



TRANSDERMAL BUPRENORPHINE PATCH – AN APPROACH FOR MANAGEMENT OF POST OPERATIVE PAIN FOLLOWING HYSTERECTOMY FOR BENIGN GYNECOLOGICAL CONDITIONS

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ABSTRACT

Background: Buprenorphine is a semisynthetic derivative of thebaine, which is 75-100 times more potent than morphine and causes less respiratory depression. Efficacy and safety of transdermal buprenorphine have been well established in chronic pain. **Aim:** To evaluate the efficacy of transdermal buprenorphine patch in postoperative pain management. **Materials and Methods:** Total 100 patients were taken as the sample size over a span of 1 year (September 2021-August 2022). Transdermal Buprenorphine patch 10 mg was applied on the upper arm on the night before surgery. Analgesic and hemodynamic effects post surgery were observed and certain parameters like time interval between first complain of pain by the patient and surgery, need of other analgesics- when and in what dosage, were taken into consideration. Visual Analog Scale was taken for pain scaling. **Results:** Patient well being was considerably increased because of remarkable decrease in pain complains, also there were no significant hemodynamic changes observed in the study group.

KEYWORDS

Analgesia, Hemodynamic, Patch, Transdermal Delivery System

INTRODUCTION

As quoted in TeLinde – “Successful surgery depends on control of Bleeding, Infection and Pain”¹, post operative pain management is a necessary component of a patient undergoing major surgery. Adequate pain management is a challenge to the surgeon as there are many adverse physiological and psychological effects associated with pain.² Pain can hamper the recovery process and increase the hospital stay and contribute towards patient dissatisfaction. Multimodal approach and drugs have been used for pain control with variable achievement. Every technique and drug has its own advantages and disadvantages. Buprenorphine is a semi synthetic derivative of thebaine, a morphine alkaloid, being a potent and safe analgesic (75 to 100 times greater than that of morphine), at 5-10% lesser receptors occupancy, causing less respiratory depression^{3,4}. The Transdermal Drug Delivery system [TDS] overcomes the pharmacokinetic problems of oral and parenteral routes.⁷

AIM

In this study, we aim to evaluate the efficacy and hemodynamic effects of transdermal buprenorphine patch (10mg) in post operative pain management of lower abdominal surgery.

MATERIALS AND METHODS

Over a span of one year, from September 2021 to August 2022, 100 patients undergoing all types of hysterectomies were taken into the study. Patients with known episode of hypersensitivity reaction to buprenorphine; respiratory, gastrointestinal, liver or renal morbidities were not taken for the study. The peak effect of buprenorphine patch is achieved at 12-24 hours⁸. All patients were premedicated on the night before surgery with ranitidine 150 mg, metaclopramide 10mg and Alprazolam 0.25 mg orally. Transdermal patch was applied to hair-less sites, with most common sites being the upper outer arm, chest, upper back, or side of the chest night before surgery. Intraoperative monitoring included non-invasive arterial blood pressure, electrocardiography, capnography, pulse oximetry and temperature. All the base line parameters (heart rate, Blood pressure, SpO₂, ETCO₂) were recorded and intravenous line was obtained with 18 gauge cannula on the dorsum of hand. After surgery, VAS score was assessed. The visual analog scale (VAS) is a validated, subjective measure for acute and chronic pain. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between “no pain” and “worst pain”. If VAS score was more than ≥ 3 , Inj. tramadol i.v. was given as a rescue analgesic. VAS scores were assessed every hour till first 12 hours on the first day, 2nd day - 7th days after surgery and Inj. tramadol was given whenever VAS score was found to be ≥ 3 .

In our study, on the 1st day 39 patients were complaining of pain and hence were given Inj Tramadol iv 2cc (50mg/ml) as additional dose. Most of them needed extra dose within 6 hours after surgery. Also, of them, 18 patients needed second dose of Inj tramadol that same day after 5 to 6 hours of the first tramadol dose. Once the peak effect of buprenorphine was established, the complaints of pain started decreasing. On 2nd post op day, only 7 patients complained of pain and were given Inj Tramadol 2cc (50mg/ml) iv stat. On 3rd day, only 1 patient complained of pain. From, 4th day to 7th day there were no

complains. The findings of our study are supported by Arshad et al., who reported that the buprenorphine TDS was significantly decreasing postsurgical pain⁹. As per that study, Buprenorphine TDS was also shown to be an effective analgesic against chronic, severe pain in this study population. Patients treated with this new formulation of buprenorphine showed improved duration of sleep and reduced need for additional oral analgesics. That study proved its usefulness in postoperative pain also. Fentanyl TDS is not extensively studied in postsurgical patient due to fear of respiratory depression.

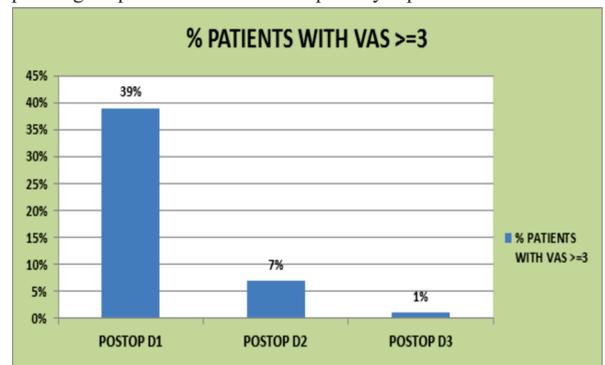


Figure 1: Percentage of Patients Required Additional Analgesic Dosage

Table 1 Vas Score of Patients During Post Operative Period

| POST OP HOUR | VAS SCORE | NO OF PATIENTS (%) |
|--------------|-----------|--------------------|
| 0 | 1 | 39 (%) |
| | 2 | 22 (%) |
| | 3 | 22 (%) |
| | 4 | 17 (%) |
| 2 | 1 | 51 (%) |
| | 2 | 17 (%) |
| | 3 | 18 (%) |
| | 4 | 14 (%) |
| 6 | 1 | 49 (%) |
| | 2 | 39 (%) |
| | 3 | 08 (%) |
| | 4 | 04 (%) |
| 12 | 1 | 88 (%) |
| | 2 | 11 (%) |
| | 3 | 1 (%) |
| | 4 | 0 (%) |
| 18 | 1 | 92 (%) |
| | 2 | 08 (%) |
| | 3 | 0 (%) |
| | 4 | 0 (%) |
| 24 | 1 | 99 (%) |
| | 2 | 1 (%) |
| | 3 | 0 (%) |
| | 4 | 0 (%) |

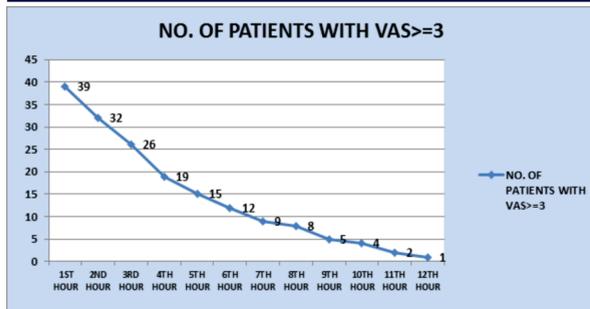


Figure 2: Decreasing Trend of Post Operative Pain After Buprenorphine Transdermal Patch

Table 2 Showing Side Effects Associated with Buprenorphine Transdermal Patch

| SIDE EFFECTS | NO. OF PATIENTS (%) |
|--------------------------------|---|
| NAUSEA | 23 (23%) – (mostly seen in patients also requiring tramadol as additional analgesia, so possibly a side effect of that) |
| VOMITING | 4 (4%) |
| CONSTIPATION | 0 (0%) |
| APPLICATION SITE RASHES | 0 (0%) |
| HEADACHE | 2 (2%) |
| OTHER HEMODYNAMIC SIDE EFFECTS | NONE SIGNIFICANT |

Few side effects were noted such as nausea, vomiting, and trivial changes in systolic blood pressure but were not found significant and to be associated with buprenorphine. 23 patients complained of nausea but of them 21 patients had had requirement of inj Tramadol 2cc (50mg/ml) as additional analgesia and nausea is a well known side effect of tramadol so statistically this was not found to be significant. 4 patients had vomiting episodes 3 of which had received Inj Tramadol. Other known side effects like headache, constipation or application site rashes were not found in our study.

The cost of the patch is around 800 to 900 rupees which is quite expensive as compared to inj tramadol and oral tablets (4 times) but it remarkably improves the well being of the patient which is the most important factor.

RESULTS & DISCUSSION

Post-surgical pain is a complex response to trauma during surgery that stimulates the central nervous system. It raises the possibility of complications, cost of medical care and healing recovery ¹⁰. Transdermal Drug Delivery System (TDDS) provides safe, convenient and reliable method of drug delivery. It is a preferable alternative to oral and parenteral drug delivery method as it avoids painful skin punctures and multiple dosing. TDS has an advantage in having a high tendency for first-pass metabolism. These can be release in small doses with a sustained blood level ¹¹.

The peak-effect of buprenorphine patch is achieved at 12-24 hours. Efficacy of buprenorphine transdermal patch was dosage dependent; mainly in the first postoperative hour where additional analgesia was required ¹². The peak-effect of buprenorphine patch was achieved at 12-24 hours, so the patients remained haemodynamically stable at intubation and thereafter ¹³. Oifa et al., also reported that the buprenorphine infusion (BUP-i) and buprenorphine bolus (BUP-b) in abdominal surgery patients provide haemodynamically stable during intra and postoperative period ¹⁴. Setti et al., also found that buprenorphine transdermal delivery system (BUP-TDS) efficacy was directly proportional to its dosage ¹⁵. No significant differences in Blood Pressure (BP) were observed. Although statistically significant, changes were physiologically not relevant and of no clinical importance.

In the present study, the rescue analgesia was required. The difference in analgesia requirement was found to be statistically significant compared to priorly when we were using only Inj Tramadol 50mg/ml as post operative analgesic at all above time intervals i.e. 24 hours postoperatively and thereafter, second, third, fourth, fifth, sixth and seventh day after surgery. The findings of our study are supported by Setti et al., Böhme and Likar who reported that the efficacy of

transdermal buprenorphine patches was directly proportional to its dosage, although additional analgesia was required, particularly in the 1st postoperative hour in gynecological surgery ^{12,15}. In a previous study Sittl et al., had found that patients treated with transdermal buprenorphine had reduced need for additional analgesics ⁵.

Other treatment related side effects such as, headache, application site pruritus, application site erythema, application site rash, dizziness, constipation and dry mouth, were not found in our study. Walsh et al., observed that the nausea, vomiting, euphoria, sedation, delayed gastric emptying and pupillary constriction were all seen to a lesser degree with buprenorphine as compared to morphine ¹⁶. This was probably due to the high lipophilicity of buprenorphine as compared to morphine.

CONCLUSION

Transdermal Buprenorphine patch (10 mg) is effective in attenuating postoperative pain, maintaining haemodynamic stability and fewer postoperative rescue analgesic requirements, for patients undergoing lower abdominal surgeries.¹⁷

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