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Original Research Article

Transdermal Drug Delivery System-Future for Post Operative Pain Management- A Study in Post MRM Patients

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Abstract

Introduction: Modified Radical Mastectomy is usually associated with severe post operative pain and sometime phantom pain .Transdermal delivery system is non-invasive method and provides sustained release of drug for prolonged period with lesser side effects with less variation in therapeutic plasma levels and less need for parentral analgesia.

Material and Methods: Sixty patients undergoing Modified Radical Mastectomy were randomly divided into two equal groups. Group "A" received Fentanyl 25 µg/hr transdermal patch and Group "B" received Buprenorphine 20 µg/ hr transdermal patch 18 hours prior to the surgery. Patients in both the groups were followed for 3 post operative days for percentage of pain relief, break through pain and any adverse effects. All the patients received injondensetron 0.15 mg/kg every morning and Injparacemol infusion 1 gm immediately after surgery. The break through dose of 75 mg inj diclofenac in IV infusion was planned and if VAS score was more than 5 after diclofenac injection then inj tramadol 100 mg IV slow was planned as extra rescue dose.

Result: The VAS score was comparable in both the groups with P value= 0.3135. The requirement of rescue dose was comparable in both the groups P=0.3317. No patient had any other side effects.

Conclusion: Fentanyl 25 ug/hr and buprenorphine 20 ug/hr transdermal patch are effective non invasive method of pain relief in post operative cases of MRM.

Keywords: Fentanyl TDS,Buprenorphine TDS,MRM

Introduction

Modified Radical Mastectomy is associated with severe post operative pain in association with neuropathic pain in chest and shoulders and sometimes phantom pain. Cancer patients due to their disease, chemotherapy and radiotherapy have poor myocardial and renal reserves.

Post operative pain management in these patients is challenging. 50-80% patients do not get adequate post operative pain relief [1] with NSAIDS and Tramadol commonly used in post operative period leading to inadequate ventilation and psychological changes. The need for background round the clock pain relief is well managed with transdermal delivery system of drugs.

Recently the role of transdermal delivery system has emerged as new modality in the treatment of acute post operative pain. The advantage of this is constant release of analgesic drug and maintenance of sustained therapeutic blood level of drug over a period of three consecutive days. This study was done at tertiary cancer institute in North India where large number of patients undergo MRM. The aim of this study was to compare whether TDS fentanyl 25µg/hr associated with superior or equivalent analgesic potency and tolerability as compared to TDS Buprenorphine 20 µg/hr.

Fentanyl is a narcotic and comes under narcotic act and thus it lacks universal availability in the market and most hospitals in northern India. Buprenorhine TDS has become attractive choice for post operative pain relief due to its easy availability, unique pharmacology and lesser side effects.

Material and Methods

After institutional ethical committee approval and written informed consent from the patients, 60 patients posted for MRM aged between 25-55 years were taken for surgery.

Patients were randomized into two groups of 30 each. Group A received transdermal fentanyl patch 25 µg/hr. 18 hours before surgery was planned. Group B received transdermal buprenorphine patch 20 µg/hr also 18 hrs before planned surgery.

Application of TDS:

Patients were explained before application of patch. The TDS was applied in the infraclavicular area of contralateral side of MRM. The area was cleaned with spirit and a transparent adhesive film dressing was used to cover the patch and the patients were instructed to avoid heat exposure.

All patients were premedicated with tab alprozolam 0.25 mg orally night before surgery. On the morning of surgery Inj. Ranitidine 150 mg, Inj. Ondensetron 0.15 mg/kg and Inj. Glycopyrrolate 0.2 mg given 1/V one hour before induction of anaesthesia.

Intraoperative monitoring includes non-invasive blood pressure, ECG, Pulse oximetry, temperature and capnography. After preoxygenation, Inj. Midazolam 1 mg IV, Inj. Propofol 2 mg/kg, Inj. Fentanyl 2 µg/kg and Inj. Diclofenac 75mg in drip given. Succinylcholine (1.2 mg/kg) was given to facilitate tracheal intubation. Anaesthesia was maintained with 40% O_2 and 60% N_2O. Isoflurane, vecuronium as muscle relaxant. Patient was ventilated and end tidal CO_2 maintained between 35-40 mm hg.At the end of surgery patients were reversed with neostigmine 0.05mg/kg with glycopyrrolate 0.005 mg/kg.

After operation patient received Inj. Paracetomol 1 gm IV infusion .VAS score were measured every 8 hourly for 3 consecutive days. Similarly Ramsay score for sedation also measured. Any incidence of break through pain, sedation, nausea, vomiting and itching was noted. All patients were given injondensetron 0.15mg/kg at 8 AM on 3 consecutive days

Break through pain was treated with inj diclofenac 75 mg in infusion. If in case the VAS score was more than 5 or 6 ,2 hrs after injection diclofenac. Then extra rescue dose was given by inj tramadol 100mg slow iv.

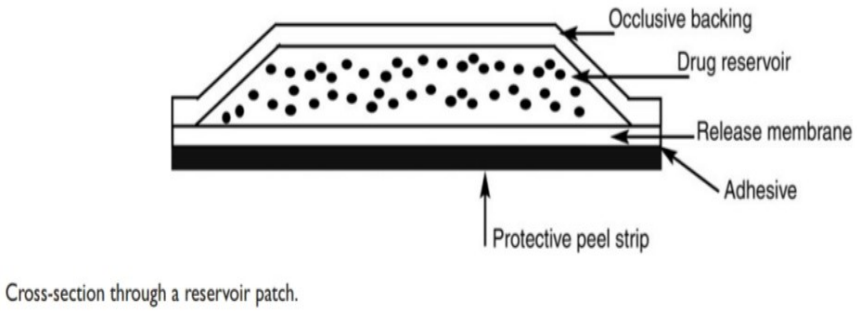

Figure 1: Cross section through a reservoir patch.

Results

All patients in both the study groups completed the study successfully. The demographic profile of age, weight and subtype of breast malignancies were comparable in both the groups. The VAS score in group A was mean 2.7 ± 0.92 SD and in group B was mean 2.93 ± 0.83 SD. The P value was 0.3135 and t=1.0167 which were statistically insignificant.

Thus the VAS score were comparable in both the groups.

Requirement of rescue dose in group A was mean 1.3±0.92 SD and in group B mean 1.53±0.90 SD. P value= 0.3317, t=0.9988 which was statistically also insignificant. Thus the requirement of rescue dose was comparable in both the groups.

No patient had complain of nausea, vomiting and itching. There was no complain of constipation in both the groups. Ramsay score was comparable in both the groups and was never more than 2. No patient needed extra rescue dose of inj. Tramadol in both the groups.

Statistics: The result was expressed as mean±standard deviation. P value was measured and students test was used for testing significance between the two study groups.

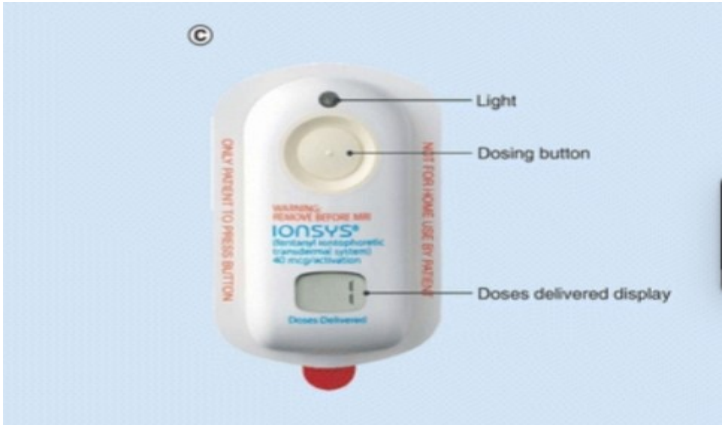

Figure 2: Fentanyl Iontophoretic Transdermal System.

Discussion

Transdermal drug delivery system offers a superior way to existing strategies for the systemic administration of analgesics. It avoids the peaks and trough of intermittent dosage regimes that can lead to side effects such as sedation, respiratory depression, nausea and vomiting. It also avoids frequent needle pricks thus improving patient compliance.

Background drug delivery via the transdermal route also by-passes first pass hepatic metabolism and circumvents common barriers to the use of oral analgesics immediately following surgery.

Drug transport across the skin occurs via stratum corneum. On applying the TDS to the skin a drug concentration gradient is developed and drug starts to move down the gradient. In this passive delivery system a second drug reservoir is created in the stratum corneum from here the drug is absorbed into the local capillary vasculature and is then transported into the systemic circulation.

There are three designs of trandermal patch currently available, the reservoir, the matrix system and iontophoretic transdermal system. Now a days for acute post operative pain relief iontophoretic fentanyl transdermal patch 40µg is used commonly, which in an active electronic device of the size of credit card. This is a patient control device (PCA) for delivering fixed amount of drug boluses but unfortunately it is not available in North India.

Although transdermal reservoir patch has been used in chronic pain management successfully [2] but TDS have also shown good results in post operative acute pain management if applied a day before operation, thus reducing the parentral opioid demand as compared to placebo [3, 4].

Fentanyl TDS are available in various concentrations12.5, 25, 50, 75 and 100 µg /hr. They are applied for 72 hours. After of application of TDS serum concentration increase gradually and levels between 12-24 hours and then decreases on second and third day due to decrease in concentration gradient. The delivery of fentanyl in affected by temperature [5].

Buprenophine transdermal patch is available in 5, 10, 20, 35 µg /hr strength. The effective plasma concentration peaks at 24 hour after application of patch but the effect continues even up to 30 hours after removed patch.

In our study we compared the efficacy of 25 µg/hr fentanyl patch with 20 µg/hr of buprenorhine patch and noted the VAS scores and number of rescue doses required. Due to pre-existing analgesic effect of perioperative period and continuous blood levels of fentanyl and buprenorhine the requirement of break through analgesia was low in both the groups and was comparable. The VAS score on day 1,2 and 3 were also comparable in both the groups.

Fentanyl is a well known potent analgesic. Buprenorphine is a partial agonist of mu receptor and its analgesic efficacy is comparable with the usual doses of other opiods such as pentazocine, morphine and pethidine.

In India due to restrictions in narcotic license fentanyl patch in not freely available in the market and hospitals. Efficacy of 25 µg/hr transdermal fentanyl patch can be compared with 20 µg TDS of buprenorphine in post operative period.

The minimal side effect observed in both the groups in our study justify the use of both types of patches in high risk cancer surgery like modified radical mastectomy.

Conclusion

Transdermal patch of 25 µg/hr of fentanyl and 20 µg/hr of buprenorphine applied 18 hours before surgery are good choice for postoperative analgesia in MRM. It can reduce the post operative rescue analgesic

consumption over a period of 52 hrs and maintain haemodynamic stability without any serious complications like sedation, respiratory depression or nausea vomiting.

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