Original Article

Use of intraoperative mild hyperventilation to decrease the incidence of postoperative shoulder pain after laparoscopic gastric sleeve surgery: A prospective randomised controlled study

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ABSTRACT

Background and Aims: Post-laparoscopic shoulder pain (PLSP) is a common problem. It is a referred type of pain resulting from irritation of phrenic nerve endings. Multiple manoeuvres were used to decrease its incidence with varying success rates. In this study, we tested the use of mild intraoperative hyperventilation to reduce PLSP in patients undergoing laparoscopic sleeve gastrectomy surgery (LSG). **Methods:** Consenting American Society of Anesthesiologists-I and II patients undergoing LSG under general anaesthesia were randomly assigned to two groups. Group A (53 patients) received intraoperative mild hyperventilation with target end-tidal carbon dioxide ($ETCO_2$) of 30–32 mmHg. Group B (51 patients) received conventional ventilation ($ETCO_2$ of 35–40 mmHg). Incidence and severity of PLSP, cumulative analgesic requirements and incidence of nausea and vomiting were recorded at 12 and 24 hours postoperatively and then followed up after discharge over the phone at 48 hours, 1 week, 1 month and 3 months. Statistical significance of differences between the two groups was defined at $P < 0.05$. **Results:** Incidence of PLSP was comparable between the two groups in the first 24 hours. The intervention group had a significantly lower incidence of PLSP throughout the remaining assessment points (56.6% vs. 80.4%, 30.2% vs. 78.4%, 15.1% vs. 70.6%, 3.8% vs. 35.3% at 36 hours, 48 hours, 1 week and 1 month, respectively, $P < 0.05$). The average PLSP pain score was significantly lower in the mild hyperventilation group at all assessment time points. Nausea and vomiting were non-significantly lower in the mild hyperventilation group. **Conclusion:** Mild intraoperative hyperventilation could be beneficial in reducing the incidence and severity of PLSP after LSG surgery.

Key words: Bariatric surgery, hyperventilation, laparoscopy, pain, shoulder

INTRODUCTION

Post-laparoscopy shoulder pain (PLSP) was first reported by gynaecologic surgeons in 1976.[1] Since then, laparoscopists have recognised it as a common patient complaint with an estimated incidence between 35% and 80%.[2] This postoperative pain can be more disturbing to the patient than the surgical site pain itself.

Almost all suggested theories explaining the pathophysiology of PLSP revolved around the belief that SP is a referred type of pain resulting from nociceptive stimulation to diaphragmatic surfaces during laparoscopy involving the C4 dermatome.

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Several methods were introduced and tested to decrease the incidence and severity of PLSP based on the suggested pathophysiologic mechanisms, with varying degrees of success. Some of these methods targeted the gas insufflation process itself by using low intra-abdominal gas pressures, slow rates of gas insufflation, use of warmed gas, and the use of gasless laparoscopy. Other interventions dealt with the pain signal itself by suppressing its initiation using anti-inflammatory medications, or blocking its transmission either locally by applying a local anaesthetic solution to the diaphragmatic surface or by using intrathecal and intraperitoneal clonidine.[3,4] Expelling the remaining intra-abdominal gas at the end of laparoscopy by active suction, or applying pulmonary recruitment manoeuvres, are also used to decrease its proposed irritating effect on the diaphragm.[5]

We hypothesised that lowering the plasma concentration of carbon dioxide during laparoscopy will reduce the incidence and severity of PLSP by reducing the concentration of carbonic acid in the diaphragmatic tissue and consequently decrease its irritation and possible sensitisation of diaphragmatic nerve endings. We tested the validity of our theory in patients undergoing laparoscopic sleeve gastrectomy (LSG). The primary aim of our study was to evaluate the effect of mild hyperventilation on the incidence and severity of PLSP compared to conventional ventilation. The secondary outcomes measured were any effects of the study intervention on the incidence of postoperative nausea and vomiting, duration of recovery and overall hospital stay.

METHODS

This prospective randomised, single-blinded study was conducted between June 2019 and February 2020 at a tertiary university teaching hospital in Irbid, Jordan. Approval of study and its protocol was obtained from institutional review board committee (#56/124/2019) on 10/06/2019. The study was registered at ClinicalTrials.gov registry database (#NCT04514887).

Patients with American Society of Anesthesiologists-I and II physical status undergoing LSG surgery were systematically approached for participation. Exclusion criteria included mentally incapacitated patients, patients with respiratory problems, patients who had previous abdominal surgery and those who received analgesic treatment in the last 24 hours before surgery. Informed consent was obtained from all participants and the study was performed following the guidelines of the Declaration of Helsinki. Qualified consenting patients were randomly assigned using a coin-tossing method to two study groups. Group A received mild intraoperative hyperventilation with a target intraoperative end-tidal carbon dioxide ($ETCO_2$) value of 30–32 mmHg and group B received traditional intraoperative ventilation with target $ETCO_2$ of 35–40 mmHg. The $ETCO_2$ values in the intervention group were chosen based on previous clinical safe use and were low enough not to intersect with normal $ETCO_2$ values. Only prime investigator who carried out the study intervention was made aware of the coin face coding of the study group.

The same bariatric surgeon performed surgery for all patients using the same five-trocar laparoscopic technique (three 5-mm, one 12-mm and one 10-mm). Carbon dioxide gas was insufflated using an open technique method. An initial gas flow rate of 3 L/min was raised gradually until a target pneumoperitoneum of 15 mmHg was reached. The gas flow required to maintain the target pressure was regulated through a high-flow gas insufflator without heating or humidification of insufflated gas. At the end of the surgery, pneumoperitoneum gas was allowed to move outside, assisted by manual abdominal compression. Active suctioning of the peritoneal cavity trocar sites was used in an attempt to expel any residual gas.

All patients received a premedication regimen of oral diazepam 10 mg and intravenous (i.v.) omeprazole 100 mg, given 2 hours before operation. After establishing routine monitoring and ensuring stable vital signs, patients were pre-oxygenated for 3 min and anaesthesia was induced with i.v. propofol 2 mg/kg and fentanyl 2 μg/kg. Oro-tracheal intubation was facilitated by rocuronium 0.6 mg/kg and anaesthesia was maintained with isoflurane in oxygen/air mixture. Volume-controlled ventilation was used in all patients with a tidal volume of 10 ml/kg of ideal body weight. In the hyperventilated group (group A), each patient's respiratory rate was increased until ETCO2 readings were lying in the range of 30–32 mmHg. In the traditionally ventilated group (group B), the respiratory frequency was adjusted to maintain ETCO2 values in the range of 35–40 mmHg.

Duration of anaesthesia, surgery, pneumoperitoneum and total gas consumption were recorded. Peak

airway pressure was maintained under an upper alarm point of 25 cm H_2O. Postoperative analgesia was as per our surgical team routine and consisted of morphine 5 mg i.v. when needed, with a 6-hour minimum dosing interval, and paracetamol 1 gm i.v. (or orally after resuming oral intake) when needed, with a 6-hour minimum dosing interval. A research team member (HH) who was unaware of the patient's group assignment did the assessment and recording of shoulder pain scores. Pain assessment was carried out at 12 and 24-hour postoperative time points. If their answer was yes, they were asked to quantify its severity on a verbal scale of 10, where zero represented no pain and 10 the worst experienced pain ever. The total rescue morphine and paracetamol requirements were recorded at these time points. Patients with uneventful surgeries were discharged from the hospital on the first postoperative day. They were contacted over the phone and asked the same questions at 2 days, 1 week, 1 month and 3 months postoperatively, and the total paracetamol consumption was recorded too.

We considered a 50% reduction in the incidence of SP to be clinically relevant. Based on previous literature, we estimated the current incidence of SP to be about 60%, and consequently, a minimum sample size of 42 patients in each group was considered adequate for enrolment.

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) Version 24.0. (Armonk, NY: International Business Machines Corp). Descriptive statistics were used to summarise demographic data using frequencies and percentages for categorical variables and mean ± standard deviation (SD) for continuous ones. Results of pain scores were summarised using median (interquartile range). The Chi-square (X^2) test was used to compare categorical variables whereas the Independent Samples *t*-test and Mann–Whitney U test were used to compare scale and categorical variables as appropriate. A *P* value of less than 0.05 was considered significant.

RESULTS

One hundred and six patients were approached for participation. Two patients declined, and 104 consenting patients were randomised into the two study groups. Fifty-three patients were enroled in Group A and 51 in group B. Follow-up was completed for all enroled patients with no post-enrolment dropouts or exclusions [Figure 1]. Basic patient demographic characteristics, duration of surgery, CO_2 pressure and gas flow used to create pneumoperitoneum were also comparable between the two study groups [Table 1].

About 80% of our study patients suffered from PLSP at one point of observation or another. This incidence was comparable in both intervention and control groups (77.4% vs. 82.4, respectively, $P = 0.526$). The shoulder pain started on the day of operation in 80 patients. Left-sided PLSP predominated over right and bilateral PLSP at all observation time points, with all patients who suffered from PLSP reporting positional change in its intensity [Table 2].

The incidence of PLSP at each time point with the corresponding average pain scores was noted [Table 3]. A significant decrease in the incidence of PLSP was observed at 36 hours' time point compared to the control group, which persisted for 1 month. However, no PLSP was reported in either of the groups at the 3-month observation point.

Pain scores were significantly lower in the intervention group compared to the control group at the 12-hour time point and continued to be so for 1 month [Table 4]. Paracetamol consumption was comparable between the two groups at 12- and 24-hour postoperative time points. This was followed by a significantly lower paracetamol consumption in the intervention group at all remaining time intervals ($P < 0.001$) [Figure 2].

Despite a lower incidence of postoperative nausea and vomiting (PONV) in the intervention group, it did not reach statistical significance at any of the observation points. No incidence of lung injury was reported in any patient. None of the patients in both groups had delayed recovery and all patients were discharged home on the first postoperative day.

DISCUSSION

Reduced postoperative pain is one of the great advantages of laparoscopic over open surgery, and this leads to a smoother recovery and earlier discharge from hospital.[2,6] Since the early days of laparoscopy, the special complaint of PLSP emerged as a concerning issue that could be more distressing to the patient than the surgical site itself. Although this type of postoperative shoulder pain is reported after open abdominal surgery, its higher incidence and severity after laparoscopic surgery indicates that another nociceptive burden was incurred by the laparoscopic approach itself.[2]

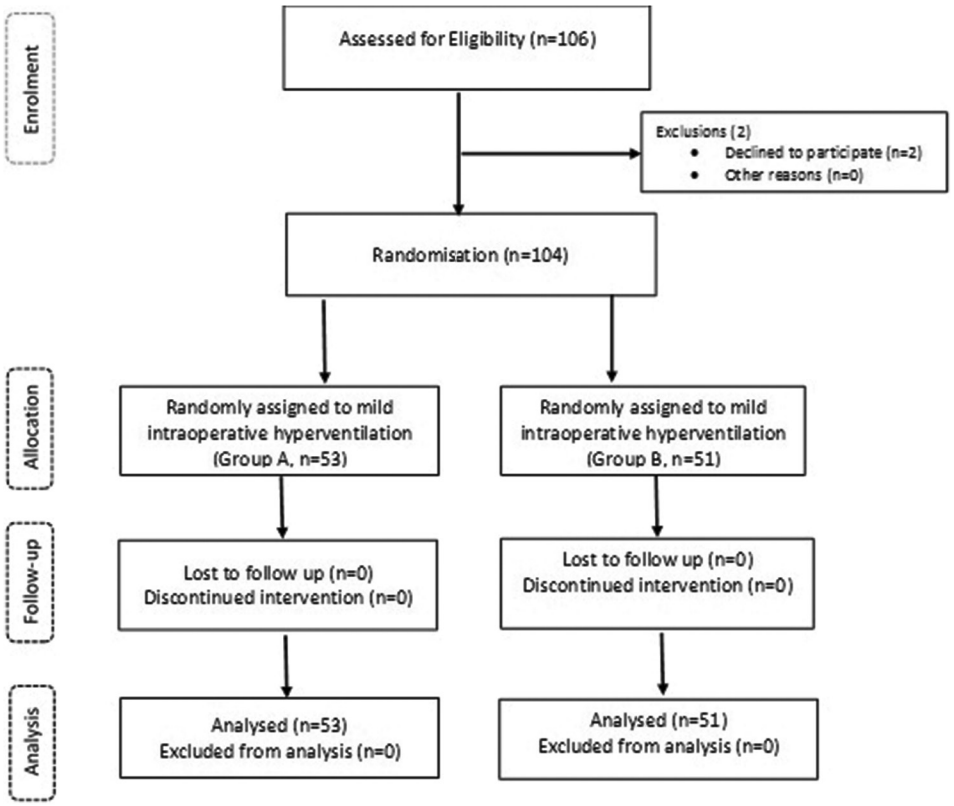

Figure 1: Flow diagram of patients' enrolment, randomisation, and follow-up

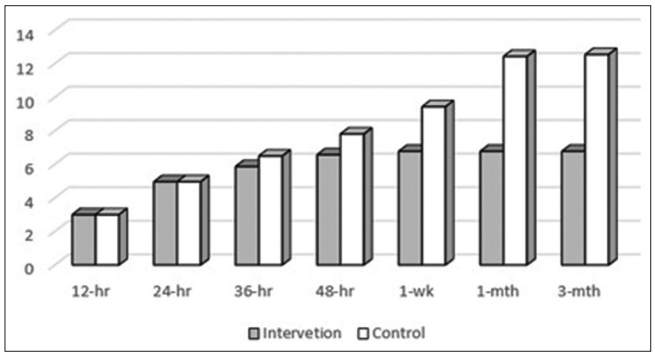

Figure 2: Cumulative paracetamol consumption (gm) by study patients

Table 1: Patient demographics and operative characteristics

Variable	Group A (*n*=53)	Group B (*n*=51)	*P*
Gender (M/F)	8/45	7/44	0.843
Age (years)	32.9 (7.6)	31.5 (9.1)	0.422
Weight (kg)	124.0 (18.9)	128.4 (17.7)	0.336
Height (cm)	164.1 (8.7)	164.3 (7.7)	0.901
Body Mass Index (kg/m^2)	46.4 (6.2)	47.4 (3.8)	0.335
Duration of surgery (min)	36.4 (8.3)	39.3 (8.0)	0.066
CO_2 pressure (cmH_2O)	14.9	15	0.329
CO_2 flow (L/min)	34.2 (4.9)	36.0 (5.3)	0.072
Respiratory rate	12-16 (14)	7-11 (9)	

Values are expressed as mean (standard deviation) or range (median).
n: number, M: Male, F: Female

The diversity of methods used to treat PLSP reflects both a multifactorial nature of its underlying mechanism and its significance as an annoying postoperative symptom. In this study, we introduced a novel method of targeting this pain at the initiation point of its course, addressing one of its most commonly accepted underlying mechanisms—carbon dioxide irritation of the diaphragm.[7]

Our study results showed a high incidence (80%) of PLSP in this group of bariatric patients undergoing LSG surgery. Dixon *et al*.[8] reported a lower PLSP incidence of 66% in bariatric patients undergoing gastric banding. Phelps *et al*.,[9] however, reported higher PLSP incidence of 83% in patients undergoing gynaecological laparoscopic surgeries. One study identified lower weight as the only one among other factors to correlate with PLSP significantly.[10] When all the above are taken together, we can assume that the high incidence of PLSP observed in our study resulted from the location of surgical intervention, as surgery in the region of the gastro-oesophageal junction is assumed to be associated with a higher incidence of shoulder pain.[8]

Table 2: Incidence of postoperative pain according to site during study period

Site of pain	12 h	24 h	36 h	48 h	72 h	1 month	3 months
Right Shoulder	34 (32.7)	35 (33.7)	32 (30.8)	25 (24.1)	19 (18.3)	6 (5.8)	0
Left shoulder	45 (43.3)	44 (42.4)	42 (40.4)	31 (29.9)	25 (24.1)	14 (13.5)	0
Both shoulders	2 (1.9)	1 (0.96)	0	0	0	0	0
Incision	3 (2.89)	3 (2.89)	0	0	0	0	0
No pain	20 (19.3)	21 (20.2)	30 (28.9)	48 (46.2)	60 (57.7)	84 (80.8)	104 (100)

Values are frequencies (percentage from total number of patients)

Table 3: The incidence of shoulder tip pain among patients at different time points during the study period

Time point after operation	Group A (*n*=53)	Group B (*n*=51)	Chi-square statistic (degrees of freedom)	*P*
12 hours	38 (71.7%)	41 (80.4%)	1.08 (1)	0.362
24 hours	39 (73.6%)	41 (80.4%)	0.68 (1)	0.488
36 hours	30 (56.6%)	41 (80.4%)	6.79 (1)	0.012
48 hours	16 (30.2%)	39 (76.5%)	22.34 (1)	<0.001
1 week	8 (15.1%)	36 (70.6%)	32.79 (1)	<0.001
1 month	2 (3.8%)	18 (35.3%)	16.63 (1)	<0.001
3 months	0 (0%)	0		

Values are frequencies (percentage within group), *n*: number

Table 4: The median scores (on a numerical scale of 10) of shoulder tip pain reported by study patients at the different observation time points

Time point after operation	Group A (*n*=53)	Group B (*n*=51)	*P*
12 hours	4.00 (3)	7.00 (1)	<0.001
24 hours	3.00 (2)	6.00 (2)	<0.001
36 hours	2.00 (3)	5.00 (8)	<0.001
48 hours	0.00 (2)	4.00 (2)	<0.001
1 week	0.00 (0)	3.00 (4)	<0.001
1 month	0.00 (0)	0.00 (2)	<0.001
3 months	0.00 (0)	0.00 (0)	-

Values are expressed as Median (Interquartile range), *n*: number

Our study showed that mild intraoperative hyperventilation effectively decreased the incidence and severity of PLSP. The effect of our study intervention on PLSP severity was earlier than its effect on PLSP incidence (12-hour vs. 36-hour time points, respectively). This discrepancy can be explained by the multifactorial nature of PLSP, where factors other than CO_2 irritation are still active in the immediate postoperative period. The lower consumption of paracetamol analgesia in the intervention group further signifies the beneficial effect of this intervention.

Techniques used in prevention of PLSP or in reducing its incidence are based on reducing either or both the chemical or physical irritation of diaphragmatic surface. The first is achieved through decreasing the amount of CO_2 in the peritoneal cavity at the end of surgery by expelling the remaining intra-abdominal gas using passive drainage or active suctioning,[11] or through applying pulmonary recruitment manoeuvres that push the gas out through the open laparoscopic holes.[12] Reduction of physical irritation can be achieved by using gas warming,[13] low pneumoperitoneal pressures, low gas insufflation rates,[14] or even use of gasless laparoscopy.[15] Moreover, other interventions dealt with the pain signal itself by suppressing its initiation using anti-inflammatory medications,[16] blocking its transmission by applying a local anaesthetic solution to the diaphragmatic surface at the end or beginning of surgery,[17-19] intraperitoneal instillation of additional dexmedetomidine or clonidine along with bupivacaine,[20] use of intraperitoneal hydrocortisone[21] or use of intrathecal clonidine.[22] The use of low-pressure laparoscopy provides a decrease in both physical and chemical irritation inputs and this explains the suggestion by Donatsky *et al*.[3] that it is the most effective strategy in decreasing the incidence of PLSP. In this context, our study introduces a new method of decreasing diaphragmatic irritation by CO_2. By the anticipated decrease in the concentration of the intermediate CO_2 metabolite of carbonic acid using mild intraoperative hyperventilation, our method seemed to successfully reduce the incidence and severity of PLSP.

The lack of a statistically significant difference in the incidence of PONV between both groups is consistent with the findings of Son and colleagues. The authors did not find an effect of different levels of $PaCO_2$ on the incidence of PONV.[23] The trend of lower incidence of PONV in our intervention group is likely due to the lower incidence and severity of pain in this group, a factor well-known for causing PONV.[24]

Our study can be criticised for the lack of a direct objective method of measuring tissue concentration of

carbonic acid and/or pH that provides a quantitative measurement of the effect of the intervention on tissue acid–base status. Unfortunately, none of these methods is available in our institution. Although $ETCO_2$ level provides an indirect indication of tissue acid–base status, the actual tissue carbonic acid level could be affected by other metabolic factors. Severe acute hypocapnia resulting from hyperventilation can result in a shift in the oxygen–haemoglobin dissociation curve and reduced oxygen delivery, cerebral vasoconstriction, hypocalcaemia or coronary vasospasm,[25,26] however, mild levels of hypocapnia are not expected to cause serious clinical effects.[27] In our study, we enroled patients with healthy lungs where the arterial-end tidal gradient of carbon dioxide is expected to be about 2–5 mmHg.[28] Accordingly, a $PaCO_2$ tension of 33–37 mmHg is anticipated in patients enroled in the intervention group in our study. This range closely resembles the 30–35 mmHg $PaCO_2$ by prehospital ventilation found to be associated with the lowest mortality in patients with traumatic brain injury compared to higher and lower ranges.[29] A preoperative baseline arterial blood gas analysis to rule out any pre-existing physiological derangements in the lung function would have been a good asset in the study design that we unfortunately missed doing. Coin tossing may not be the ideal randomisation method, however, we chose it because of its simplicity. Although most literature states that PLSP lasts no longer than 3 days, we followed our patients for 3 months especially as PLSP was not studied before in similar bariatric surgery patients. Other types of pain like upper abdominal pain by the locally sequestered CO_2 between the diaphragm and liver were not assessed in our study wherein we focused only on shoulder pain.

In summary, we have proposed and tested a new clinical method to decrease the incidence of PLSP in patients undergoing LSG using mild intraoperative hyperventilation. The effect of this method is assumed to be through the resulting decrease in tissue level of carbonic acid proposed to be responsible for phrenic nerve irritation.

CONCLUSIONS

We found that mild intraoperative hyperventilation as described in our study reduced the incidence and severity of PLSP after LSG compared with traditional ventilation. These results support the hypothesis of CO_2-mediated irritation of the phrenic nerve as the underlying cause of shoulder tip referred pain. Further similar studies, preferably with quantitative measurement of tissue pH and/or carbonic acid concentration, are recommended to test for reproducibility of our results in different types of laparoscopic surgeries.

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Conflicts of interest

There are no conflicts of interest.

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