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Original Research Article

The Role of Port Site Oxytocin in Alleviating Postoperative Pain after Laparoscopic Surgery under General Anaesthesia

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Conflict of interest: Nil

Abstract

Background and Objectives: Recently, oxytocin has garnered recognition as a pivotal mediator of endogenous analgesia. This study aims to evaluate the efficacy of pre-emptive subcutaneous oxytocin infiltration at port sites in reducing post-operative pain, contrasting its effectiveness with post-operative infiltration in patients undergoing laparoscopic surgeries.

Methods: This randomized controlled study involved 88 patients, selected based on predefined inclusion and exclusion criteria. Participants were randomly assigned to two groups: the study group, receiving preincisional subcutaneous Inj. Oxytocin at each port site incision, and the control group, receiving post-surgical subcutaneous Inj. Oxytocin at each port site incision. Each group comprised 44 patients. Intraoperative hemodynamic parameters, surgery duration, analgesia characteristics, and post-operative pain intensity assessed using the Visual Analogue Scale (VAS) during recovery and 24 hours post-surgery were recorded.

Results: Both groups exhibited comparable demographic and general clinical characteristics. The study group demonstrated significantly lower postoperative pain intensity at 2, 4, 6, and 24 hours compared to the control group. The study group also displayed a notable attenuation of hemodynamic response (mean heart rate, systolic and diastolic blood pressure) during surgery, a response not observed in the control group.

Conclusion: Pre-emptive/preincisional subcutaneous oxytocin infiltration at port sites effectively reduced post-operative pain in adult patients undergoing laparoscopic surgeries under general anaesthesia when compared to controls. Additionally, this intervention demonstrated effectiveness in blunting the cardiovascular response to intra-operative nociceptive stimuli in contrast to the control group.

Keywords: Oxytocin, Post-operative pain, Laproscopy, General anesthesia.

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Introduction

Laparoscopic surgical procedures have gained popularity due to lower complication rates, minimized incision size, and reduced trauma, leading to faster postoperative recovery and discharge. Compared to open surgery, laparoscopic surgeries exhibit a decreased incidence of post-operative pain and reduced analgesic requirements. However, postoperative pain in laparoscopic procedures, attributed to port pain, pelvic organ nociception, and diaphragmatic irritation from residual pneumo-peritoneum, is often brief but intense, impacting patient recovery [1-3]. Postoperative pain is a complex and multifactorial phenomenon, necessitating a judicious selection of various perioperative analgesic modalities for optimal clinical outcomes. The increasing use of multimodal analgesic approaches involves the incorporation of drugs, regional blocks with local anaesthetics, and general anaesthesia. Single wound infiltration with local anaesthetic (WI) or continuous local anaesthetic infusion through catheters placed into surgical wounds has been reintroduced as components of multimodal analgesia for post-operative pain control [4-7]. Pre-emptive analgesia,

an anti-nociceptive intervention administered before incision or surgery, aims to reduce sensitization of peripheral and central pain pathways to the transmission of pain signals elicited by tissue damage. Proposed by Wall in 1988, pre-emptive analgesia, besides its potential efficacy, possesses neuroprotective properties [8, 9].

While local infiltration with local anaesthetics and adjuvants is commonly used in pre-emptive analgesia, their adverse effects significantly limit their application. Hence, there is a considerable need for newer and safer analgesics. Oxytocin, an endogenous nonapeptide, has recently emerged as a crucial mediator of endogenous analgesia, showing promise in animal and limited human studies. Its central (intrathecal), peripheral (subcutaneous), and intranasal administration have been explored in a limited number of studies [10-14].

Considering the scarcity of studies exploring the peripheral role of oxytocin in reducing post-operative pain, the present study aimed to evaluate the effectiveness of pre-emptive port site subcutaneous oxytocin infiltration in reducing post-operative pain compared to post-operative infiltration in patients undergoing laparoscopic surgeries.

Material and Methods

The eligible study population encompassed patients aged 18 to 50 years, classified as American Society of Anaesthesiologists (ASA) physical class I and II, scheduled for elective laparoscopic surgeries.

Exclusions comprised individuals on chronic analgesic treatment (e.g., non-steroidal anti-inflammatory drugs, opioids), and those with hypersensitivity to the study drug. Patients encountering intra-operative complications such as excessive bleeding (>500cc) or requiring conversion to open laparotomy were also excluded. Data collection employed a structured proforma encompassing sociodemographic details, surgery indication, anaesthetic specifics, intra-operative monitoring parameters, postoperative vitals, and Visual Analogue Scale (VAS) scores. A total of 88 patients were included.

Preoperatively, patients were briefed on the VAS score, ranging from 0 (no pain) to 10 (excruciating worst possible pain). Premedication involved IV Inj. Glycopyrrolate (0.005mg/kg), Inj. Ondansetron (0.1 mg/kg IV), Inj. Midazolam (0.02 mg/kg), and Inj Fentanyl (0.002mg/kg IV).

Aesthetic procedures included attaching standard monitors, recording baseline heart rate (HR), mean arterial pressure, and oxygen saturation (SpO2). Patients were randomly assigned to two groups: Group I (study group) received pre-incisional subcutaneous infiltration with Inj. Oxytocin 4 µg (2.5 IU) diluted to 4 cc at each port site incision, and Group II (control group) received post-surgical infiltration with Inj. Oxytocin 4 µg (2.5 IU) diluted to 4 cc at each port site incision. Each group consisted of 44 patients. Standard anaesthetic techniques were employed, with muscle relaxation achieved by Inj. Atracurium (0.5 mg/kg). Anaesthesia maintenance involved Air in O2 and Isoflurane. Intra-abdominal pressure was maintained at 12–15 mmHg during surgery.

Postoperatively, patients were observed in the post-anaesthesia care unit for 2 hours. Vital signs and VAS scores were recorded at intervals. In cases of inadequate analgesia (VAS > 3), both groups received IV Inj. Paracetamol (15 mg/kg) as rescue analgesia. Parameters assessed postoperatively included the quality and duration of analgesia, hemodynamic parameters, time to the first dose of rescue analgesia, sedation, and any postoperative complications or side effects. Duration of analgesia was defined as the time from oxytocin administration to the first dose of rescue analgesic.

Results

The demographic and clinical characteristics of participants in both the study and control groups did not exhibit statistically significant differences. There were no significant variations in the total duration of analgesia and surgical procedures between the study and control groups. However, the total duration of post-operative analgesia was notably reduced in the control group. Notably, the control group demonstrated a higher requirement for rescue analgesia at 4 and 12 hours, with significantly increased total doses of rescue analgesia. Assessment of Visual Analogue Scale (VAS) scores at various time points, including 15 minutes, 30 minutes, 45 minutes, 60 minutes, 2 hours, 4 hours, and 6 hours, revealed comparable post-operative analgesia between both groups initially (upon arrival in PACU). However, at 2 hours, 4 hours, 6 hours, and 24 hours, VAS scores were significantly elevated in the control group, indicating a greater degree of discomfort. A comprehensive comparison of general and clinical variables between the study and control groups is provided in Table 1.

In the pre-emptive subcutaneous oxytocin infiltration group, the mean heart rate, systolic and diastolic blood pressure was significantly lower compared to the post-operative oxytocin infiltration group.

This suggests a substantial attenuation of the nociceptive response to surgical incisions and trocar insertions. Mean systolic and diastolic blood pressure at various assessment points are illustrated in Figure 1.

Table 1: Clinico-demographic parameters of study participants

Characteristic	Study Group	Control Group	P-Value
Age (in years)	39.2 ± 15.8	36.7 ± 12.9	0.06
Gender (Males/ Females)	25/19	21/23	0.31
Mean Heart rate (BPM)	92.1 ± 17.3	90.3 ± 18.7	0.73
Mean arterial pressure (mmHg)	88.6 ± 11.5	94.7 ± 10.2	0.08
Mean Systolic blood pressure (mmHg)	125.2 ± 14.4	127.5 ± 11.1	0.66
Mean Diastolic blood pressure (mmHg)	73.8 ± 10.8	78.2 ± 11.2	< 0.05
Mean SPO2 (%)	97.9 ± 1.2	98.4 ± 1.0	0.21
Total Duration of Surgery (Min)	75.6 ± 32.1	72.5 ± 36.8	0.70
Total Duration of Anaesthesia (Min)	81.4 ± 33.8	78.2 ± 37.6	0.71
Total Duration Of Post-Op Analgesia (Hours)	9 (7, 10)	6 (5, 7)	< 0.05
Total Doses of Rescue Analgesia	3 (2, 4)	2 (2, 2)	< 0.05
Mean VAS Score			
15 min	1 (1,1)	1 (1,1)	1.00
30 min	1 (1,1)	1 (1,1)	1.00
45 min	1 (1,1)	2 (1,2)	0.06
60 min	1 (1,2)	2 (2,2)	0.06
2 hours	2 (1,2)	2 (2,2)	<0.05
4 hours	2 (2,2)	3 (2,3)	<0.05
6 hours	2 (2,3)	3 (3,3)	<0.05
24 hours	2 (2,3)	3 (3,3)	<0.05

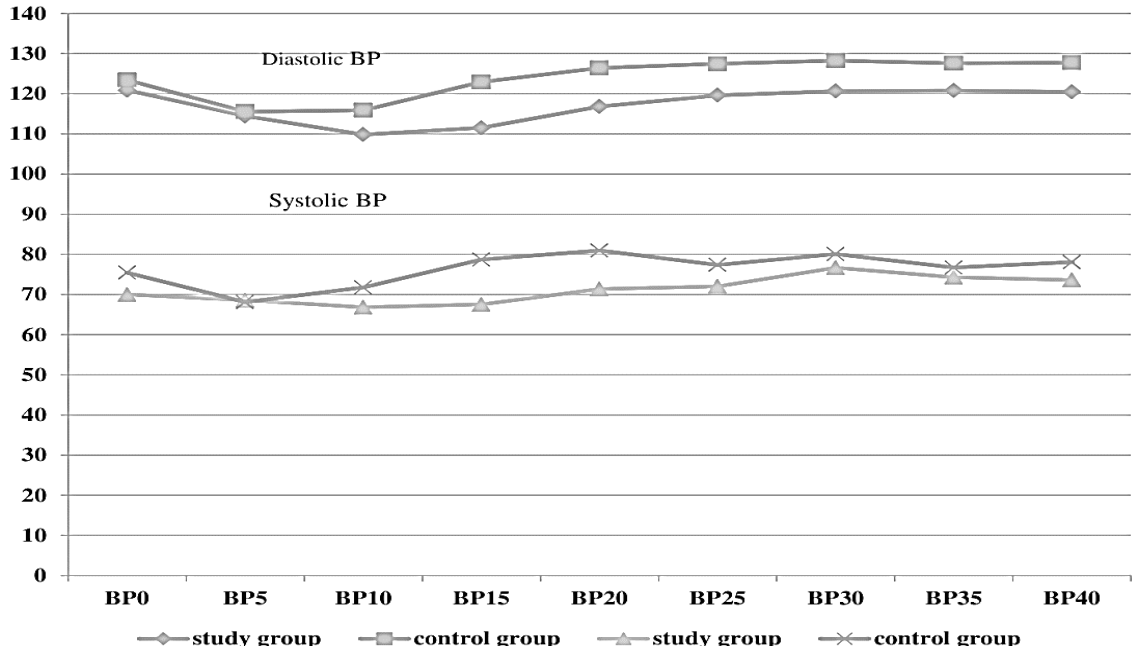

Figure 1:

Discussion

In recent years, there has been a notable trend favouring regional anaesthesia techniques for post-operative pain management in procedures conducted under general anaesthesia. These techniques encompass pre and post-operative wound infiltration (WI), involving both single and continuous infiltration (CWI) of local anaesthetic agents, with or without adjuvants. Such approaches have demonstrated significant antihyperalgesic effects. Oxytocin, originating primarily in the supraoptic and paraventricular nuclei (SON & PVN, respectively) of the hypothalamus, exerts peripheral and central actions. Oxytocinergic neurons from the PVN project axons to the spinal cord, forming synaptic connections with dorsal horn neurons.

Beyond its well-established roles in parturition and lactation, oxytocin is intricately involved in social and psychological functions, including maternal attachment, anxiety, depressive mood, memory, appetite, sexual function, and stress regulation. Oxytocin, administered exogenously, directly and indirectly affects pain by modulating nociceptive transmission, pain perception, and reducing pain sensitivity [12, 15-18]. In our study, pre-emptive (preincisional) subcutaneous infiltration of oxytocin

at the port site proved significantly more effective in reducing post-operative pain compared to post-surgical oxytocin infiltration in the control group. A recent study by Zayas-González H et al. [10] reported a similar efficacy of subcutaneous oxytocin over lidocaine. Notably, only these two studies, including our present investigation, have assessed the analgesic effects of subcutaneous oxytocin infiltration. These findings align with recent basic science studies [19] demonstrating that activation of peripheral oxytocin receptors in skin nerve terminals can produce enduring inhibition of nociception. In our study, the study group exhibited a blunted cardiovascular response to nociceptive stimuli during surgery compared to the control group. This reduction in cardiovascular response has been linked to effective post-operative pain control [10]. Uchida et al. [20] suggested that heart rate variability may predict the onset of postoperative pain, although results may vary with anaesthetic agents.

Additional clinical evidence is crucial to further assess the relationship between opioids, inhalation anaesthesia, duration of exposure to halogenated agents, and the autonomic nervous system response [12, 21]. Effective approaches to significantly decrease post-operative pain involve a combination of pre-emptive analgesia and multimodal pain management. Multimodal analgesic techniques, which decrease the dosage of individual drugs and mitigate associated adverse effects, include agents such as dexmedetomidine, lidocaine, with or without non-opioid adjuvants (NSAIDs, beta-blockers, ketamine, gabapentin, etc.). Oxytocin could prove effective as an inclusion in this group [15].

The outcomes of our current investigation contribute to the scant evidence available on the efficacy of pre-emptive subcutaneous oxytocin infiltration in mitigating postoperative pain among patients undergoing laparoscopic surgeries. It is imperative to acknowledge that our study was conducted at a single centre and had a relatively limited sample size. To advance the understanding of the role of pre-emptive subcutaneous oxytocin infiltration in reducing post-operative pain and enhancing clinical outcomes, there is a critical need for multicentre randomized controlled trials incorporating multiple arms and larger participant cohorts. Such comprehensive studies would provide a more robust and generalizable assessment of the potential benefits of pre-emptive subcutaneous oxytocin infiltration in the context of various surgical settings.

Conclusion

The pre-emptive or preincisional subcutaneous infiltration of oxytocin was efficacious in diminishing post-operative pain in adult individuals undergoing laparoscopic surgeries with general anaesthesia when compared to the control group. Moreover, it demonstrated effectiveness in mitigating the cardiovascular response to intraoperative nociceptive stimuli in the study group as opposed to the control group.

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