

# A Comparative Study of Transdermal Fentanyl Patch Vs Sustained Release Oral Morphine in Patients on Palliative Care in Sms Hospital with Special Reference to Bowel Function Discomfort

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## Abstract

**Objective:** The aim of study was to compare quality of life, side effects especially GI side effects and efficacy between transdermal fentanyl and oral morphine in palliative care.

**Materials and methods:** A hospital based prospective randomized observational study done on 240 eligible cases in Palliative care center, R.K. Birla cancer center, SMS hospital, Jaipur. In this study 240 cases of malignancies reporting in palliative care reported during one year of study period were put on oral morphine & transdermal fentanyl patch. EORTC\_QLQ\_C30 score was analyzed using paired -t test. Continuous data were expressed in the form of proportions.

**Results:** There was no statistically significant difference in EORTC global quality of life between transdermal fentanyl and oral morphine ( $P>0.05$ ). Fentanyl was associated decreased incidence of constipation ( $P<0.001$ ), no significant difference in nausea and vomiting ( $P>0.05$ ) compare to morphine. There was no significant difference in effectiveness of management for pain between both treatment groups.

**Conclusions:** we conclude that compared with oral morphine, fentanyl transdermal patch equally controls cancer pain and it has lesser side effects in term of constipation.

**Keywords:** Palliative care, transdermal fentanyl patch, sustained release oral morphine, side effects of opioids, cancer pain management

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## Introduction

Cancer is a major public health issue all around the world. A new study [1] in US suggested that cancer is second leading cause of death in the United States and it may replace to heart diseases as the leading cause of death in the coming years. About 6% of all deaths in India are due to

cancers which contribute to 8% of global cancer mortality [2]. Every patient of cancer having significant reduction in quality of life due to pain and side effects of pain treatment [3]. Cancer pain is one of the commonest reasons for visiting a doctor in palliative care.

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life threatening illness, through the prevention and relief of suffering by means of early identification, impeccable assessment and treatment of pain and their problems, physical, psychological and spiritual.

“Palliative care is a human right” was the theme for world palliative care day celebration for the year 2008, which stressed the importance of people dying without distressing symptoms including pain. Studies found that one million people suffer from cancer pain in India, but only 0.4 % of them are able to access oral morphine [4]. Despite the WHO and other local palliative care guidelines for cancer pain management, 50% of patient with cancer pain experience inadequate analgesia [5-6].

Opioids are the mainstay of management of cancer pain, providing effective pain relief [7-8]. Few strong opioids available in our country are morphine, buprenorphine pethidine, and fentanyl as oral, sublingual, and transdermal respectively.

Morphine is the standard opioid which is being used since years for the treatment of pain. A WHO guideline in 1986 recommended that morphine should be used for severe cancer pain management [9]. Many publications reported that severe constipation, a persistent complication of oral morphine may affect some patients' quality of life more than their pain [10]. Other significant side effects are nausea and vomiting, somnolence, urinary retention [3].

Fentanyl is a lipid soluble synthetic opioid. Low molecular weight and high lipid solubility makes it suitable for good skin absorption effect [11-13]. So fentanyl is available in the form of transdermal patch providing continuous and controlled systemic delivery up to 72 hours [12].

Studies suggested that transdermal fentanyl have analgesic efficacy in cancer pain [14-18] Side effects of fentanyl are constipation, nausea, vomiting and skin irritation. Some published study suggested respiratory depression occurs due to the long duration of blood concentration [19].

In moderate to severe cancer pain oral morphine is mostly used over fentanyl patch in palliative care settings. We conducted a study to compare quality of life, efficacy and side effects specially constipation of transdermal fentanyl patch with sustained release oral morphine in cancer pain management.

### Materials and Methods

This study was a Hospital based prospective randomized observational study. This study was done in Palliative care center, R.K. Birla cancer center, SMS hospital, Jaipur after approval from ethics committee. Patients with cancer pain who were not getting relief by tramadol with analgesics and were receiving 10mg every 4 hourly stable dose of morphine since last 48 hours were invited to our study. The written informed consent was taken after explaining the trial. Patients with deranged RFT, LFT and altered sensorium were excluded out in study.

240 patients in Sample size were required as 120 in each group at 95% confidence and 80% power to verify the minimum expected difference. Randomization was done in two groups using computerized random number table. Blinding was not possible as transdermal patch was visible.

Intention to treat concept was followed in the entire study. Cases were considered in the same initial group irrespective of dropout or change of treatment etc.

In those two groups one was getting sustained release oral morphine 30mg BD and another one was on fentanyl patch 25mcg/hr. Both groups were given treatment for 14 days. Each patch was changed every 72hourly. Conversion ratio

for oral morphine to transdermal fentanyl was 100:1. Immediate release morphine was used for break through pain in both groups.

Baseline clinical characteristics including demographic, clinical and biochemical data were collected at first visit. Patients were given EORTC QLQ C-30 questionnaire to be filled up by themselves at day 1 and day 14.

This questionnaire is extensively used in cancer patients for quality of life, side effects and functional score assessment. Continuous follow up was done up to day 14 for patient’s complaints and treatment compliance. Patients at day 14 reevaluated for his/her complaints for further treatment plan and were offered to complete same questionnaire on same day for evaluation of quality of life, side effects and functional score assessment.

All the original individual score as well as overall scores were converted to a scale of 0-100 as per the EORTC module8s. All scores were expressed as mean and standard deviation. For functioning scales, a higher score indicates better function whereas on other hand other scale’s higher

score indicates a worse problem. Change in scores before and after therapy was analyzed using paired t test. A p value < 0.05 was taken as statistically significant.

**Results**

In our study the maximum number of patients i.e. 27.5% in morphine group & 30% in transdermal fentanyl group were seen in 40-49 years of age group.

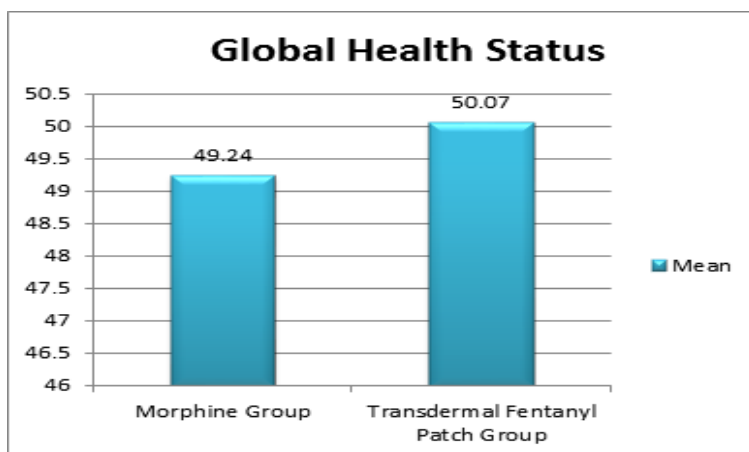
Male to female ratio was 1.72:1 in morphine group & 1.55:1 in transdermal fentanyl group. Most patients were having malignancy of oral cavity (35.83%) in morphine group & 30.83% in transdermal fentanyl group.

**Quality of Life/Global health status**

The EORTC questionnaire revealed both treatments showing significant improvement in global health status/ Quality of Life. But when both treatments were compared with each other it was found that there was no significant difference in quality of life, thus showing both treatments are equally efficacious to improve quality of life. [table 1] & [figure 1]

**Table 1: Comparison of global health status / Quality of life score morphine & transdermal fentanyl patch group after therapy**

Global health status	Morphine group	transdermal fentanyl patch group	Difference of mean	P-value
Mean±SD	49.24±11.59	50.07±10.05	0.833±1.400	0.5522 NS



**Figure 1: Comparison of global health status / Quality of life score morphine & transdermal fentanyl patch group after therapy**

**Analgesic Efficacy**

Pain control was assessed using EORTC questionnaire revealed no significant difference were detected between the transdermal fentanyl and oral morphine [table 2]. This result showed that transdermal fentanyl had similar analgesic efficacy when compared with oral morphine. [Figure 2]

**Constipation and Nausea-Vomiting**

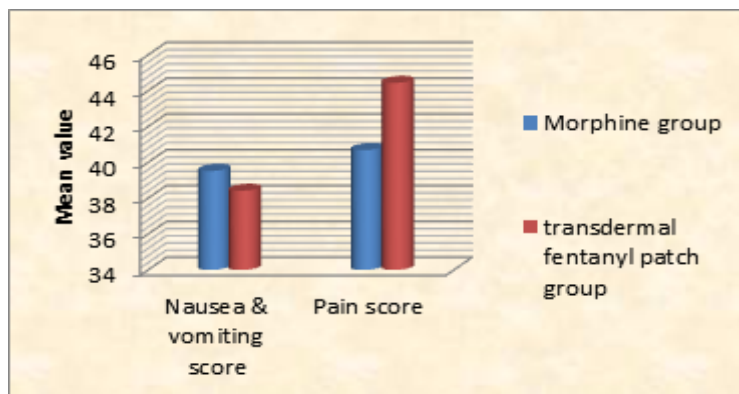
In our study incidence and degree of nausea & vomiting were similar between

transdermal fentanyl patch and oral morphine both [table 2].

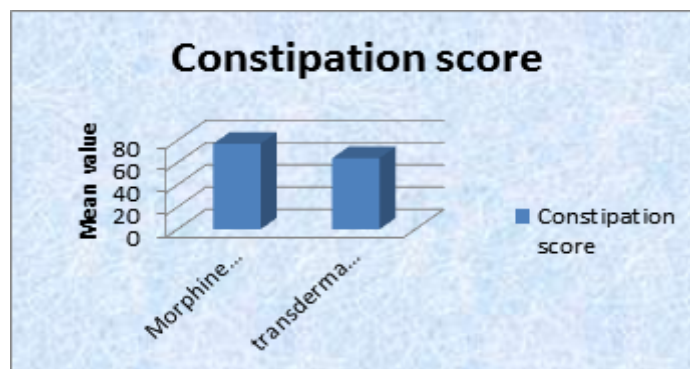
There was a significant difference in incidence of constipation with use of transdermal fentanyl patch compared to oral morphine. The mean constipation score after morphine therapy was 76.94±21.95, which decreased to 63.92±20.13 after transdermal fentanyl patch therapy. The comparison of mean was found to be statistically significant (P=0.0001). [Figure 3]

**Table 2: Comparison of Symptoms score morphine & transdermal fentanyl patch group after therapy**

Symptoms Score	Morphine group	transdermal fentanyl patch group	Difference of mean	P-value
Constipation score	76.94±21.95	63.92±20.13	13.02±2.113	0.0001
Nausea & vomiting score	39.53±17.45	38.42±15.32	1.111±2.312	0.6473
Pain score	40.69±16.14	44.44±14.22	3.750±1.964	0.0574



**Figure 2: Comparison of Pain score and nausea & vomiting score morphine & transdermal fentanyl patch group after therapy**



**Figure 3: Comparison of constipation score morphine & transdermal fentanyl patch group after therapy**

## Discussion

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life threatening illness, through the prevention and relief of suffering by means of early identification, impeccable assessment and treatment of pain and their problems, physical, psychological and spiritual.

Quality of life refers to the level of health, happiness and comfort you experience in life. Maximizing quality of life during cancer treatment involves responding to the physical, emotional and mental well-being of cancer patients. Maximizing quality of life for cancer patients means that cancer treatment is focused on treating both the disease and the person.

Transdermal fentanyl patch equally effective to improve quality of life compare to oral morphine. These results support that the QLQ-C30 is a reliable and valid measure of quality of life in cancer patients receiving cancer pain management. In a Korean study done by Kaasa and Loge et al found that the EORTC QLQ-C30 can be used effectively in the palliative care settings in order to assess the effects of cancer pain management on quality of life of advanced-stage cancer patients [20].

Pain in cancer patients significantly impact on quality of life so pain control itself improves quality of life in patients suffering from malignancy. Transdermal fentanyl patch and oral morphine are equally effective for the treatment of cancer pain [21-25], and both are first line management in palliative care centers across the world. Wang DD et al [26] found no statistically significant difference with regard to the effectiveness of management for cancer pain between the use of transdermal fentanyl patch and oral morphine. This is consistent with our study. In this total of 35 studies involving

3406 participants met the inclusion criteria for meta-analysis and made reliable conclusions.

There was a significant difference in incidence of constipation with use of transdermal fentanyl patch compared to oral morphine. Sam Ahmedzai [17] found fentanyl treatment was associated with significantly less constipation than morphine.

A trial by Donner et al [15] also found that patients receiving fentanyl suffered less constipation and required fewer laxatives than when taking morphine. Ludo Haazen et al [27] found low incidence of gastrointestinal side effects compared to transdermal fentanyl with oral morphine. The more favorable constipation and analgesia ratio of fentanyl relative to morphine was found. [28]

In our study incidence and degree of nausea & vomiting were similar between transdermal fentanyl patch and oral morphine both. This is consistent with Sam Ahmedzai<sup>17</sup> study which suggested that nausea & vomiting, dyspnoea, appetite loss, and diarrhea were not significant between the two treatment groups.

## Conclusion

Based on this study we conclude that compared with oral morphine, fentanyl transdermal patch equally controls cancer pain and it has lesser side effects in term of constipation.

Palliative care is a very important modality to enhance quality of life cancer patients. Early implementation of palliative care improves the standard of life, alleviates co-existing symptoms, improves quality of life, gives pain relief, and improves functioning within the family.

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