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EFFICACY OF INTRAPERITONEAL BUPIVACAINE INSTILLATION FOR POSTOPERATIVE PAIN CONTROL: A QUALITY IMPROVEMENT STUDY

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ABSTRACT

Laparoscopic surgery is associated with better pain experience, reduced Length of Hospital Stay and better scar. However, the resulting postoperative pain is distinct and can be disturbing, hence the need for multimodal analgesia. The side effects of parenteral analgesics and low practice of regional anaesthesia has limited their role in multimodal analgesia. Therefore, strategies that limit the reliance on these pain control modalities will be beneficial. Our study evaluated the efficacy of intraperitoneal instillation of plain bupivacaine after laparoscopic surgeries. The double blinded randomized study enrolled 50 consenting patients who fulfilled recruitment criteria. The bupivacaine group received 20mls of 0.25% plain Bupivacaine while the saline group received 20mls normal saline instillation into the peritoneal cavity via the umbilical port of the laparoscopy device. Visual Analogue Scale (VAS) was assessed at presentation at the Post anaesthesia care unit (PACU) and at 4, 8, 12, 16, 20, 24 hours afterward. In addition, the interval between end of surgery, first request for analgesia and total analgesic requirements were recorded. The VAS at presentation was significantly lower in the Bupivacaine group compared to the saline group, however, there was no statistically significant difference at other times. In addition, there was a significant difference in time to first analgesic request in both groups. The only observed post operative complications were nausea and vomiting. Intraperitoneal Instillation of Bupivacaine is an easy, non-invasive, cheaper and safer method of pain control following laparoscopic surgery in carefully selected patients.

Keywords: Intraperitoneal Bupivacaine, Laparoscopy, Pain management, Bupivacaine instillation, Multimodal analgesia

INTRODUCTION

Laparoscopic or minimally invasive procedures are popular for abdominal surgeries because of better postoperative pain experience, reduced length of hospital stay (LOS) and better scar, and reduces the consequences of inadequate pain control(Ekwunife & Njike, 2013). Despite these obvious advantages, pain after laparoscopic surgery is peculiar and can be very disturbing(Ekstein et al., 2006; Li et al., 2021; Sao et al., 2019; Tobias, 2013). As laparoscopic surgical procedures gradually evolve in our study environment, there is need to optimize patient's comfort and improve the care of these patients. Patients may experience laparoscopic surgery-related pain due to stretching of the intra-abdominal cavity and peritoneal inflammation as a result of pneumoperitoneum or shoulder pain resulting from phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity(Ekstein et al., 2006; Li et al., 2021). Whereas, parietal pain is less severe due to the small size surgical incision.

As a result, providing adequate postoperative analgesia after laparoscopic surgery especially in the first 24 hours after surgery should aim to meet the discharge criteria within a reasonable time may be a challenge[4]. To improve post-operative pain control, multimodal analgesia is necessary to reduce the high dose of single agents especially opioids. Several regimens such as the administration of non-steroidal anti-inflammatory drugs (NSAIDS) and opioids, local wound infiltration, and intraperitoneal saline have been used in previous studies to relieve pain after laparoscopic surgery(Bonnet & Marret, 2007; Mayoral Rojals et al., 2022). Opioids provide effective analgesia but can further increase the risk of nausea and vomiting, delay the return of gastrointestinal motility, pruritus or produce excessive sedation after surgery, which may be intolerable and may increase LOS(Mayoral Rojals et al., 2022). In addition, the side effects of NSAIDs such as platelet dysfunction, renal and gastrointestinal toxicity and the low practice of regional anaesthesia in our environment, has limited the available options for multimodal analgesia(Mayoral Rojals et al., 2022). Therefore, there is the need to develop strategies that reduce the opioid requirement after laparoscopic surgery at minimal.

Local anaesthetic (LA) instillation after laparoscopic surgery, an uncommon modality of pain management in our environment, is relatively safe when used within the recommended dosage and can provide adequate pain relief(Kahokehr, 2013). The rationale for selecting the intraperitoneal route for administering bupivacaine is to block the transmission of pain signals from the internal organs and potentially modify the perception of visceral pain in order to provide pain relief. Intraperitoneal local anaesthesia (IPLA) has been used for visceral blockade since the 1950s and its use in postoperative pain relief after laparoscopic surgery has recently become popular. Among the various techniques for administering drugs for pain relief9–11, intraperitoneal instillation of local anaesthetic may be best suited for our environment12. In addition, it is relatively safe, cheap and easy to perform13–15. If implemented as a part of a multimodal pain strategy in our environment, we anticipate it will improve the quality and cost of postoperative pain control after laparoscopic surgery.

In this quality improvement study, we hypothesized that intraperitoneal instillation of bupivacaine following laparoscopic surgery will not have any significant effect on pain reduction and opioid consumption. Therefore, our study assessed the effect of intraperitoneal instillation of Bupivacaine on reduction of postoperative pain as part of a

multimodal analgesia approach to the management of acute pain after gynaecological and general surgery laparoscopic surgeries.

MATERIALS AND METHODS

This study is a prospective, double-blinded, randomized and controlled quality improvement study that was performed on fifty American Society of Anesthesiologists (ASA) physical status class I to III patients aged between 18 and 60 years scheduled for elective laparoscopic surgery at the General and Gynaecological surgery units of the Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. Only patients assessed as stable ASA class III were included in the study. Approval of the Hospital Ethics Committee (UDUTH/HREC/2015/NO59) was obtained before conducting this study from November 2016 to June 2017. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all patients after thorough explanation of the purpose and scope of the study. Patients with allergy to the study drugs, chronic analgesic use before presentation, morbidly obese, refuse consent, lack the capacity to use the visual analogue score (VAS) or provide history of cardiovascular, hepatic or renal insufficiency were excluded from the study.

Study Drugs

Pethidine injection (Martindale Pharmaceuticals. Lot No. 0022255), Plain Bupivacaine (Duracaine®, Myungmoon pharm. Co. LTD. Batch No. E1427).

Study Protocol

After patient recruitment and randomization, consenting patients were educated on the use of VAS scale. Routine pre-anaesthetic evaluation was done a day to the surgery following departmental protocol., and patients were instructed to fast according to the departmental fasting guidelines. Fifty (50) consecutive patients scheduled for laparoscopic surgery were randomized into either of two groups (Group B and group S) after fulfilling study selection criteria. Group B received bupivacaine instillation via the umbilical port while group S was instilled with equal volume as saline through the same port. Both solutions were prepared and labelled 'B' or 'S' by the researcher before handing it over to the research assistant. The research assistant removes the seal before handing over the solution to the surgeon for instillation. The Surgeon and Researcher were blinded to the instilled study drug.

Procedure

All patients had intravenous access with two (2) wide bore canulae, base line vital signs were taken after premedication with 0.01mg/kg intravenous (IV) glycopyrrolate, 0.15mg/kg IV dexamethasone and 50mg IV ranitidine before induction of anaesthesia. General anaesthesia was induced with 2-2.5mg/ kg IV propofol, 2µg/kg IV fentanyl and 0.5mg/kg IV atracurium to facilitate tracheal intubation. A nasogastric tube was inserted and left in situ to decompress the gastrointestinal tract while anaesthesia was maintained with 1% Isoflurane in oxygen and intermittent bolus atracurium at 0.2mg/kg. Ventilation was controlled at tidal volume of 7- 10ml/kg which was adjusted to maintain end tidal carbon dioxide ($ETCO_2$) 35–40 mmHg. Fentanyl 0.5 – 1µg/kg was administered intravenously to provide intraoperative analgesia. Intraoperative monitoring consists of non-invasive blood pressure (NIBP) measured every 5minutes and continuous pulse rate (PR), oxygen saturation (SPO_2), $ETCO_2$ and ECG.

The study drug was instilled by the Surgeon at the end of surgery, after CO_2 was carefully evacuated as much as possible via the umbilical port. The time of instillation was noted and recorded. Each patient was tilted in Trendelenburg, reverse Trendelenburg, left lateral decubitus, right lateral decubitus, and then supine position consecutively after every 2 minutes to facilitate a spread of the instilled solution.

Afterwards, isoflurane and atracurium were discontinued and fresh gas flow of oxygen (O_2) was increased. In addition, the nasogastric tube removed before extubation. Extubation was performed after the patient was fully awake and obeys simple commands. They were transported to the post anaesthetic care unit (PACU) on supplemental O_2 and pulse oximeter monitor. Outcome measures were assessed and recorded at the PACU. Patients were discharged from PACU after fulfilling the departmental discharge criteria. Subsequent VAS scores were assessed in the ward at 4 hourly intervals over 24 hours.

Data collection

The time and VAS score on arrival at the PACU was assessed and recorded by the researcher as the zero hour respectively. Data on postoperative pain score on admission into PACU (zero hour), time to first analgesic request, postoperative pain scores at 4 hourly intervals for 24 hours, total pethidine consumption for the first 24 hours period, Presence/absence of procedure- and drug-related complications were collected during the study. The VAS score was obtained and recorded in the PACU at 0^{th}, 4^{th}, 8^{th}, 12^{th}, 16^{th}, 20^{th}, and 24^{th} hour after surgery. The VAS score was interpreted as: 0, 1 to 3, 4 to 6, 7 to 9 and 10 indicating no pain, mild pain, moderate pain, severe pain and worst possible pain respectively[9]. Intravenous pethidine titrated to a maximum of 0.5mg/kg was used as rescue analgesic to keep VAS score ≤ 4. The time interval between end of surgery and the first administration of pethidine was noted and recorded as time to first analgesic request (TFA). Patients not fully recovered from anaesthesia at presentation at the PACU were excluded from the final analysis.

Management of Adverse Effects

Patients were closely monitored for post-operative complications for the first 24 hours after the surgical procedure. Nausea and vomiting were managed by re-assurance of patient for mild symptoms and treatment with intravenous metoclopramide 10mg.

Statistical Analysis

The sample size was calculated based on figures from a similar study by Dinesh et al16. A sample size of 50 patients were recruited for the study after applying a 10 % attrition. Statistical analysis of data collected was performed with the use of IBM SPSS version 20. Results were expressed as mean ± SD except where otherwise stated. Differences in postoperative data between the two groups were analysed by using the χ^2 test and unpaired Student's *t*-tests for nonparametric and parametric variables, respectively. Differences in VAS scoring between the two groups were evaluated with Student's *t*-tests. The time to first analgesic request (TFA), was analysed with the unpaired Student's t-test after logarithmic transformation to ensure a normal distribution. *p*- value <0.05 was considered significant.

RESULTS AND DISCUSSION

There was no significant difference in the clinical characteristics of the patients shown in table 1. However, the mean difference in intraoperative fentanyl was slightly significantly higher in group S compared to group B.

Table 1: Clinical Characteristics of Patients

Variables	Group B (Mean±SD)	Group S (Mean±SD)	p-value
Age	33.52 (±11.52)	35.84 (±10.35)	0.65
BMI (kg/m^2)	23.31(±3.28)	24.28(±4.16)	0.42
Duration of surgery (mins)	88.72(±31.54)	89.12(±34.61)	0.97
Intraoperative fentanyl*	18.72(±4.80)	19.68(±4.89)	0.48

*Time from last intraoperative fentanyl dose in minutes

Laparoscopic adhesiolysis and cholecystectomy, and laparoscopy and dye test were the least and most performed procedures respectively (Table 2).

Table 2: Pattern of Laparoscopic Procedures

Variables	Group B	Group S
Laparoscopy and dye test	14(56)	13(52)
Cholecystectomy	1(4)	2(8)
Appendectomy	3(12)	2(8)
Ovarian drilling	3(1)	4(16)
Diagnostic laparoscopy	2(8)	3(12)
Laparoscopic adhesiolysis	2(8)	1(4)

Table 3 shows that VAS score at the time of admission into PACU was significantly lower in group B compared to group S. Although not significant, the mean VAS score was lower in group B compared to group S over 20th and 24th hours after surgery.

Table 3: Postoperative Pain Scores

Time (hour)	Group B (Mean±SD)	Group S (Mean±SD)	p-value
0*	2.82(±0.57)	3.38(±0.61)	0.02**
4	3.88(±0.57)	4.06(±0.74)	0.34
8	4.61(±0.97)	5.00(±0.80)	0.13
12	4.56(±0.52)	4.60(±0.50)	0.82
16	4.60(±0.59)	4.96(±0.83)	0.87
20	4.28(±0.38)	4.40(±0.42)	0.3
24	4.07(±0.30)	4.02(±0.27)	0.56

*Time of presentation at PACU, **p-value is significant. Pain scores were assessed using visual analogue scale scores in cm.

The corresponding pethidine consumption revealed higher consumption in group S compared to group B, but significance was recorded only at the 4th and 8th hours after surgery (table 4). Whereas, the mean cumulative pethidine consumption was higher but not significant in the group S compared to groups B (Table 5).

Table 4: Pethidine Consumption

Time (hour)	Group B (Mean±SD)	Group S (Mean±SD)	p-value
0*	1.55(±7.00)	3.92(±10.85)	0.37
4	6.52(±12.46)	19.38(±16.93)	0.04**
8	20.96(±15.28)	30.25(±10.16)	0.01**
12	27.36(±11.95)	23.83(±15.96)	0.39
16	29.80(±9.24)	32.79(±4.17)	0.15
20	27.84(±12.22)	32.75(±4.14)	0.07
24	27.24(±13.39)	26.42(±12.45)	0.83

*Pethidine consumption at presentation into the PACU, **p-value is significant.

Table 5: Pethidine Consumption and Time to First Analgesic Request

Variable	Group B	Group S	p-value
Pethidine consumption* (mg)	145.12(±42.58)	166.48(±41.11)	0.08
TFA (hour)**	8.16(±3.56)	5.92(±3.67)	0.03***

*Mean cumulative pethidine consumption in mg, **Time to first analgesic request, ***p-value is significant.

The TFA was higher for group B compared to group S over the study duration (table 5). None of the patients experienced severe adverse effect during the study (table 6).

Table 6: Postoperative Complications

Complications	Group B n(%)	Group S n(%)
Nausea	5(12)	18 (72)
Vomiting	0(0)	2(8)

Discussion

Our study demonstrated that intraperitoneal instillation of 20ml of 0.25% plain bupivacaine reduces the intensity of postoperative pain following laparoscopic surgery without severe adverse effects. The significant difference in mean VAS score and pethidine consumption for group B compared to group S at presentation in PACU may be because of the instilled bupivacaine in the former, however, the residual effect of the intraoperative analgesia might have contributed to this finding.

There was no significant difference in VAS scores from the 4th to the 24th hour postoperatively between the groups, lower values were still recorded for group B throughout this period. Although not significant, our findings of lower value of VAS score from the 4th to the 24th hour postoperatively might be because patients received pethidine at 4 hourly intervals to keep VAS score ≤ 4 or the wearing off effect of the instilled bupivacaine, though, only 2 % of the study population underwent laparoscopic cholecystectomy. In contrast, the study by Zmora O. et al(Zmora et al., 2000) reported that intraperitoneal instillation of bupivacaine does not attenuate pain following laparoscopic cholecystectomy. Perhaps because the dose of bupivacaine and the technique of instillation used by Zmora O. et al(Zmora et al., 2000) was different from the dose administered to patients in our study. In addition, the bupivacaine group received reduced dose of Bupivacaine, which was instilled into the gall bladder bed and at right subphrenic space only(Zmora et al., 2000). Meanwhile, VAS score was assessed at intervals over the 14th hours postoperatively(Zmora et al., 2000).

Our study found that patients in group B had a significantly longer time before requesting their first analgesic compared to those in group S, which is comparable with the findings of Bhardwaj et al(Bhardwaj et al., 2002). It is worth noting that the majority of our study population underwent laparoscopic cholecystectomy. Bhardwaj et al(Bhardwaj et al., 2002) reported lower visual analogue scale (VAS) scores up to 8 hours after surgery, although this difference was not statistically significant. Comparably, our study revealed that this technique of management of postoperative pain significantly reduced the need for postoperative pethidine in the same first 8 hours. Furthermore, Sherwinter et al(Sherwinter et al., 2008) revealed that the analgesic effect of intraperitoneal bupivacaine instillation can be prolonged further by placing an intraperitoneal catheter for continuous infusion.

Although not significant, our study revealed the mean cumulative pethidine consumption over 24 hours was higher in group S compared to group B. Similar finding was reported by Yadava et al(Yadava et al., 2016) in a similar study. However, the use of magnesium sulphate as adjuvant in their study might have influenced their outcomes. Adjuvants such as dexamethasone and magnesium sulphate may prolong onset and duration of analgesic effect of bupivacaine when instilled intraperitoneally(Fares et al., 2015; Yadava et al., 2016).

Although no major side effect, our study revealed more patients in the group S significantly experienced nausea and vomiting compared to the group B despite premedication with intravenous dexamethasone. The higher consumption of intravenous pethidine in the group S compared to group B may explain this finding. Opioid use may increase the risk of postoperative nausea and vomiting (PONV)(Yari et al., 2014). It is likely that higher values would have been recorded in both groups if these patients were not premedicated with dexamethasone(Fares et al., 2015).

The side effect profile in our study revealed that the use of IPLA with bupivacaine may be relatively safer at the concentration and volume of the local anaesthetic used for the study. In addition, our study revealed that IPLA with bupivacaine resulted in better pain experience. The heterogeneity in surgical procedures among the studied population, not analysing vital signs and not measuring the serum level of bupivacaine were concerns in our study.

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