPLA in the studies reviewed.

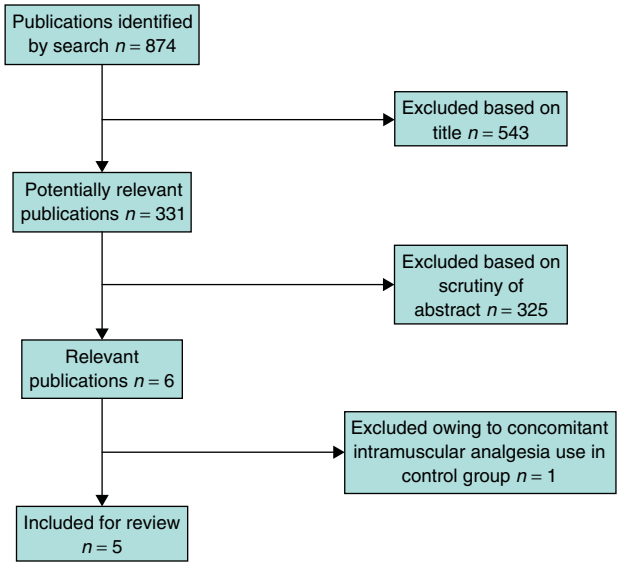

Fig. 1 Selection of articles for review

Abdominal pain outcomes

Three trials that investigated postoperative abdominal pain intensity in a total of 119 patients were used for meta-analysis[21,22,24]. There was a reduction in pain scores with the use of IPLA at each time point after surgery. The overall mean difference, based on a total of 426 observations at several time points, was −1·64 (−2·09 to −1·19 ($P < 0{\cdot}001$) (*Fig. 2*). The funnel plot was symmetrical (results not shown) and overall heterogeneity was not significant ($\chi^2 = 10{\cdot}27$, 10 d.f., $P = 0{\cdot}42$, $I^2 = 3$ per cent). Further analysis was therefore not indicated.

Shoulder tip pain

The incidence of postoperative shoulder tip pain was investigated in three trials[20,21,24] in a total of 90 patients. Meta-analysis of these trials showed a reduction in shoulder tip pain: overall odds ratio 0·15 (0·05 to 0·44; $P < 0{\cdot}001$) (*Fig. 3*). The funnel plot was symmetrical (results not shown) and heterogeneity was not significant ($\chi^2 = 1{\cdot}78$, 2 d.f., $P = 0{\cdot}41$, $I^2 = 0$ per cent). Further analysis was therefore not indicated.

Postoperative opioid use

All five trials reported on postoperative opioid use, in 273 patients[20–24]. Meta-analysis showed a reduction in admission total opioid use with IPLA: overall mean difference −3·23 (−4·81 to −1·66; $P < 0{\cdot}001$) (*Fig. 4*). The funnel plot was symmetrical (results not shown)

Table 1 Randomized controlled trials of intraperitoneal local anaesthetic in laparoscopic general surgical procedures

Reference	Procedure and no. of patients	Timing of IPLA use* and method of delivery	Agent used	Pain outcome and analgesia use	Bowel outcome, PONV	Original authors' conclusion, other relevant findings	Jadad score Data used in meta-analysis
Cunniffe *et al.*[20] 1998	Fundoplication IPLA 11 Control 10	Before; sub-diaphragmatic irrigation applied equally to each diaphragmatic dome	10 ml 0·5% bupivacaine in 500 ml NS Control: NS	Reduced STP intensity for 24 h, reduced i.m. morphine use	NP	Reduced STP severity and frequency with potential to reduce morbidity	4 STP incidence, analgesia use
Palmes *et al.*[21] 2007	Fundoplication IPLA before 20 IPLA after 20 Control 20	Before and after; upper surfaces of both lobes of liver	50 ml 0·5% lidocaine Control: NS	Reduced abdominal pain, STP and piritramide use in group given IPLA before dissection	NP	Reduced pain and analgesia consumption in operations with prolonged pneumo-peritoneum	4 Pain, analgesia use, STP incidence
Symons *et al.*[23] 2007	Roux-en-Y gastric bypass IPLA 65 Control 68	Before; on to oesophageal hiatus	15 ml 0·5% bupivacaine Control: NS	No difference in pain, reduced oral hydrocodone/ paracetamol use	No difference in antiemetic use	Reduced oral analgesia use but no other clinical difference	5 Analgesia use
Sherwinter *et al.*[24] 2008	Gastric banding IPLA 15 Control 15	After; i.p. infusion catheter placed between gastric band	2 ml/h 0·375% bupivacaine infusion for 48 h Control: NS	Reduced pain, no difference in analgesia use	No difference in nausea	Safe and effective to use infusion system; need to evaluate cost saving	3 Pain, analgesia use, STP incidence
Alkhamesi *et al.*[22] 2008	Roux-en-Y gastric bypass IPLA 25 Control 25	After; aerosolized using purpose-built device	10 ml 0·5% bupivacaine Control: NS	Reduced pain, no difference in analgesia use	NP	Reduced pain, safe	3 Pain, analgesia use
Paech *et al.*[25] 2008	Various, including cholecystec-tomy and gynaecological IPLA 50 Control 50	After; on to operative bed under direct vision	20 ml 0·75% ropivacaine Control: NS and i.m. meperidine	No difference in pain or analgesia use	NP opioid	No difference in pain compared with systemic opioid	5 Excluded from meta-analysis as concomitant i.m. meperidine used in control group

*Before or after dissection. IPLA, intraperitoneal local anaesthetic; PONV, postoperative nausea and vomiting; NS, normal saline; STP, shoulder tip pain; NP, not published; i.m., intramuscular, i.p., intraperitoneal.

and heterogeneity was low ($\chi^2 = 6{\cdot}92$, 4 d.f., $P = 0{\cdot}14$, $I^2 = 42$ per cent). Further analysis was therefore not indicated.

Discussion

This systematic review identified five randomized double-blinded trials that reported use of IPLA for pain outcomes in laparoscopic gastric procedures for non-inflammatory conditions. Meta-analysis of these trials revealed an overall reduction in abdominal pain intensity, reduced incidence of shoulder tip pain and decreased opioid analgesia use. There was no report of adverse effects in any patient. This approach should be particularly useful in the ambulatory setting that laparoscopic procedures are increasingly being performed in.

A large meta-analysis has similarly confirmed the benefits of pain reduction with IPLA use after laparoscopic cholecystectomy[26]. The present review further supports the concept that pain arising from the parietal and visceral peritoneum can be controlled locally and IPLA may be used safely as part of multimodal, balanced analgesia after laparoscopic surgery.

The mechanism of action of IPLA probably involves blockade of free afferent nerve endings in the peritoneum. Systemic absorption of local anaesthetic from the peritoneal cavity may also play a part in reduced nociception, although this would be expected to occur after any local anaesthetic technique. Systemic levels of

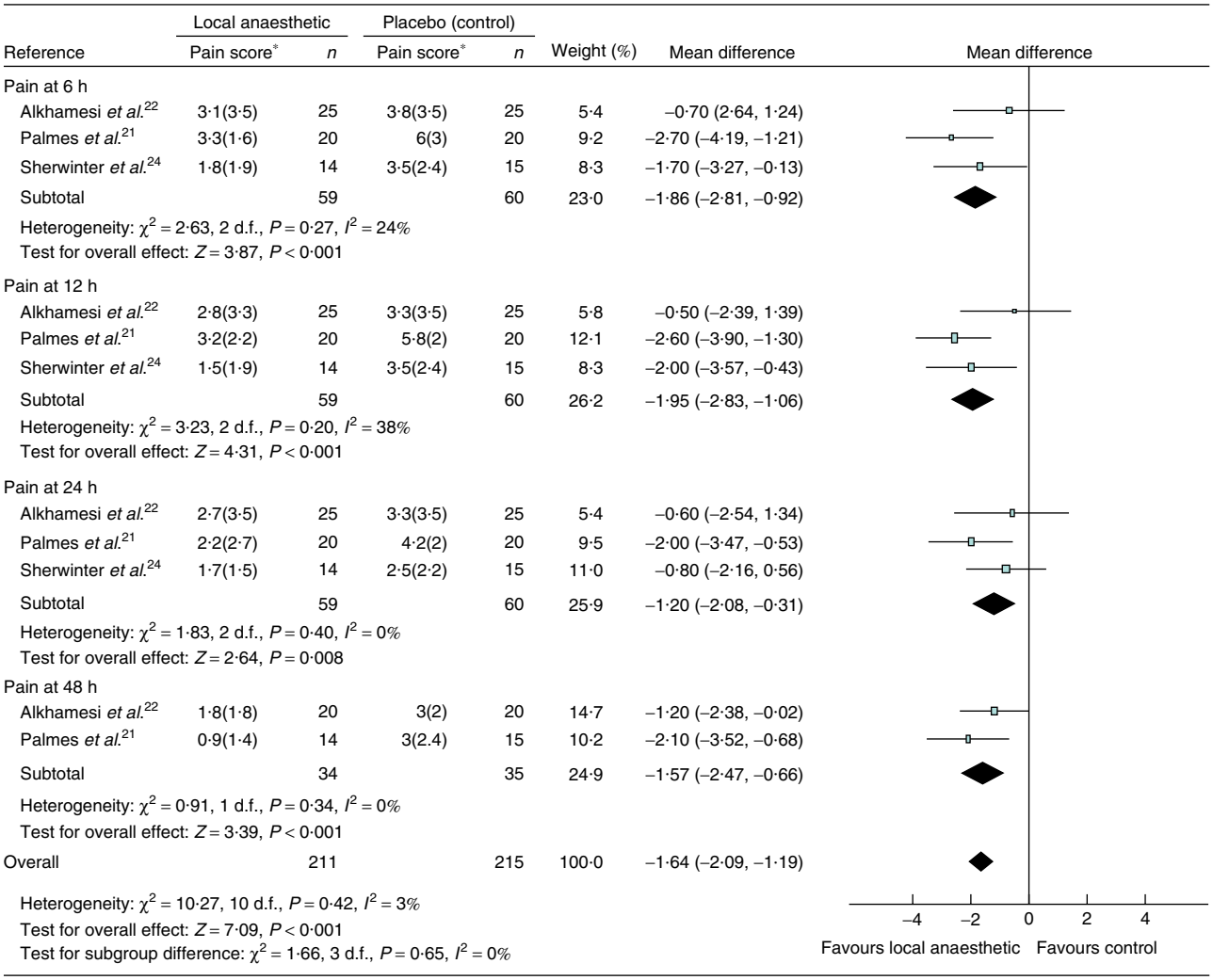

Fig. 2 Forest plot showing meta-analysis of pain scores after laparoscopic gastric procedures with intraperitoneal local anaesthetic *versus* placebo (control). An inverse variance fixed-effects method was used. *Values are mean(s.d.). Mean differences are shown with 95 per cent confidence intervals

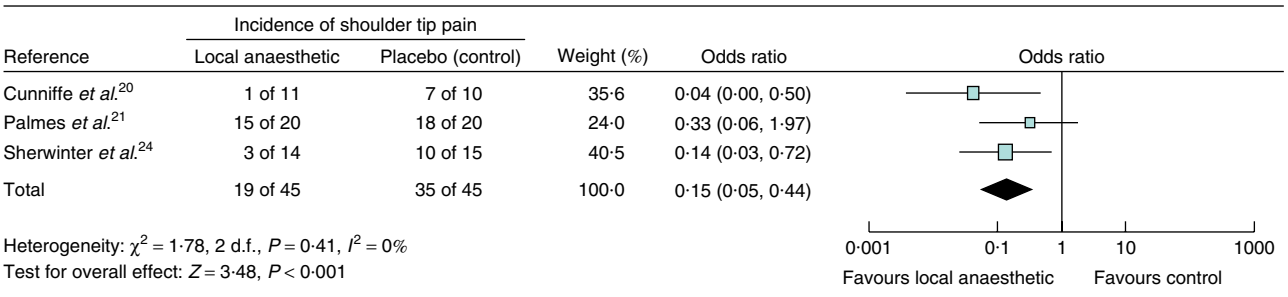

Fig. 3 Forest plot showing meta-analysis of incidence of shoulder tip pain after laparoscopic gastric procedures with intraperitoneal local anaesthetic *versus* placebo (control). A Mantel–Haenszel fixed-effects method was used. Odds ratios are shown with 95 per cent confidence intervals

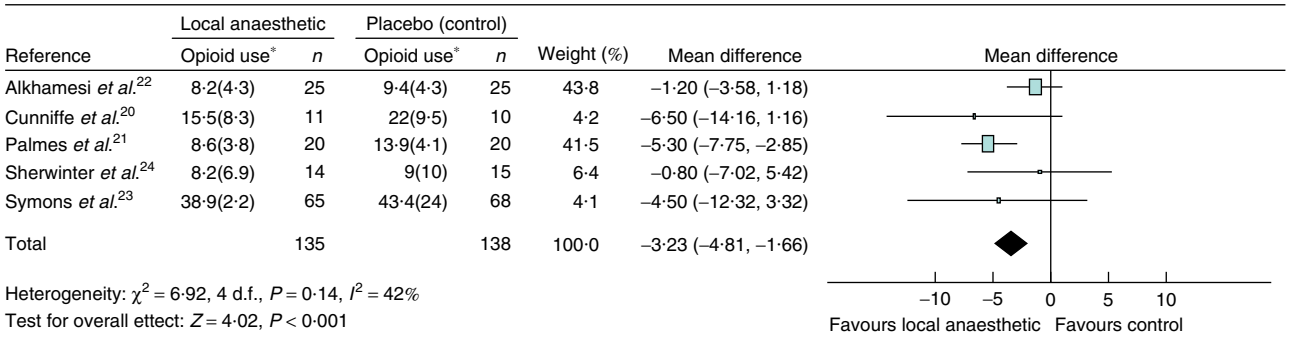

Fig. 4 Forest plot showing meta-analysis of total opioid use after laparoscopic gastric procedures with intraperitoneal local anaesthetic *versus* placebo (control). An inverse variance fixed-effects method was used. *Values are mean(s.d.). Mean differences are shown with 95 per cent confidence intervals

local anaesthetic are detectable in the serum as soon as 2 min after bolus instillation into the peritoneum[27], and a systematic review has recently confirmed that low-dose intravenous local anaesthetic infusion is advantageous compared with parenteral opioid administration alone in patients having abdominal operations[28]. Local anaesthetics also have anti-inflammatory actions[29,30]. Topical intraperitoneal lidocaine and bupivacaine have been shown to inhibit chemical peritonitis in an animal model[31]. Intraperitoneal infusion of procaine significantly reduced adhesion formation and density after abdominal surgery in rabbits[32].

Cervero and Laird[4] argue that, although visceral nociception is not easily excitable in health, there is sensitization in inflammation, for example after visceral surgery. Afferent signalling may therefore be greater in magnitude and prolonged in duration after surgical insult[4]. A proinflammatory cytokine cascade in the peritoneal cavity, with direct action on the visceral afferents and the vagus as a major vehicle, is a feasible contributor to postoperative visceral pain perception and the 'sickness response'[33]. By using IPLA it may be possible to modulate peritoneal and visceral signalling to the brain, thereby attenuating the metabolic impact of visceral surgery.

It is therefore logical that IPLA should be used in addition to other perioperative pharmacological agents after visceral surgery. Furthermore, novel methods of delivery of agents to the peritoneal cavity are emerging with the advent of a peritoneal nebulizer, and the use of elastomeric pumps to maintain a continuous infusion system for drug delivery[34–38]. These should perhaps be trialled in the expanding field of natural orifice surgery in order to study visceral nociception as a clinically relevant issue.

This systematic review included only randomized double-blinded trials. The analysis was limited by the outcomes reported in these studies. Most trials did not report on other outcomes of interest such as recovery of bowel function, which may also be improved. The nature of clinical trials in surgery meant that a variety of different local anaesthetic agents and methods of administration was used. Given the likely variation in degree of intraperitoneal inflammation caused by different surgical procedures, it would have been ideal to compare the technique of local anaesthetic delivery for each procedure separately. However, meta-analysis of individual procedures is not currently feasible owing to the paucity of data. Therefore, to assess the degree of difference between procedures, validated heterogeneity testing was carried out. As overall heterogeneity was low and not significant, the authors believe the results of this meta-analysis to be valid despite the variety of gastric procedures.

Acknowledgements

This research was conducted during tenure of the Ruth Spencer fellowship from the Auckland Medical Research Foundation held by A.K. and S.S. The authors declare no conflict of interest.

References

1 Wills VL, Hunt DR. Pain after laparoscopic cholecystectomy. *Br J Surg* 2000; **87**: 273–284.
2 Kuon Lee S, You YK, Park JH, Kim HJ, Lee KK, Kim DG. Single-port transumbilical laparoscopic cholecystectomy: a preliminary study in 37 patients with gallbladder disease. *J Laparoendosc Adv Surg Tech A* 2009; **19**: 495–499.
3 Gumbs AA, Fowler D, Milone L, Evanko JC, Ude AO, Stevens P *et al.* Transvaginal natural orifice translumenal endoscopic surgery cholecystectomy: early evolution of the technique. *Ann Surg* 2009; **249**: 908–912.

4 Cervero F, Laird JM. Visceral pain. *Lancet* 1999; **353**: 2145–2148.
5 Burns AJ, Pachnis V. Development of the enteric nervous system: bringing together cells, signals and genes. *Neurogastroenterol Motil* 2009; **21**: 100–102.
6 Bielefeldt K, Christianson JA, Davis BM. Basic and clinical aspects of visceral sensation: transmission in the CNS. *Neurogastroenterol Motil* 2005; **17**: 488–499.
7 Grundy D, Al-Chaer ED, Aziz Q, Collins SM, Ke M, Taché Y *et al*. Fundamentals of neurogastroenterology: basic science. *Gastroenterology* 2006; **130**: 1391–1411.
8 Kehlet H, Liu SS. Continuous local anesthetic wound infusion to improve postoperative outcome: back to the periphery? *Anesthesiology* 2007; **107**: 369–371.
9 Hanson IR, Hingson RA. The use of xylocaine, a new local anesthetic, in surgery, obstetrics and therapeutics. *Curr Res Anesth Analg* 1950; **29**: 136–147.
10 Griffin EM, Prystowsky H, Hingson RA. The use of topical anaesthesia of the peritoneum in poor risk surgery and in augmenting inadequate vertebral conduction anaesthesia. *N Z Med J* 1951; **50**: 31–33.
11 Ajao OG. The use of local anaesthetics for emergency abdominal operations. *Trop Doct* 1978; **8**: 73–75.
12 Penfield AJ. Laparoscopic sterilization under local anesthesia. 1200 cases. *Obstet Gynecol* 1977; **49**: 725–727.
13 Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097.
14 Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ *et al*. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996; **17**: 1–12.
15 Higgins JPT, Green S (eds). *Cochrane Handbook for Systemic Review of Interventions, Version 5.0.1*. The Cochrane Collaboration: Oxford, 2008.
16 Pereira J, Lawlor P, Vigano A, Dorgan M, Bruera E. Equianalgesic dose ratios for opioids. A critical review and proposals for long-term dosing. *J Pain Symptom Manage* 2001; **22**: 672–687.
17 Lawlor P, Pereira J, Bruera E. Dose ratios among different opioids: underlying issues and an update on the use of the equianalgesic table. In *Topics in Palliative Care*, Bruera E, Portenoy RK (eds), vol. 5. Oxford University Press: New York, 2001; 247–276.
18 Higgins JPT, Green S (eds). *Cochrane Handbook for Systematic Reviews of Interventions, Version 5.0.2* [updated September 2009]. The Cochrane Collaboration. http://www.cochrane-handbook.org [accessed 12 May 2010].
19 Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557–560.
20 Cunniffe MG, McAnena OJ, Dar MA, Calleary J, Flynn N. A prospective randomized trial of intraoperative bupivacaine irrigation for management of shoulder-tip pain following laparoscopy. *Am J Surg* 1998; **176**: 258–261.
21 Palmes D, Röttgermann S, Classen C, Haier J, Horstmann R. Randomized clinical trial of the influence of intraperitoneal local anaesthesia on pain after laparoscopic surgery. *Br J Surg* 2007; **94**: 824–832.
22 Alkhamesi NA, Kane JM, Guske PJ, Wallace JW, Rantis PC. Intraperitoneal aerosolization of bupivacaine is a safe and effective method in controlling postoperative pain in laparoscopic Roux-en-Y gastric bypass. *J Pain Res* 2008; **1**: 9–13.
23 Symons JL, Kemmeter PR, Davis AT, Foote JA, Baker RS, Bettendorf MJ *et al*. A double-blinded, prospective randomized controlled trial of intraperitoneal bupivacaine in laparoscopic Roux-en-Y gastric bypass. *J Am Coll Surg* 2007; **204**: 392–398.
24 Sherwinter DA, Ghaznavi AM, Spinner D, Savel RH, Macura JM, Adler H. Continuous infusion of intraperitoneal bupivacaine after laparoscopic surgery: a randomized controlled trial. *Obes Surg* 2008; **18**: 1581–1586.
25 Paech MJ, Ilett KF, Hackett LP, Page-Sharp M, Parsons RW. Disposition and clinical outcome after intraperitoneal meperidine and ropivacaine administration during laparoscopic surgery. *Anesth Analg* 2008; **106**: 278–286.
26 Kahokehr A, Sammour T, Soop M, Hill AG. Intraperitoneal use of local anesthetic in laparoscopic cholecystectomy: systematic review and metaanalysis of randomized controlled trials. *J Hepatobiliary Pancreat Sci* 2010; **17**: 637–656.
27 Fuhrer Y, Charpentier C, Boulanger G, Menu N, Grosdidier G, Laxenaire MC. [Analgesia after laparoscopic cholecystectomy by intraperitoneal administration of bupivacaine.] *Ann Fr Anesth Reanim* 1996; **15**: 128–134.
28 Marret E, Rolin M, Beaussier M, Bonnet F. Meta-analysis of intravenous lidocaine and postoperative recovery after abdominal surgery. *Br J Surg* 2008; **95**: 1331–1338.
29 MacGregor RR, Thorner RE, Wright DM. Lidocaine inhibits granulocyte adherence and prevents granulocyte delivery to inflammatory sites. *Blood* 1980; **56**: 203–209.
30 Martinsson T, Oda T, Fernvik E, Roempke K, Dalsgaard CJ, Svensjö E. Ropivacaine inhibits leukocyte rolling, adhesion and CD11b/CD18 expression. *J Pharmacol Exp Ther* 1997; **283**: 59–65.
31 Rimbäck G, Cassuto J, Wallin G, Westlander G. Inhibition of peritonitis by amide local anesthetics. *Anesthesiology* 1988; **69**: 881–886.
32 Zhitniuk RI, Kataeva GA. [Intraperitoneal infusions of novocaine after laparotomies for the prevention of intraperitoneal adhesions.] *Khirurgiia (Mosk)* 1974; (Oct): 67–69.
33 Maier SF, Goehler LE, Fleshner M, Watkins LR. The role of the vagus nerve in cytokine-to-brain communication. *Ann N Y Acad Sci* 1998; **840**: 289–300.
34 Alkhamesi NA, Ridgway PF, Ramwell A, McCullough PW, Peck DH, Darzi AW. Peritoneal nebulizer: a novel technique for delivering intraperitoneal therapeutics in laparoscopic

surgery to prevent locoregional recurrence. *Surg Endosc* 2005; **19**: 1142–1146.

35 Greib N, Schlotterbeck H, Dow WA, Joshi GP, Geny B, Diemunsch PA. An evaluation of gas humidifying devices as a means of intraperitoneal local anesthetic administration for laparoscopic surgery. *Anesth Analg* 2008; **107**: 549–551.

36 Gupta A, Perniola A, Axelsson K, Thorn SE, Crafoord K, Rawal N. Postoperative pain after abdominal hysterectomy: a double-blind comparison between placebo and local anesthetic infused intraperitoneally. *Anesth Analg* 2004; **99**: 1173–1179.

37 Ilfeld BM, Morey TE, Enneking FK. New portable infusion pumps: real advantages or just more of the same in a different package? *Reg Anesth Pain Med* 2004; **29**: 371–376.

38 Rawal N, Axelsson K, Hylander J, Allvin R, Amilon A, Lidegran G *et al*. Postoperative patient-controlled local anesthetic administration at home. *Anesth Analg* 1998; **86**: 86–89.