Research Article

Comparison of Diclofenac Transdermal Patches versus Extended Release Tablets of Tramadol in Pain Management of Cancer Patients

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ABSTRACT

The study aims the comparison of the effect of diclofenac transdermal patches 100mcg and extended release tablets of tramadol 100mg in pain management of cancer patients. A prospective observational comparative study was carried out in 40 patients at a multi-specialty hospital in Tamil Nadu for nine months using a well-structured proforma. The pain intensity level of the patient was assessed, which showed a significant difference and the comparison of patient satisfaction score of diclofenac was 70% and tramadol 80%. The pain relief score was also determined, diclofenac showed 55% and tramadol 60%. It was concluded that tramadol extended release 100mg tablets were more effective in reducing severe cancer pain while diclofenac 100mcg transdermal patches subsides mild to moderate pain.

Keywords: Cancer, Diclofenac transdermal patches, Tramadol extended release tablets, Pain.

INTRODUCTION

Cancer is one of the leading causes of death in the world, particularly in developing countries. In 2012, approximately 14 million new cases and 8.2 million cancer related deaths.[1] About 1,685,210 new cancer cases are expected to be diagnosed in 2016.[2] Cancer is a class of disorders or diseases characterized by uncontrolled division of cells and the ability of these cells to invade other tissues, either by direct growth or by implantation in distant site by metastasis. This unregulated growth is caused by damage to DNA, resulting in mutations to genes that encode for proteins controlling cell division. Many mutation events may be required to transform a normal cell into a malignant cell. These mutations can be caused by chemicals or physical agents called carcinogens, by close exposure to radioactive materials, or by certain viruses that can insert their DNA into the human genome. Mutations occur spontaneously, or are passed down generations as a result of germ line mutations.[3] Many forms of cancer associated with exposure to environmental factors such as tobacco chewing, tobacco smoking, radiation, alcohol and certain viruses.[4]

Pain management is one of the objective of palliative care where pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.[5,6] It is estimated that 70% - 90% of patients with advanced cancer experience significant cancer pain.

Pain in cancer can be grouped into four causal categories: Cancer itself (soft tissue, visceral, bone, neuropathic, metastatic), Treatment related (mucositis, postoperative syndromes, radiation induced), Debility (constipation, muscle spasm/tension), Concurrent disorder (spondylosis, osteo – arthritis).[7]

Acute pain comes on abruptly and generally lasts for a short period of time. **Chronic pain** lasts for longer than the healing time of an injury. Most cancer pain can be classified as chronic pain. Chronic pain can be broken up into a few different categories as well:

- Intermittent pain is long term chronic pain that comes and goes. It may occur in waves or patterns, and is generally treated with short acting narcotics.
- *Persistent pain* lasts 12 hours a day or more every day for more than three months. Persistent pain is usually treated with long acting pain medications that treat the pain all day long.
- Breakthrough pain comes on suddenly above and beyond the medicine you use to treat persistent pain. Breakthrough pain may happen several times a day or be associated with certain activities. Breakthrough pain is usually treated with short acting narcotics.

Types of pain includes: Nerve pain, Bone pain, Soft tissue pain, Phantom pain, Referred pain.[8] Pain can be managed by non-opiods and opiods. Non–opiods control mild to moderate pain. It includes NSAIDs (aspirin, ibuprofen, ketoprofen, naproxen sodium, diclofenac, indomethacin). These medicines are used alone or with non-opioids to treat moderate to severe pain.

Opioids are much like natural substances (called endorphins) produced by the body to control pain. Hydromorphone codeine, levorphanol, methadone morphine, oxycodone, meperidine, oxymorphone, fentanyl, Tramadol. Adjuvant drugs commonly used to relieve cancer pain are antidepressants, antihistamines, anti anxiety drugs, anticonvulsants, steroids, stimulants

and amphetamines.[9] Tramadol, a centrally-acting analgesic has a higher affinity to bind with opioid receptors to inhibit the uptake of norepinephrine and serotonin, suggesting that its antinociception activity. Diclofenac responsible for its anti-inflammatory/antipyretic/analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX).[10]

MATERIALS AND METHODS

A prospective observational comparative study was carried out in 40 patients at a multi-specialty hospital in Tamil Nadu for 9 months. A well-structured pro-forma was adopted which includes demographic details, diagnosis, present and past medical/medication history, pain intensity scale[11], pain relief scale[12], patient satisfaction scale[13], pain management index by Cleeland.[14]

Patient Inclusion Criteria

- Patient who was diagnosed as cancer and pain related to cancer
- Pain related to cancer therapy
- Both genders
- Age above 20 years

Patient Exclusion Criteria:

- Pregnant or lactating women
- Previous history of allergy to NSAID's
- Peptic ulcer patients
- Non – Solid tumours
- Surgery

The patients who satisfied our inclusion criteria were included in the study after obtaining the consent form. The data collected from patients through the designed data entry format by the regular ward rounds were thoroughly assessed and analyzed by using Student t Test.

RESULTS AND DISCUSSION

This study was designed to compare the effect of Diclofenac transdermal patches 100mcg versus extended release tablets of Tramadol 100mg in pain management of cancer patients.

In this study 40 cancer patients were selected on the basis of inclusion and exclusion criteria.

Out of 40 patients 20 patients were treated with diclofenac transdermal patches100 mcg (Group A) and 20 patients were treated extended release tablets of tramadol 100mg (Group B).

At the time of diagnosis, the initial pain intensity were taken as base and followed by three days (1st day, 2nd day, 3rd day) and were categorized into no pain, mild, moderate and severe pain. Pain relief and patient satisfaction management were taken at the end of 3rd day. Pain management score were calculated on the basis of Cleeland's pain management index by using patient's pain intensity and analgesics prescribed.[14]

Of all patients, 19 were male (48%) and 21 were female (52%). The analysis revealed that the distribution of the study population between the age of 31-40 years were 2 patients (5%), 41-50 years were 5 patients (12.5%), 51-60 years were 14 patients (35%), 61-70 years were 17 patients (42.5%),and 71-80 were 2 patients(5%). The social status of study population revealed that 17 patients were smokers, 12 patients were alcoholics, 8 patients were found to have habituation of tobacco usage and 6 were found to be chewing pan masala.

The total cases were categorized based on the diagnosis as in Table 1.

Type of cancer treatment received among the 40 patients included 18 patients (45%) on chemotherapy, 20 patients (50%) receiving radiation therapy, and 2 patients (5%) receiving radiation therapy and chemotherapy.

The pain located in the study population was head face, mouth, breast and thoracic region, abdominal region, lower limbs, anal canal, cervix and genital region, around neck and ears as described in Table 2.

The patients treated with diclofenac transdermal patches (group A) have shown decreasing effect of pain intensity from mean of 5.3500 (±0.3925) to 1.5990 (±2723) Table 7. The patients treated with extended release tablets of Tramadol (Group B) have shown decreasing effect of pain intensity from mean of 7.8500 (± 0.1957) to mean of 2.2170 (±0.2279).

Table 8: Both the groups were found to be extremely statically significant. The pain intensity level of both the groups shown in Table 3 and 4.

The pain intensity level of both groups were compared and tabulated in Table 5.

Table 1: Type of Cancer among the Patients

Type of Cancer	Number of Patients	Percentage (%)
Cervix	7	17.5
Tongue	5	12.5
Stomach	3	7.5
Anal Canal	1	2.5
Neck	6	15
Uterus	3	7.5
Breast	4	10
Maxilla	1	2.5
Mouth	2	5
Lower limbs	2	5
Oropharynx	4	10
Hypopharynx	2	5

Table 2: Pain Location

Pain Location	Number of Patients (n=40)	Percentage (%)
Head, Face, mouth	3	7.5
Breast, thoracic region	4	10
Abdominal region	6	15
Lower limbs	2	5
Anal canal, cervix and genital region	8	20
Around neck and ears	17	42.5

Pain Intensity Measurements

Table 3: Pain intensity in patients receiving diclofenac transdermal patches 100 mcg (Group A)

Patient ID	Pain intensity base	I day	II day	III day
A1	3	2.67	1.67	0.33
A2	5	2.0	1.67	1.0
A3	4	3.67	2.0	1.0
A4	5	3.0	2.67	2.0
A5	3	2.67	2.0	1.67
A6	6	5.0	4.33	2.0
A7	8	7.3	6.3	4.67
A8	4	3.67	2.67	0.67
A9	3	2.0	1.33	1.0
A10	5	2.67	3.0	1.33
A11	7	6.3	4.67	1.3
A12	6	4.67	3.0	0.67
A13	8	6.67	5.0	3.0
A14	5	2.0	1.0	1.0
A15	4	3.0	2.67	1.0
A16	7	6.67	4.0	2.0
A17	3	2.0	1.0	0.67
A18	6	5.0	4.0	1.0
A19	8	7.67	6.0	4.67
A20	7	6.0	4.0	1.0
Mean ± STDE	5.3500 ± 0.3925	4.2315 ± 0.4377	3.1475 ± 0.3545	1.5990 ± 0.2723
P-Value				<0.0001

Table 4: Pain intensity in patients receiving extended release tablets of tramadol 100 mg (Group B)

Patient ID	Pain intensity base	I day	II day	III day
B1	8	6.67	5.0	3.0
B2	7	6.3	4.67	2.3
B3	8	7.67	5.0	2.67
B4	8	6.67	5.0	4.3
B5	7	6.67	4.0	2.0
B6	8	5.67	3.3	1.0
B7	6	4.67	4.0	3.0

B8	9	6.0	3.67	1.3
B9	8	5.0	3.67	2.0
B10	8	7.67	6.0	4.67
B11	6	5.0	3.67	1.3
B12	8	7.3	5.67	3.0
B13	8	6.3	4.67	1.0
B14	9	6.0	4.0	2.3
B15	8	5.0	3.0	1.3
B16	9	6.0	4.0	2.0
B17	8	6.67	5.67	2.3
B18	7	6.67	4.0	1.3
B19	8	7.3	5.0	2.3
B20	9	6.0	3.67	1.3
Mean ± STDE	7.8500 ± 0.1957	6.2615 ± 0.1980	4.3830 ± 0.1883	2.2170 ± 0.1279
P-Value				0.0001

Table 5: Comparison of pain intensity level in patients receiving diclofenac transdermal patches 100mcg and extended release tablets of tramadol 100 mg

Pain Intensity Level	Diclofenac Transdermal Patches 100 mcg Number of patients (n=20)		Extended Release Tablets of Tramadol 100 mg Number of patients (n=20)	
	At base	After 3 days	At base	After 3 days
No pain	0	0	0	0
Mild pain	4	18	0	18
Moderate pain	10	2	2	2
Severe pain	6	0	18	0

Table 6: Comparison of pain relief score among the patients receiving diclofenac transdermal patches and extended release tablets of tramadol

Response	Diclofenac Transdermal Patches (n=20)	Percentage (%)	Extended release tablets of Tramadol (n=20)	Percentage (%)
Complete Relief	11	55	12	60
Strong Relief	6	30	6	30
Moderate Relief	3	15	2	10
Slight Relief	0	0	0	0
No Relief	0	0	0	0
Worsening pain	0	0	0	0

Table 7: Comparison of patient satisfaction score receiving diclofenac transdermal patches and tramadol extended release tablets

Response	Diclofenac Transdermal Patches (n=20)	Percentage (%)	Extended release tablets of Tramadol (n=20)	Percentage (%)
Very satisfied	14	70	16	80
Somewhat Satisfied	3	15	4	20
Satisfied nor dissatisfied	3	15	0	0
Dissatisfied	0	0	0	0
Very dissatisfied	0	0	0	0

Pain Relief Score and Patient Satisfaction Scale

Pain relief score among the patients in both group A and B were compared in Table 6.

The comparisons of patient satisfaction score between the two groups were also done and the results are represented in Table 7.

Pain Management Index

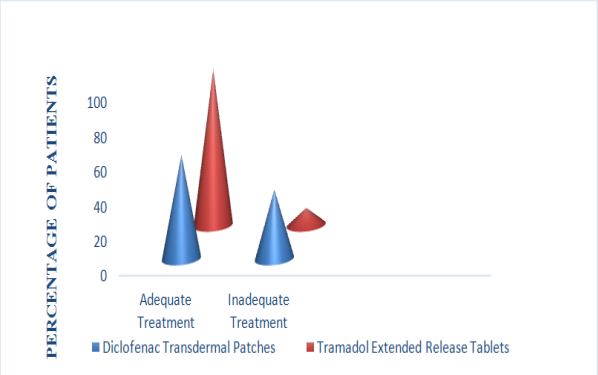

Figure 1: Comparison of pain management index of diclofenac transdermal patches and tramadol extended release tablets.

Pain management index were calculated for each patient to determine whether they received adequate treatment or not as per Figure 1.

Similar study was conducted by McNeil, in pain management outcomes for hospitalized Hispanic patients and concluded pain management index scores revealed 36% of the participants inadequately treated for pain.[13] McNicol says that NSAIDs appears to be more effective than placebo for cancer pain while Daniel proposed that tramadol is effective in the treatment of neuropathic cancer pain and appears to improve the quality of life in the cancer patients.[15,16]

Grond suggested that tramadol can be used for the treatment of cancer pain, when non-opiods alone are not effective. High doses of tramadol are effective and safe.[17] Maltoni recommended that pain is treated during active therapy by the patients' oncologists in collobration with a palliative care specialist.[18]

CONCLUSION

From the results of our study, we found that there was a significant variation in the pain intensity level while using diclofenac transdermal patches 100mcg and extended release tablets of tramadol 100mg.

The pain relief score obtained from the patients of both group depicted a slight increase in the efficacy of tramadol to reduce the pain. The patient satisfaction score documented at the end of the third day showed a greater satisfaction with the use of tramadol extended release tablet 100 mg.

Here comes the role of clinical pharmacist to evolve and implement the algorithmic treatment to reduce pain from non-opioids to strong opioids and to determine the appropriate dose for the analgesics used for the pain management to improve the pharmaceutical care, hasten the patient pain relief, and thus improve the quality of life.

Inadequately treated pain results in less pain relief and greater pain-related impairment of function.

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