Compliance for Transdermal Fentanyl Patch versus Sustained Release Oral Morphine in Cancer Pain

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ABSTRACT

Introduction: Cancer pain management is an art as it needs to be individualized according to the type and site of cancer and variability of response among patients to different pain medications and treatments. The emergence of the concept of 'total pain' alleviation emphasizes both on physical and psychological factors to improve the overall quality of life and decrease the work loss and disability. This study was done at a tertiary cancer care centre of North India.

Material and methods: 40 patients with moderate to severe cancer pain were randomized into two equal groups. Group-A received 75 µg/hr Fentanyl patches to be changed at 72 hours and Group B received 30 mg sustained release oral morphine tablet 12 hourly. This study was done on outdoor patient basis in patients having VAS scores >6 according to WHO regime. VAS, incidence of break through pain, compliance and adverse effect were noted. For breakthrough pain fixed dose of 10 mg immediate release morphine was used with 4 hr locking period. The study period was 12 weeks.

Results: Incidence of breakthrough pain and adverse effects were more in group B patients having VAS score >8. Compliance in fentanyl patch group was poor in patients who belong to low socio-economic status, villagers and illiterate.

Conclusion: Fentanyl patch provided better quality and intensity of analgesia with fewer adverse effect than morphine but compliance in villagers and illiterate patients was poor.

Keywords: Transdermal Fentanyl Patch, Oral Morphine, Cancer Pain

INTRODUCTION

Pain occurs in up to 70% of patient with advanced cancer. The management of pain is an essential aspect of comprehensive cancer care. The emergence of new, slow release dosage forms has simplified round the clock administration of maintenance pain therapy and has improved patient compliance and comfort. Patients can now benefit from the controlled release forms which can conventionally be given by oral and transdermal routes to relieve chronic pain.

In UP oral malignancies are common due to tobacco chewing. Fentanyl patch is the boon in late stages of oral and esophageal cancers where swallowing in a problem.[1]

The aim of this study was to determine the compliance, analgesic efficacy and side effects of transdermal fentanyl as compared to oral sustained release morphine for relief of moderate to severe pain.

MATERIAL AND METHODS

Clinical experience in palliative care has shown that optimal dose cannot be determined in advance and that it must be personalized for each patient. Thus we carried out a pilot study before our main study to titrate the right dose which provided adequate analgesia without opioid intoxication.

After obtaining institutional ethical committee approval and informed written consent from the patients. 40 patients with chronic moderate to severe pain were included in this prospective comparative study. Patients were randomized into two groups of 20 each. Group A received fentanyl patch 75 µg /hr every 72 hours and group B received oral sustained release tablet of morphine 30 mg 12 hourly.

Patients having hepatic and renal insufficiencies, true allergy, intolerance, nausea, vomiting, medical conditions which are likely to interfere with drug absorption were excluded from the study. Nonopioid analgesics such as nonsteroidal anti-inflammatory drugs acetaminophen, adjuvant drugs that had been part of the patients therapy as baseline were continued at the same fixed dose level throughout the study period (Table-1).

Pain score were measured on visual analogue pain scale and numerical scale. Patients having VAS between 6-8 were marked as moderate pain and VAS between 8-10 were marked as severe pain with VAS 10 as excruciating pain. Patient's compliance for drug and adverse effects were noted in both the groups.

Before application of fentanyl patch the hairs were clipped off (not shaved). The area was cleaned with spirit. The skin was allowed to completely dry before application of the patch. Patch can be applied at chest, back, flank or upper arm.

In our study patch was applied at fixed place i.e. on chest throughout the study. As the problem of adhesion exist so we used transparent adhesive film dressing. Patients were

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Drugs	Indications
Non-steroidal anti-inflammatory drugs (NSAIDs)	• Bone pain • Soft tissue filtration • Hepatomegaly
Corticosteroids	• Raised intracranial pressure • Soft tissue infiltration • Nerve compression • Hepatomegaly
Antidepressants and anticonvulsants	• Nerve compression or infiltration • Paraneoplastic neuropathies
Bisphosphonates	• Bone pain
Ketamine (specialist use only)	• Refractory pain • Neuropathic pain • Ischaemic limb pain

Table-1: Adjuvent analgesics for cancer pain

instructed to avoid direct heat exposure and hot baths. Patients receiving fentanyl were never exposed to morphine before.

Breakthrough pain

Breakthrough pain is a transitory severe acute pain that occurs on a background of chronic pain that is controlled by round the clock opioid regimen. The use of supplemental doses offered as needed in combination with a fixed scheduled opioid regimen, is known as rescue dosing.

Rescue dosing is usually done with immediate release morphine or transmucosal fentanyl lozenges. As we had no facility of transmucosal fentanyl, we used 10 mg morphine tablets for break through pain as the dose of rescue dose is calculated as 1/6th of the total daily dose of morphine. The locking period for rescue dose was fixed at 4 hours.

STATISTICAL ANALYSIS

The results were expressed as mean ± standard deviation. Student's 't' test was used for testing the significance between the two study groups.

RESULTS

All patients in both the study groups completed the study successfully. The demographic profile of age, sex, weight and the type of malignancies were comparable in both the groups. The main sites of malignancies were oral, breast, cervix, uterus, lungs, gallbladder and sarcomas.

The VAS score in group A was 0.75±0.78 which was significantly less than that in group B, 1.75± 0.71. P <0.0001. Requirement of rescue dose in group A was 0.35± 0.48 which was significantly less than that in group B 2.10 ±0.71, P < 0.0001.

6 out of 20 patients in fentanyl group showed poor compliance while in group II all the patients showed good compliance.

Intensity of constipation and drowsiness in group A was less than in group B rest of the side effects were comparable in both the groups.

DISCUSSION

Pain is a multifaceted sensation involving the entire nervous system. Pain occurs in up to 75% of patients with advanced cancer. Cancer pain especially caused by metastasis to bone is excruciating type.[2] Unrelieved or under relieved cancer pain is a cause of major suffering world-wide. Cancer pain may be due to tumor, surgery, radiotherapy, chemotherapy or metastasis.

The goal of chronic analgesic therapy is to achieve continuous suppression of pain. This requires administration of analgesics on a regular basis[3], the next dose to be given before the effects of the previous dose have finished. The continuous suppression of pain erases the memory and fear of pain as well as reduce anxiety associated with its anticipated return.

Sustained release oral and subcutaneous formulations are designed to maintain effective plasma drug levels throughout and have been shown to provide effective analgesia round the clock. Clinical experience in palliative care has shown that optimal dose cannot be determined in advance and that it must be personalized for each patient. Thus, we carried out a pilot study to titrate the right dose which provide adequate pain relief without opioid intoxication.

In the pilot study 25 µg /hr fentanyl patch which was equivalent to 60 mg of oral morphine and 50 µg /hr fentanyl patch equivalent to 135 mg of oral morphine did not relieve severe pain. As the adverse effects were tolerable so we tried 75 µg /hr patch which was almost equivalent to 225 mg of morphine and which relieved severe pain without much side effects.

Fentanyl is a synthetic opioid that acts on mu opioid receptors. Fentanyl is 80-100 times more potent than morphine Fentanyl is available as transdermal patch[4] and oral lozenzes. wadays fentanyl is the most widely used opioid for cancer pain. Fentanyl is highly lipophilic it diffuses across the skin and makes depot under the skin from where it is slowly released in blood. It takes 8-16 hours for the full effect of transdermal fentanyl patch.

Although there is interpatient variability but we used fixed dose of fentanyl patch i.e., 75 µg/hr as it was the only strength available in our hospital. The fentanyl patch is designed to release drug at a constant rate upto 72 hours. It may take 34-38 hrs to reach a maximum serum concentration of fentanyl and steady state is reached by 6th day. Studies show that extraneous heat application to fentanyl patch has increased systemic absorption of the drug.[5] So we advised our patients

not to do any outdoor activity in the sun, avoid hot baths and sunbaths.

As most of our patients were uneducated and belonged to low socio-economic status 6 out of 20 patients had poor compliance as they threw away the patches during bathing or patch came out due to sweating. Later on we used occlusive transparent dressing over the patch to improve skin adhesion and patients were educated and trained about the use of patch. The new patch was put in the same location.

In fentanyl group VAS and incidence of breakthrough pain was significantly less than in morphine group. P <0.0001 The incidence of breakthrough pain was more in morphine group where VAS was more than 8. The compliant patient in fentanyl group were more satisfied.[6] Constipation and drowsiness were the most common limiting adverse effects observed in our study. Constipation and drowsiness were found to be more prominent in morphine group then in fentanyl[6,7,8] group inspite of the fact that we used high dose of fentanyl which was equivalent to 225-314 mg of morphine. Except for the 6 illiterate patient compliance[6] was good in both the groups.

CONCLUSION

Fentanyl patch produced better pain relief for most patient with moderate to severe pain than with sustained release oral morphine. Fentanyl patch is particularly useful in patient having gastric intolerance, esophageal and oral cancers as the drug can be absorbed through the skin.

The ability of transdermal fentanyl to maintain a relatively steady serum concentration in the blood and the brain can lead to better control of cancer pain. It also decreases the need to take pain medication several times a day as patch can last for 3 days. The noted side effect like constipation and drowsiness were also less as compared to morphine. The poor compliance in illiterate patients can be overcome by education and awareness programme. Patients in fentanyl group were happier and satisfied and had less work loss days.

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