Brief Communication

Feasibility and efficacy of sublingual buprenorphine tablets in managing acute postoperative pain after elective breast cancer surgeries: A series of 10 cases

INTRODUCTION

Poorly controlled perioperative surgical pain is a consistent risk factor for developing post mastectomy pain syndrome (PMPS).[1] The incidence of chronic pain after mastectomy is as high as 25-60%, which is a range derived from several studies.[2] American Society of Anesthesiologists (ASA) recommends a multimodal approach to postoperative pain management whenever possible which includes use of non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, alpha-2 agonists, N-methyl D-aspartate receptor antagonists, gabapentinoids, dexamethasone, anti-depressants and peripheral nerve blocks.[3]

Buprenorphine hydrochloride is a partial μ-receptor agonist, OLR-1 (Oxidized Low-density lipoprotein Receptor) agonist, delta and kappa receptor antagonist approved for managing acute surgical pain, cancer pain and non-cancer pain.[4] Sublingual (SL) buprenorphine is available in the form of 200 μg tablets which has been used with good results for managing acute postoperative pain.[5] In the present case series, we have investigated the feasibility and efficacy of SL buprenorphine in managing acute postoperative pain after mastectomy.

CASE SERIES

After Institutional Ethics Committee (IEC) approval, we enrolled 10 American Society of Anesthesiologists-Physical Status (ASA-PS) I-II patients scheduled for elective breast cancer surgeries (modified radical mastectomies, mastectomy with sentinel lymph node biopsy) in this study after obtaining informed consent to understand safety and efficacy of SL buprenorphine. Patients currently using opioids, respiratory, renal or hepatic failure, predisposition to vomiting, weight less than 50 kg or patients unwilling to participate in study were excluded. Demographic details and parameters like postoperative nausea/vomiting (PONV), respiratory rate, sedation score and requirement of rescue analgesic are shown in Table 1.

All patients were thoroughly evaluated at pre-anaesthesia clinic for fitness. Relevant investigation (complete blood picture, creatinine, blood group, viral markers) were advised for all patients. A 12-lead electrocardiogram and two-dimensional echocardiogram were advised if they had received anthracycline-based chemotherapy preoperatively. After confirming nil by mouth status and securing appropriate intravenous (IV) access on contra lateral hand, patients were shifted to operating room. Non-invasive blood pressure (NIBP), heart rate (HR), and oxygen saturation (SPO2) were noted. All patients were premedicated with IV 0.03 mg/kg midazolam and 1.5 μg/kg fentanyl (maximum 100 ug). General anaesthesia was induced with IV propofol 2-2.5 mg/kg and the airway secured with an appropriately sized supraglottic airway (SGA), AMBU® Aura40™. Neuromuscular block was achieved with 0.5 mg/kg atracurium. General anaesthesia was maintained with oxygen-medical air and isoflurane using volume-controlled ventilation, and dial concentration was adjusted to target a minimum alveolar concentration of 1. Intraoperative monitoring was as per ASA standards (electrocardiogram, non-invasive blood pressure, oxygen saturation and end-tidal carbon dioxide). Fentanyl (1 μg/kg) IV was administered to all the patients who had sympathetic response to pain on incision i.e. if the vitals raised by at least 20% of baseline. At the end of surgery, SGA was removed after reversing neuromuscular blockade with 0.05 mg/kg neostigmine and 0.01 mg/kg glycopyrrolate. Patients were then transferred to a high-dependency unit. The visual analogue scale (VAS) was used to assess pain postoperatively. Intravenous Paracetamol 1 gram 8th hourly was continued in the postoperative period. All patients received 200 μg buprenorphine tablet SL (ADDNOK®, Rusan Pharma Ltd.) after surgery when they were awake and ready for clear liquids (usually 1 hour after surgery). IV morphine 3 mg was the rescue analgesic planned if the VAS score was more than 4 in spite of paracetamol and buprenorphine. Respiratory rate, Ramsay sedation score, PONV score and VAS was noted for all patients during the 24 hr stay in HDU. None of the patients had respiratory depression due to buprenorphine (respiratory rate <12 min), all patients had an acceptable sedation score (2-3) and a VAS less than 4 in 24 hour duration. 4 patients had one episode of PONV, which was

Table 1: Showing demographic details and other information like side operated, type of breast surgery, intraoperative fentanyl used, PONV score in all 10 patients

Age (yrs)	Weight (kgs)	BMI (kg/m^2)	ASA-PS	Side	Surgery	Intraoperative Fentanyl (μg)	PONV	Rescue analgesia
50	75	29.67	II	Left	MRM	150	No	No
56	70	39.57	II	Right	BCS	150	2	No
45	70	25.4	II	Left	MRM	150	1	No
35	65	27.41	II	Right	MRM	150	No	No
54	68	22.29	II	Right	MRM	150	No	No
57	56	24.2	I	Left	MRM	150	No	No
39	76	28.26	I	Right	MRM	150	No	No
44	84	34.52	I	Left	MRM	200	No	No
43	53	25.67	II	Left	MRM	150	1	No
65	77	36.62	II	Left	WLE + AC	150	1	No

BMI – Body mass index; ASA-PS – American Society of Anesthesiologists-Physical Status; MRM – Modified radical mastectomy; BCS – Breast conservation surgery; AC – Axillary clearance; PONV – Postoperative nausea and vomiting

unrelated to the timing of SL buprenorphine. None of the patients required rescue analgesic.

DISCUSSION

Thoracic paravertebral block is a time tested regional anaesthesia (RA) technique, which not only provides good perioperative analgesia but also has shown to reduce incidence of post mastectomy pain syndrome.[6] Several RA techniques are now practiced with good results for managing acute postoperative pain after breast surgeries like pectoralis blocks (1 and 2), serratus anterior plane (SAP) block, erector spinae plane block (ESPB).[7,8] The recently described RA techniques provided good postoperative opioid sparing pain relief. However, right now its efficacy in preventing cancer recurrence and preventing PMPS is not established. Moreover, these techniques need ultrasound (US) guided injections which needs training and expertise. Opioids, NSAIDs and acetaminophen continue to be used for managing mastectomy pain. Tramadol is the commonly used postoperative opioid as it can be administered orally and IV. However, nausea and vomiting are the potential adverse effect with the use of tramadol via any route.[9] Female gender and preoperative chemotherapy are additional risk factors for contributing to PONV.

Buprenorphine is a partial μ-receptor agonist available for IV use, as per rectal suppository, as a transdermal patch and as a sublingual preparation (tablet and film). Analgesic potency of buprenorphine is 25-40 times greater than that of morphine sulfate. US-FDA has approved buprenorphine for 3 indications: opioid detoxification, opioid maintenance, and pain management. Buprenorphine undergoes extensive first pass metabolism enzyme by CYP3A4 in the gastrointestinal tract when taken orally. However, when used SL, there is 30-60% of bioavailability as hepatic first pass metabolism is avoided, due to which SL buprenorphine can be used effectively for managing acute pain. SL buprenorphine gets dissolved in 10 minutes and takes around 60-90 minutes to achieve peak plasma concentration. A single SL dose offers pain relief for up to 6 hrs. Being a partial agonist; addiction, abuse, tolerance are less with buprenorphine use. Due to these properties, SL buprenorphine has been found useful in managing breakthrough cancer and non-cancer pain.[10] However, in case of accidental overdose, naloxone does not help in reversing respiratory depression.

This is possibly the first study in which SL buprenorphine has been used for managing acute postoperative mastectomy pain.

CONCLUSION

In conclusion, SL buprenorphine appears to a safe and efficacious analgesic in managing acute postoperative pain after mastectomy. Further studies can establish its safety and efficacy when compared to conventional opioids like morphine and tramadol.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Krishna Sumanth D, Abhijit S Nair, Srinivasa S P Mantha, Basanth K Rayani

Department of Anaesthesiology, Basavatarakam Indo-American Cancer Hospital and Research Institute, Hyderabad, Telangana, India

Address for correspondence:
Dr. Abhijit S Nair,
Department of Anaesthesiology, Basavatarakam Indo-American Cancer Hospital and Research Institute, Hyderabad - 500 034, Telangana, India.
E-mail: abhijitnair@rediffmail.com

Received: 08th May, 2019
Revision: 01st September, 2019
Accepted: 11th September, 2019
Publication: 11th December, 2019

REFERENCES

1. Gartner R, Jensen MB, Nielsen J, Ewertz M, Kroman N, Kehlet H. Prevalence of and factors associated with persistent pain following breast cancer surgery. JAMA 2009;302:1985-92.
2. Andersen KG, Kehlet H. Persistent pain after breast cancer treatment: A critical review of risk factors and strategies for prevention. J Pain 2011;12:725-46.
3. Helander EM, Menard BL, Harmon CM, Homra BK, Allain AV, Bordelon GJ, *et al*. Multimodal analgesia, current concepts, and acute pain considerations. Curr Pain Headache Rep 2017;21:3.
4. White LD, Hodge A, Vlok R, Hurtado G, Eastern K, Melhuish TM. Efficacy and adverse effects of buprenorphine in acute pain management: Systematic review and meta-analysis of randomised controlled trials. Br J Anaesth 2018;120:668-78.
5. Lim SC, Schug S, Krishnarajah J. The pharmacokinetics and local tolerability of a novel sublingual formulation of buprenorphine. Pain Med 2019;20:143-52.
6. Terkawi AS, Tsang S, Sessler D, Terkawi RS, Nunemaker MS, Durieux ME, *et al*. Improving analgesic efficacy and safety of thoracic paravertebral block for breast surgery: A mixed-effects meta-analysis. Pain Physician 2015;18:E757-80.
7. De Cassai A, Bonvicini D, Correale C, Sandei L, Tulgar S, Tonetti T. Erector spinae plane block: A systematic qualitative review. Minerva Anestesiol 2019;85:308-19.
8. Garg R. Regional anaesthesia in breast cancer: Benefits beyond pain. Indian J Anaesth 2017;61:369-72.
9. Dhesi M, Maani CV. Tramadol. [Updated 2019 Jan 06]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537060/. [Last accessed on 2019 May 05].
10. Khanna IK, Pillarisetti S. Buprenorphine - an attractive opioid with underutilized potential in treatment of chronic pain. J Pain Res 2015;8:859-70.

Access this article online	
Quick response code	Website: www.ijaweb.org
	DOI: 10.4103/ija.IJA_361_19

How to cite this article: Sumanth DK, Nair AS, Mantha SS, Rayani BK. Feasibility and efficacy of sublingual buprenorphine tablets in managing acute postoperative pain after elective breast cancer surgeries: A series of 10 cases. Indian J Anaesth 2019;63:1036-8.