

Randomized clinical trial of the influence of intraperitoneal local anaesthesia on pain after laparoscopic surgery

D. Palmes¹, S. Röttgermann², C. Classen², J. Haier¹ and R. Horstmann²

¹Department of General Surgery, Münster University Hospital, Münster, and ²Department of Surgery, Herz-Jesu-Krankenhaus, Münster-Hiltrup, Germany

Correspondence to: Dr R. Horstmann, Department of Surgery, Herz-Jesu Hospital Münster, Westfalenstrasse 109, 48165 Münster, Germany (e-mail: chirurgie@herz-jesu-kh-ms.de)

Background: There is controversy about the effectiveness of intraperitoneal local anaesthesia (LA) in laparoscopic surgery. The aim of the present randomized clinical trial was to compare the analgesic effect of pre-emptive (preoperative) *versus* postoperative intraperitoneal LA in two different types of laparoscopic surgery.

Methods: Between July 2004 and January 2005, 133 consecutive patients scheduled to undergo laparoscopic fundoplication or hernia repair were randomly assigned to one of three treatments: placebo solution (50 ml 0.9 per cent saline) or LA (50 ml 0.5 per cent lidocaine) administered immediately after creation of the pneumoperitoneum, or LA (50 ml 0.5 per cent lidocaine) at the end of the operation. Analgesic requirements were analysed, and pain was assessed using a visual analogue scale (VAS) from 0 to 100 at 6, 12, 24 and 48 h after surgery.

Results: The duration of pneumoperitoneum (median 66 *versus* 46 min respectively; $P < 0.001$) and overall pain intensity (median VAS score 46.7 *versus* 6.5; $P < 0.001$) were higher for laparoscopic fundoplication than for hernia repair. Preoperative application of LA reduced abdominal pain (median 28.6 *versus* 74.9; $P < 0.005$), shoulder pain (median 24.3 *versus* 43.8; $P = 0.004$) and analgesic consumption (mean(s.d.) 11.1(5.0) *versus* 18.5(5.4) mg piritramide per 48 h; $P = 0.002$) after fundoplication, but had no analgesic effects after hernia repair.

Conclusion: Pre-emptive application of LA reduced postoperative pain and analgesic requirements after laparoscopic fundoplication.

Paper accepted 11 January 2007

Published online in Wiley InterScience (www.bjs.co.uk). DOI: 10.1002/bjs.5810

Introduction

Laparoscopic procedures have become popular in recent years, as they are associated with rapid postoperative recovery, low postoperative complication rates, and early mobilization and discharge home^{1,2}. Although previous studies have shown that laparoscopy is associated with less pain than laparotomy, it is not pain free²⁻¹⁰. A recent randomized controlled trial has shown that there may be more intense pain and greater analgesia requirements in the immediate postoperative period after laparoscopic surgery than after open laparotomy².

Improved understanding of the pathogenesis of postoperative abdominal and shoulder pain after laparoscopy gave rise to the use of intraperitoneal local anaesthesia (LA) to reduce pain and the need for analgesia after laparoscopy,

but the results have been variable³ as the published studies are heterogeneous⁴⁻⁹ and often lack appropriate controls. No definitive conclusion regarding the value of intraperitoneal LA can yet be made¹⁰.

The aim of this study was to examine the effect of intraperitoneal LA on the requirement for postoperative analgesia and pain intensity after two types of laparoscopic surgery in a randomized clinical trial.

Methods

This randomized double-blind placebo-controlled study was designed to examine the analgesic effects and impact of timing of administration (pre-emptive application before surgery *versus* postoperative application) of intraperitoneal

LA in laparoscopic hernia repair and laparoscopic fundoplication. The study was approved by an independent ethics committee and carried out according to the principles of the Declaration of Helsinki, 1989. Consent was obtained from all participants before inclusion in the trial.

Between July 2004 and January 2005, 160 consecutive patients were scheduled to undergo laparoscopic fundoplication (79 patients) or hernia repair (81). Patients eligible for laparoscopic fundoplication had gastro-oesophageal reflux disease (GORD), an American Society of Anesthesiologists physical status score of I or II, and were scheduled for elective surgery. Patients with GORD-related morphological alterations (upside-down stomach, Barrett's metaplasia, etc.) were excluded from the study. Those eligible for laparoscopic hernia repair had a non-incarcerated unilateral inguinal hernia and had opted for elective laparoscopic hernia repair by the transabdominal preperitoneal procedure. Patients with bilateral hernia were excluded. In general, all patients with recurrent reflux disease or recurrent hernia, extensive intraperitoneal adhesions, a history of drug or analgesic abuse, drug allergy or indigestion, or intraoperative lavage of more than 500 ml were excluded from the study. Some 133 patients (83.1 per cent), 66

(81 per cent) of those undergoing laparoscopic fundoplication and 67 (85 per cent) of those having laparoscopic hernia repair, fulfilled the inclusion criteria and were included in the study (Fig. 1).

These patients were randomly assigned to one of three groups by means of sealed envelopes, which were opened in the operating theatre. Patients in group 1 (placebo control) received 50 ml 0.9 per cent saline immediately after creation of a pneumoperitoneum and placement of the first two trocars before fundoplication or hernia repair. Those in group 2 (preoperative LA) received 50 ml 0.5 per cent lidocaine, corresponding to 0.25 mg, before fundoplication or hernia repair. Patients in group 3 (postoperative LA) received 50 ml 0.5 per cent lidocaine after fundoplication or hernia repair.

Surgical technique

All operations were carried out by the same team of surgeons; six surgeons carried out the hernia repairs and three the fundoplications. Standard procedures for laparoscopic inguinal hernia repair and fundoplication

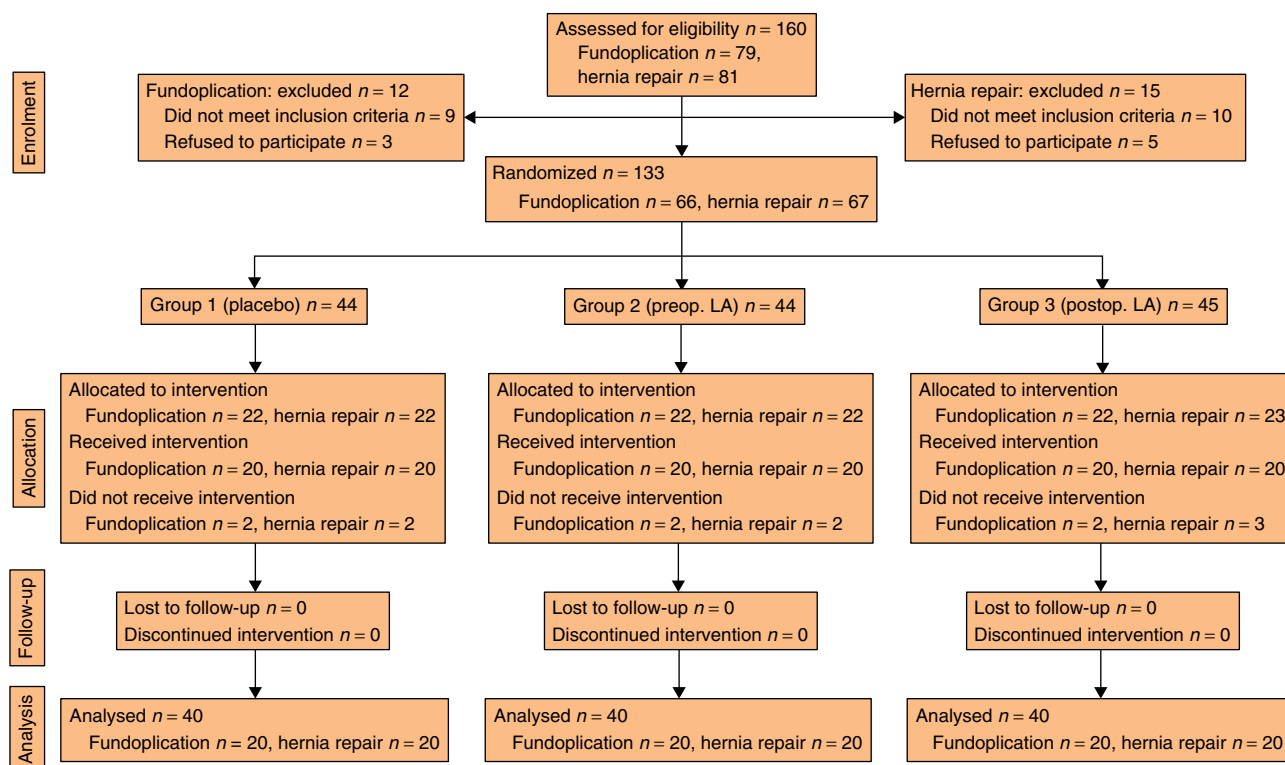
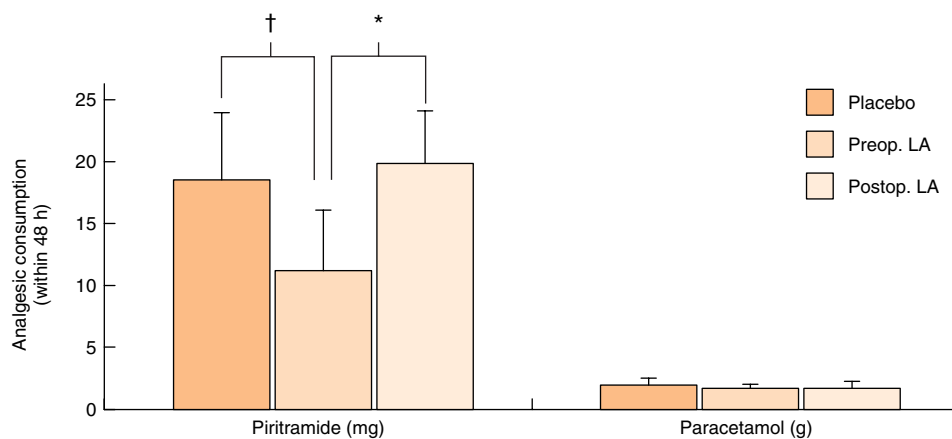
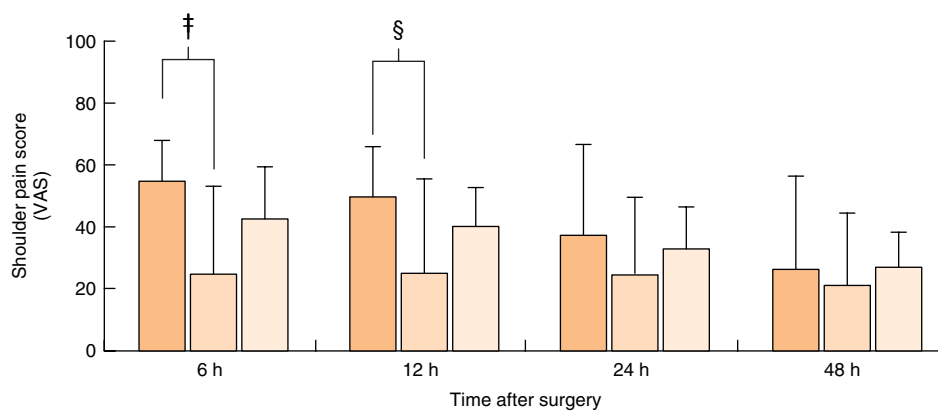


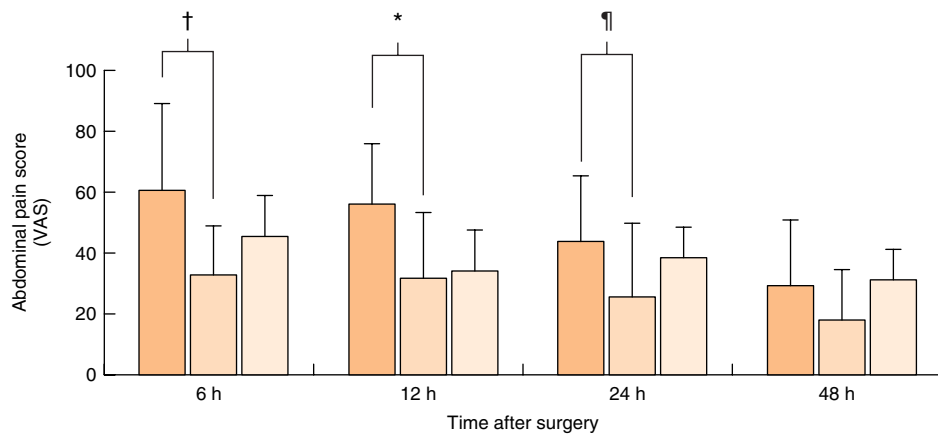
Fig. 1 Trial profile. LA, local anaesthesia



a Analgesic consumption



b Shoulder pain



c Abdominal pain

Fig. 2 Influence of intraperitoneal local anaesthesia. **a** Analgesic consumption, and **b** shoulder pain and **c** abdominal pain scores measured on a visual analogue scale (VAS), after laparoscopic fundoplication. Values are mean(s.d.). LA, local anaesthesia. * $P = 0.002$, † $P = 0.003$, ‡ $P = 0.013$, § $P = 0.014$, ¶ $P = 0.015$ (Kruskal–Wallis test)

Table 1 Patient characteristics

	Fundoplication			Hernia repair		
	Placebo (Group 1)	Preop. LA (Group 2)	Postop. LA (Group 3)	Placebo (Group 1)	Preop. LA (Group 2)	Postop. LA (Group 3)
No. of patients	20	20	20	20	20	20
Sex ratio (M:F)	12:8	14:6	11:9	18:2	20:0	19:1
Age (years)*	50.1 (25–73)	52.7 (27–69)	51.8 (23–81)	55.2 (21–74)	54.4 (31–75)	58.1 (26–79)
Body mass index (kg/m ²)†	25.5(2.3)	24.9(2.3)	26.3(2.1)	26.4(2.7)	25.8(2.5)	25.7(2.9)
Duration of pneumoperitoneum (min)†	67.2(17.1)	71.7(16.3)	69.3(14.8)	43.3(16.2)	51.2(10.2)	51.7(18.2)
Duration of surgery (min)†	79.1(16.9)	85.2(16.5)	81.4(15.4)	53.0(16.3)	61.4(11.0)	63.3(16.0)
Incidence of abdominal pain	20 of 20	20 of 20	20 of 20	18 of 20	16 of 20	19 of 20
Incidence of shoulder pain	18 of 20	15 of 20	20 of 20	7 of 20	8 of 20	7 of 20

*Values are mean (range); †values are mean(s.d.). LA, local anaesthesia.

were used^{11,12}. In all patients access to the peritoneal cavity was established through a 2-cm umbilical incision. A carbon dioxide pneumoperitoneum was created using an insufflation pressure of 12 mmHg and a maximum flow of 2 l/min, which was restricted electronically during creation of the pneumoperitoneum and at later stages of the procedure. Laparoscopic fundoplication was conducted in the lithotomy position in a 20° anti-Trendelenburg position, with the surgeon standing between the patient's legs. Five trocars were inserted into the abdomen between the xiphoid and the umbilicus, at the epiphrenium (each 10 mm), below the left (12 mm) and right (5 mm) costal arch, and on the left side (10 mm). Laparoscopic hernia repair was conducted with the patient in a 20° Trendelenburg position using three periumbilical trocars (12, 10 and 5 mm).

General anaesthesia

All patients received 10 mg diazepam orally approximately 1 h before transfer to the operating room. All operations started between 08.00 and 12.00 hours. Anaesthesia was induced with 4–5 mg/kg intravenous thiopental, 0.1 mg/kg intravenous vecuronium bromide and 15 mg/kg intravenous fentanyl. After tracheal intubation, general anaesthesia was maintained with 0.2–0.3 per cent levoflurane (end-tidal concentration). During surgery, all patients received an intravenous infusion of lactated Ringer's solution at a rate of 5–7 ml per kg per h and 1–2 ml per kg bodyweight during the following 24 h.

Peritoneal topical anaesthesia

In groups 1 and 2, immediately after creation of a pneumoperitoneum and placement of the first two trocars, 50 ml of the appropriate solution (local anaesthetic or

placebo) was sprayed on to the upper surface of the right and left liver lobe such that it would diffuse into the hepatodiaphragmatic space. This was done using a catheter inserted into the second trocar under direct laparoscopic control. In group 3, at the end of the operation and before withdrawing the first trocar, 50 ml solution was sprayed on to the same area as described for the other groups. In all groups, patients were maintained in a 15–20° head-down position for about 2 min after spraying the solution. The surgeon was unaware of the content of the solution (placebo or local anaesthetic).

Outcome measures

The primary endpoint was the consumption of analgesics. Secondary endpoints were the degree of spontaneous postoperative abdominal and shoulder pain, and blood pressure and heart rate.

Before the induction of anaesthesia, patients were given instructions in the use of a 10-cm vertical visual analogue scale (VAS) for measurement of pain; the scale ranged from 0 (no pain) to 100 (worst possible pain). Before surgery patients were informed that they could request postoperative pain relief if required. For postoperative analgesia, patients received 1 g paracetamol immediately after extubation. Additional doses were given for shoulder or abdominal pain at the patient's request. If the patient was not satisfied with the level of analgesia achieved, an additional 3.75 mg piritramide was administered intravenously if the pain was severe (VAS score of 20 or more) or 1 g paracetamol otherwise (score less than 20). The consumption of analgesics (paracetamol and piritramide) was recorded.

The degree of spontaneous postoperative abdominal and shoulder pain was assessed at rest using a VAS at 6, 12, 24 and 48 h after surgery. Blood pressure, heart rate and

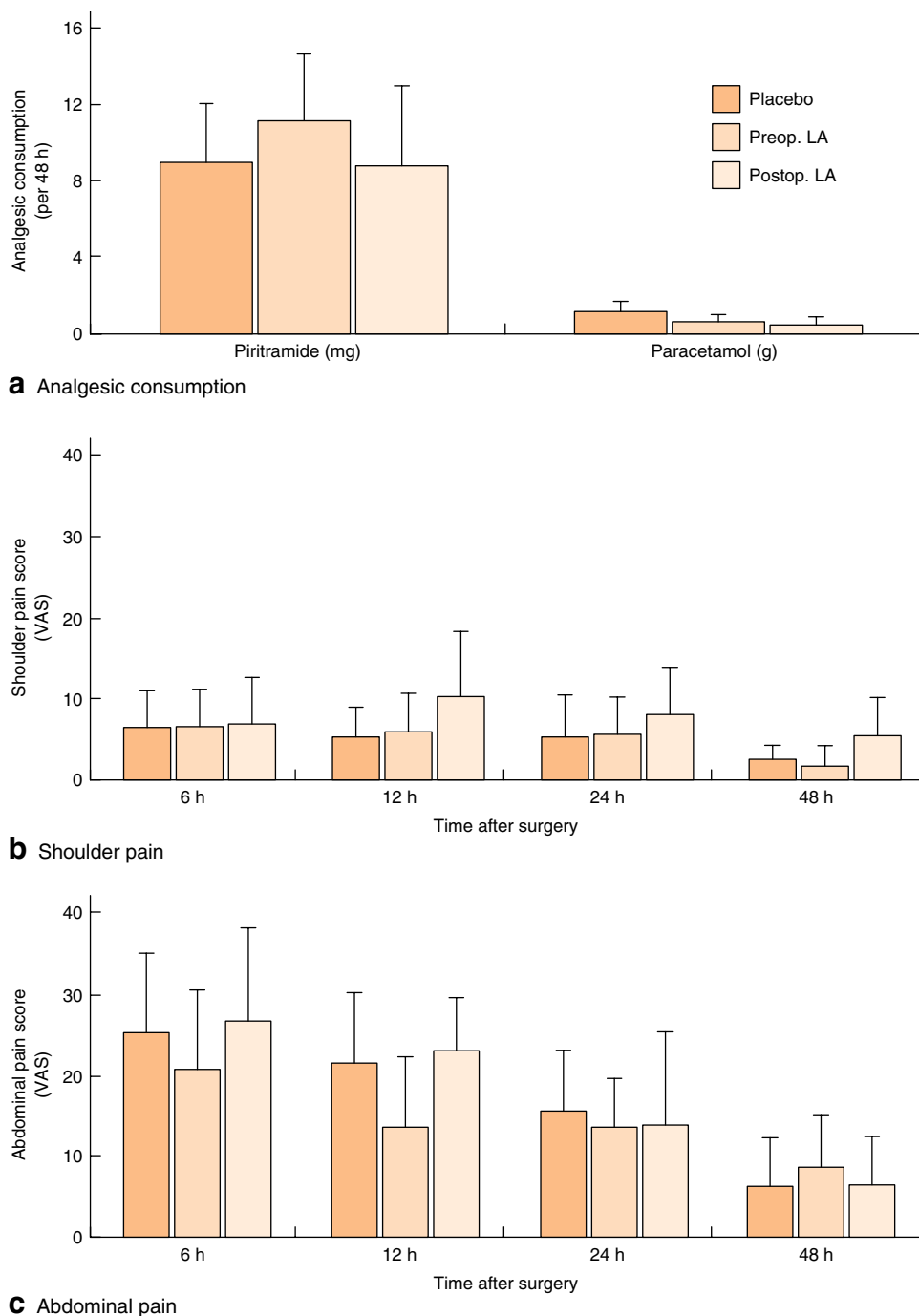


Fig. 3 Influence of intraperitoneal local anaesthesia. **a** Analgesic consumption, and **b** shoulder pain and **c** abdominal pain scores measured on a visual analogue scale (VAS), after laparoscopic hernia repair. Values are mean(s.d.). LA, local anaesthesia

respiratory rate were also monitored. Data collection was carried out by medical staff. Neither the patients nor the medical staff knew the group assignments. Blinding was maintained throughout the procedure and follow-up in all patients.

Statistical analysis

It was calculated that a total of 118 patients would be needed to enable the detection of a 20 per cent difference in analgesic use with a power of 80 per cent. In all groups,

those patients treated in accordance with the protocol were included in the statistical analysis. An intention-to-treat analysis was not performed because all drop-outs were related to predefined intraoperative exclusion criteria.

Data are presented as mean(s.d.) unless indicated otherwise. For group comparisons at each time point, k-independent ANOVA (Kruskal–Wallis test) with consecutive comparison of pairs at $P < 0.050$ was performed. A significant difference was assumed only for time points and group comparisons with $P < 0.0167$ (Bonferroni α error correction). Analgesic consumption was considered as the independent primary variable. Because pain scores were influenced by the application of analgesics according to on-demand management, these values were compared as secondary variables. SPSS version 12.0[®] (SPSS, Chicago, Illinois, USA) was used for statistical analysis.

Results

After randomization, four patients were excluded from group 1, four from group 2 and five from group 3 (Fig. 1). Reasons for exclusion were extended lavage in patients undergoing laparoscopic fundoplication and intraoperative diagnosis of a bilateral hernia in patients having laparoscopic hernia repair. The three groups of patients were well matched in terms of age, weight and body mass index (Table 1).

The overall duration of pneumoperitoneum (mean 69.4(3.2) versus 48.7(14.9) min, $P < 0.01$; median 66 versus 46 min, $P < 0.001$) and of surgery (mean 81.9(16.3) versus 59.2(14.4) min, $P < 0.01$) was significantly higher after fundoplication than after hernia repair. No patient had intraoperative complications that necessitated conversion to open operation.

Analgesic consumption

Control patients (group 1) required larger doses of piritramide after fundoplication than after hernia repair (18.5(5.4) versus 8.9(3.3) mg per 48 h; $P < 0.01$). Pre-emptive application of LA (group 2) significantly reduced the postoperative dose of piritramide (11.1(5.0) versus 18.5(5.4) mg per 48 h; $P = 0.003$), but not of paracetamol, during the 48 h after laparoscopic fundoplication, whereas application of anaesthetic at the end of the operation (group 3) had no effect (Fig. 2). LA administered either before or after surgery had no effect on analgesic consumption in patients undergoing laparoscopic hernia repair (Fig. 3).

Pain scores

Patients scheduled for hernia repair experienced no abdominal or shoulder pain before surgery, whereas four of 60 patients with GORD reported minor abdominal pain (VAS score 10–15) but no shoulder pain.

A comparison of patients who underwent hernia repair and those who had fundoplication showed that the incidence and intensity of shoulder pain (VAS score 42.2(8.8) versus 5.0(1.5); $P < 0.001$) and abdominal pain (VAS score 47.1(3.4) versus 17.3(1.7); $P < 0.001$) was higher after fundoplication than after hernia repair within the first 48 h after operation. Overall pain intensity was greater after laparoscopic fundoplication (median VAS score 46.7 versus 6.5; $P < 0.001$).

Among patients undergoing laparoscopic fundoplication who received the placebo, the maximum intensity of shoulder and abdominal pain was registered at 6 h after surgery, decreasing to half of this level by 48 h. Pre-emptive application of LA reduced overall abdominal pain scores (median 28.6 versus 74.9 in placebo group; $P < 0.005$) and shoulder pain scores (median 24.3 versus 43.8; $P = 0.004$) after laparoscopic fundoplication. In particular, significant differences were noted in abdominal pain after 6 h ($P = 0.003$), 12 h ($P = 0.002$) and 24 h ($P = 0.015$) after surgery, and in shoulder pain at 6 h ($P = 0.013$) and 12 h ($P = 0.014$) (Fig. 2). By contrast, patients receiving LA at the end of the operation showed no significant difference in postoperative abdominal or shoulder pain compared with placebo controls.

Patients undergoing laparoscopic hernia repair with placebo experienced the maximum shoulder and abdominal pain intensity 6 h after operation, and showed a continuous pain reduction down to 40 per cent (shoulder pain) and 25 per cent (abdominal pain) after 48 h. LA administered either before or after surgery had no effect on shoulder or abdominal pain intensity (Fig. 3).

Arterial blood pressure and heart rate

There were no significant differences in systolic and diastolic arterial pressures or heart rate between the groups (data not shown).

Discussion

This study demonstrated that patients having laparoscopic fundoplication experienced significantly more abdominal and shoulder pain after operation than those undergoing hernia repair, and that this might be related to the longer duration of pneumoperitoneum needed for fundoplication. Pre-emptive administration of LA resulted in reduced

postoperative analgesic consumption and lower pain intensity after fundoplication, but such effects were not seen with local anaesthetic administered at the end of operation or in patients who underwent laparoscopic hernia repair.

The origin of pain after laparoscopy is multifactorial. Pain after laparoscopy can be differentiated into abdominal pain and shoulder pain⁶. The exact reasons for such pain are still unknown. Besides the underlying disease, wound pain arising from the port sites, the surgical procedure and the pneumoperitoneum itself may contribute to abdominal pain. Peritoneal biopsies taken after laparoscopy show peritoneal inflammation, capillary rupture and neuronal rupture¹³. Chemical irritation, intraperitoneal acidosis, mucosal ischaemia and compression of the splanchnic nerve as a result of the pneumoperitoneum may also be contributory factors^{14–16}. Shoulder pain after laparoscopy is attributed to stretching of subdiaphragmatic fibres of the phrenic nerve by the increased concavity of the diaphragm, which is induced by the pneumoperitoneum and the resulting loss of visceral surface tension¹⁷.

The present study showed a potential relationship between the incidence of shoulder pain and the duration of pneumoperitoneum, as shoulder pain intensity was significantly greater after laparoscopic fundoplication than hernia repair, and fundoplication required a longer period of pneumoperitoneum. There are several other possible explanations for the greater pain intensity after fundoplication. First, postoperative pain intensity correlates with the preoperative pain level¹⁸ and more patients with GORD reported preoperative pain in this series. Second, the longer duration of operation and the resulting volume of insufflated gas¹⁹, and greater size and number of trocars used^{20,21}, might have contributed to the increased pain after fundoplication. Finally, the sex distribution might influence pain scores¹⁸ and a larger number of women underwent fundoplication than hernia repair in this series.

The rationale for using intraperitoneal LA in laparoscopic surgery is that the anaesthetic inhibits nociception by affecting nerve membrane-associated proteins, and by inhibiting the release and action of prostaglandins and other agents that sensitize or stimulate the nociceptors and contribute to inflammation²². Previous studies have provided conflicting data on the benefit of intraperitoneal LA after laparoscopy. Approximately half of the available studies have shown some benefit in terms of pain reduction after laparoscopic cholecystectomy, whereas the gynaecological literature has shown significant relief of pain by intraperitoneal application of LA³. Weaknesses in study design, and variation in timing and sites of administration

of anaesthetic may have contributed to the contradictory results.

The present randomized clinical trial was designed to overcome some of the shortfalls of previous studies. The effect and timing of administration of intraperitoneal LA on pain after two different laparoscopic procedures was examined. Postoperative pain was evaluated blindly using a VAS, which is thought to be more sensitive for the detection of small differences in pain levels than a verbal rating scale^{3,23}. Abdominal pain is most intense within the first 24 h after laparoscopy and shoulder pain often occurs as a second peak of pain on the second day after laparoscopy^{2,3,6,24}. Patients were therefore monitored for 48 h after operation in this study, although shoulder and abdominal pain actually peaked at 6 h. Piritramide and paracetamol, administered according to patient demand, were chosen for postoperative analgesia instead of non-steroidal anti-inflammatory drugs, which have been associated with the development of acute renal failure after laparoscopy owing to reduced renal blood flow during pneumoperitoneum^{3,25,26}. However, despite on-demand analgesic management, patients who received placebo in the fundoplication group especially had severe pain for up to 24 h after surgery. Other studies have demonstrated the beneficial effect of non-steroidal anti-inflammatory drugs administered periodically after surgery²⁷, and it is clear that further evaluation of different regimens for postoperative analgesia in combination with pre-emptive local anaesthesia is needed in order to optimize pain management after laparoscopic surgery.

Lidocaine was used as the local anaesthetic, because of its relatively slow rate of adsorption from the peritoneal cavity and its negligible side-effects at the dose used²⁸. Lidocaine was only effective in lowering postoperative pain and the consumption of analgesics if administered immediately after creation of the pneumoperitoneum and before starting dissection. This finding is consistent with the theory that an afferent block is achieved after preoperative administration of LA before nociceptive stimuli can modify the behavioural response and neuronal sensitization of posterior horn neurones^{10,13}. Application of LA at the end of surgery was ineffective as it did not pre-empt the trauma of surgery. It has been suggested that the application of saline alone may also reduce postoperative pain by restoration of visceral surface tension and dilution of the localized peritoneal acidosis after carbon dioxide pneumoperitoneum¹⁷, but this was not the case in the present study.

Although the differences in analgesic use and pain scores were relatively modest, this randomized double-blind study has shown that preoperative administration

of LA can significantly reduce analgesic requirements and postoperative pain in patients undergoing operations with long-lasting pneumoperitoneum, such as laparoscopic fundoplication. The results concur with those of another recent study that demonstrated the value of pre-emptive local analgesia in laparoscopic cholecystectomy using bupivacaine injection²⁷.

References

- Eypasch E, Sauerland S, Lefering R, Neugebauer EA. Laparoscopic versus open appendectomy: between evidence and common sense. *Dig Surg* 2002; **19**: 518–522.
- Ekstein P, Szold A, Sagie B, Werbin N, Klausner JM, Weinbroum AA. Laparoscopic surgery may be associated with severe pain and high analgesia requirements in the immediate postoperative period. *Ann Surg* 2006; **243**: 41–46.
- Slim K. Pain after laparoscopic cholecystectomy. *Br J Surg* 2000; **87**: 1249.
- Alexander JL. Pain after laparoscopy. *Br J Anaesth* 1997; **79**: 369–378.
- Cunniffe MG, McAnena OJ, Dar MA, Callearly 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.
- Joris J, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy: characteristics and effect of intraperitoneal bupivacaine. *Anesth Analg* 1995; **81**: 379–384.
- Hernandez-Palazon J, Tortosa JA, Nuno de la Rosa V, Gimenez-Viudes J, Ramirez G, Robles R. Intraperitoneal application of bupivacaine plus morphine for pain relief after laparoscopic cholecystectomy. *Eur J Anaesthesiol* 2003; **20**: 891–896.
- Mraovic B, Jurisic T, Kogler-Majeric V, Sustic A. Intraperitoneal bupivacaine for analgesia after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 1997; **41**: 193–196.
- Maestroni U, Sortini D, Devito C, Pour Morad Kohan Brunaldi F, Anania G, Pavanelli L *et al.* A new method of preemptive analgesia in laparoscopic cholecystectomy. *Surg Endosc* 2002; **16**: 1336–1340.
- Pasqualucci A, de Angelis V, Contardo R, Colo F, Terrosu G, Donini A *et al.* Preemptive analgesia: intraperitoneal local anesthetic in laparoscopic cholecystectomy. A randomized, double-blind, placebo-controlled study. *Anesthesiology* 1996; **85**: 11–20.
- Horstmann R, Classen C, Rottgermann S, Langer M, Palmes D. Long-term experience of treating 185 patients with gastroesophageal reflux disease (GERD) by anti-reflux surgery respecting the functional-morphological restoration of the esophagus. *Langenbecks Arch Surg* 2006; **391**: 24–31.
- Horstmann R, Hellwig M, Classen C, Rottgermann S, Palmes D. Impact of polypropylene amount on functional outcome and quality of life after inguinal hernia repair by the TAPP procedure using pure, mixed, and titanium-coated meshes. *World J Surg* 2006; **30**: 1742–1749.
- Woolf CJ, Mannion RJ. Neuropathic pain: aetiology, symptoms, mechanisms, and management. *Lancet* 1999; **353**: 1959–1964.
- Volz J, Koster S, Weiss M, Schmidt R, Urbaschek R, Melchert F *et al.* Pathophysiologic features of a pneumoperitoneum at laparoscopy: a swine model. *Am J Obstet Gynecol* 1996; **174**: 132–140.
- Windsor MA, Bonham MJ, Rumball M. Splanchnic mucosal ischemia: an unrecognized consequence of routine pneumoperitoneum. *Surg Laparosc Endosc* 1997; **7**: 480–482.
- Neuhaus SJ, Watson DI. Pneumoperitoneum and peritoneal surface changes: a review. *Surg Endosc* 2004; **18**: 1316–1322.
- Tsimoyiannis EC, Glantzounis G, Lekkas ET, Siakas P, Jabarin M, Tzourou H. Intraperitoneal normal saline and bupivacaine infusion for reduction of postoperative pain after laparoscopic cholecystectomy. *Surg Laparosc Endosc* 1998; **8**: 416–420.
- Ure BM, Troidl H, Spangenberg W, Dietrich A, Lefering R, Neugebauer E. Pain after laparoscopic cholecystectomy. Intensity and localization of pain and analysis of predictors in preoperative symptoms and intraoperative events. *Surg Endosc* 1994; **8**: 90–96.
- Korell M, Schmaus F, Strowitzki T, Schneeweiss SG, Hepp H. Pain intensity following laparoscopy. *Surg Laparosc Endosc* 1996; **6**: 375–379.
- Kehlet H, Gray AW, Bonnet F, Camu F, Fischer HB, McCloy RF *et al.* A procedure-specific systematic review and consensus recommendations for postoperative analgesia following laparoscopic cholecystectomy. *Surg Endosc* 2005; **19**: 1396–1415.
- Prospect. Procedure specific postoperative pain management. <http://www.postoppain.org> [accessed 15 Oct 2006].
- Louizos AA, Hadzilia SJ, Leandros E, Kouroukli IK, Georgiou LG, Bramis JP. Postoperative pain relief after laparoscopic cholecystectomy: a placebo-controlled double-blind randomized trial of preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25%. *Surg Endosc* 2005; **19**: 1503–1506.
- Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. *Pain* 1986; **27**: 117–126.
- Jorgensen JO, Gillies RB, Hunt DR, Caplehorn JR, Lumley T. A simple and effective way to reduce postoperative pain after laparoscopic cholecystectomy. *Aust N Z J Surg* 1995; **65**: 466–469.
- Koivusalo AM, Kellokumpu I, Ristkari S, Lindgren L. Splanchnic and renal deterioration during and after laparoscopic cholecystectomy: a comparison of the carbon dioxide pneumoperitoneum and the abdominal wall lift method. *Anesth Analg* 1997; **85**: 886–891.

- 26 Feldman HI, Kinman JL, Berlin JA, Hennessy S, Kimmel SE, Farrar J *et al.* Parenteral ketorolac: the risk for acute renal failure. *Ann Intern Med* 1997; **126**: 193–199.
- 27 Barczynski M, Konturek A, Herman RM. Superiority of preemptive analgesia with intraperitoneal instillation of bupivacaine before rather than after the creation of

- pneumoperitoneum for laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study. *Surg Endosc* 2006; **20**: 1088–1093.
- 28 Narchi P, Benhamou D, Fernandez H. Intraperitoneal local anaesthetic for shoulder pain after day-case laparoscopy. *Lancet* 1991; **338**: 1569–1570.