Case study

COMPARING THE THERAPEUTIC EFFICACY OF TRANSDERMAL PATCHES OF KETOPROFEN WITH THAT OF FENTANYL IN PAIN CONTROL IN POST-OPERATIVE PATIENTS OTHER THAN SPINE SURGERY: A CASE REPORT

Abstract:

Background: After surgery, many patients will not get recovered from the symptoms as soon because the therapeutic efficacy of drug in patient may differ. The current case report objective is to compare therapeutic efficacy of two patches that are ketoprofen and fentanyl in post-operative patients.

Case presentation: We present a case report on extent of pain relief comparison with visual analog scale scores (VAS score) by studying ketoprofen transdermal patch and fentanyl transdermal patch to the patients after the post-operative surgery other than spine surgery. The subjects are divided into two groups which includes male and female gender and the treatment was continued up to three days.

Conclusion: After complete study, we concluded that the subjects group received ketoprofen therapy was found with highest VAS score when compared to that of fentanyl therapy and the complete reduction of pain was observed in three days. The statistical analysis was appeared as highly significant.

Keywords: Pain, Patch, Therapeutic efficacy, VAS score

UNDER PEER REVIEW

Introduction:

Pain, it's a vital function of the nervous system in providing the body with a warning of potential or actual injury. It is both a sensory and emotional experience affected by psychological factors, such as past experience beliefs about pain, fear or anxiety [1]. Undertreated pain has significant physical psychological, and financial consequences [2]. Recently introduced joint commission was introduced on accreditation of health care organizations (JCAHO) standards for pain assessment and management represents a giant step forward in improving pain management. Despite of this, a world-scale epidemiology report of 2008 produced by Tsang et al. shows an age-standardized prevalence of chronic pain conditions in the previous 12 months of 37.3% in developed countries and 41.1% in developing countries, with an overall prevalence of 38.4% [3].

A 2006 study state that approximately 20% of the adult European population was having chronic pain with fewer than 2% of sufferers ever attend a pain clinic and one-third of the chronic pain sufferers were currently not being treated [4]. There is not a clear relationship between age and onset of pain conditions [5-6], but generally speaking, there is a higher prevalence of chronic pain in older age [7]. Regarding this, recent studies have found that pain remains a prevalent and serious problem in older age, the prevalence of chronic pain in older people (>65 years) living in the community ranges from 25.0% to 76.0%, while the prevalence of chronic pain in older people living in residential care is much higher and ranges from 83.0% to 93.0% [7]. Medications used for pain management have various purposes. As part of a comprehensive pain management plan, a MAPS physician (a pain medication specialist) may prescribe one or more of the pain management medications described as opioids, hydrocodone and morphine etc., Nonsteroidal anti-inflammatory drugs like aspirin and ibuprofen etc., many literature reviews are available with respect to pain but the current research was stating few literature reports those are Langford and Richard, et al. (2006) studied on transdermal application of fentanyl for improvement of pain and functioning in osteoarthritis. Strong Opioids have been used to successfully treat several types of noncancer pain but have rarely been tested in controlled studies. They tested the effects of transdermal Fentanyl (TDF) in patients with moderate to-severe osteoarthritic (OA) pain, in a placebo-controlled study. Cohort studies comprised of patients with radiologic ally confirmed OA of the hip or knee requiring joint replacement and with moderate-to-severe pain that had been inadequately controlled. The patients were randomized to receive TDF or placebo for 6 weeks after a 1-week pretreatment run-in phase. Patients treated with NSAIDs and simple analgesics were continued, but weak Opioids were discontinued. Pain was recorded on a visual analog scale (VAS), and function was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The results of these studies suggest that TDF may be better tolerated than oral strong Opioids, particularly because TDF causes less constipation [8]. Reetu verma et al., (2016) conducted study on transdermal patches of diclofenac and ketoprofen for postoperative analgesia in lower limb orthopaedic surgery compared the efficacy and safety of transdermal patches of both the drugs in a randomized single blind study by assessing the pain with VAS score. Study concluded that transdermal patch of ketoprofen and diclofenac both are effective for post-operative analgesia in lower limb orthopedic surgery under spinal anesthesia

but in diclofenac more patients required rescue analgesic as compared to ketoprofen group [9]. Esmat et al., (2016) reported on a study evaluated the efficacy of transdermal Fentanyl (TDF) delivery system or transdermal melatonin (TDM) delivery system preoperatively for acute postoperative pain after lumbar laminectomy compared to placebo group. There was a significant reduction in the visual analogue scale (VAS) score, total pethidine requirements and significantly higher patient‘s satisfaction in TDF and TDM groups when compared with the C group 6 h postoperatively. The sedation score and surgeons‘satisfaction was significantly higher associated with a significant decrease in MAP and intraoperative bleeding in TDM group compared to groups C and TDF 6 h postoperatively [10]. Aim of the current work is to observe the efficacy and safety of transdermal patches of ketoprofen compared to that of fentanyl in pain control in post-operative patients other than spine surgery.

Case presentation

The work focused on the development of randomized study design which is interventional, prospective, cohort and parallel type of design. It is an interventional because, post-operative patients, who are recruited into the study, are assigned to a particular treatment, intentionally, to determine the effect of the therapy being used. It would be a parallel design because one group receives only treatment. And the other group receives only treatment B. It would be a cohort and prospective study because a group of patients having a common characteristic are being recruited into the study and are being studied over a period of time starting from the present and going six months into future. The present study was carried out in the orthopaedics department of King George Hospital at Visakhapatnam, Andhra Pradesh, India. It is a 1300 bedded hospital with an occupancy rate of 100 percent. Study criteria was classified into inclusion and exclusion criteria.

Inclusion criteria includes

Post-operative patients other than spine surgery of age above 18 years are selected those are belongs to orthopaedics Department of King George Hospital, Visakhapatnam. The primary concerns for the study are subjects must give informed consent, male as well as female patients can be selected and those must be capable of proper compliance.

Exclusion criteria includes

UNDER PEER REVIEW

If the subjects had been suffering/not willing to participate in the study, subjects who suffer with past or current history of chronic inflammatory diseases (e.g.: Gout, Reactive arthritis or Psoriatic arthritis), other autoimmune rheumatic diseases (e.g.: Systemic lupus erythematosus, mixed connective tissue disease, scleroderma or polymyositis), neuropsychiatric disorders (e.g.: Fibromyalgia), subjects with other health problems like asthma, COPD, evidence of GIT, Renal diseases, hypotension, evidence of impaired liver functions and pregnant or lactating women.

Study procedure involves

Initial submission of protocol and obtaining the permission of the institutional ethics committee in King George Hospital, Visakhapatnam. Enlisting the patients into the study as per the inclusion criteria. A cohort group would be selected. A cohort group is a group with common characteristics. Baseline data such as age, sex, weight, height, job, marital state, occupational habits and education were taken from all the participants in the study. To conduct cohort study, subjects would be divided into two groups each consisting of 30 subjects. group 1(ODD) would start treatment with ketoprofen transdermal patch and group 2(EVEN) would receive treatment with Fentanyl transdermal patch respectively. After starting the treatment with transdermal patches of ketoprofen and Fentanyl, Assessment of pain is done by using Visual Analog Scale (VAS), Western Ontaric and McMaster Universities Osteoarthritis Index (WOMAC), helps in estimating the neurophysiologic and psychological domains of pain. The subject's data would be analyzed by using standard statistical tools.

Statistical Methods

Data was analyzed using the graph pad software. Descriptive statistics (mean, standard deviation, standard error of mean), students t-test were used in the study.

Discussion:

In the present case report the effect of ketoprofen transdermal patch was compared with fentanyl transdermal patch. group 1 received a dose of ketoprofen of 20 mg whereas group 2 received fentanyl 1.25 after the post-operative surgery other than spine surgery. The extent of pain relief was compared with VAS scores. Two groups of patients each containing 30 subjects received above the treatment, group 1 received the ketoprofen 20 mg therapy and received the fentanyl 1.25 mg therapy. Both the groups contain different age groups of both male and female and the results are presented in the following Table 1, shows the VAS score of group 1 treated with the ketoprofen therapy Table 2 shows the VAS scores of group 2 treated with fentanyl therapy

UNDER PEER REVIEW

scores reached particular low level value compared. The study was continued for three days. It was observed group 1 who received the ketoprofen therapy indicated highest VAS score when compared to that of fentanyl therapy. The VAS score was compared using the student t-test and the significance difference was observed between the two groups. Hence it was concluded that group 2 therapy was more useful compared to group 1. As the two groups contain different age groups, the effect of combination therapy was assessed on different age groups of all the 30 subjects involved in each group divided into different age groups of 18-38, 38-58 and 58-78 years and the data was presented in the form of histograms in (Fig 1, 2, 3and 4). It was observed that the first group where the age group is between 18-38 there is a significant difference between the VAS score of the first and second group t-test is significantly different from each group. It was observed that in the second group where the age group is between 38-58 there is a significant difference between the VAS group of the first and second group, as the t-test is significant different from each other it was observed that the third group where the age group is between 58-78 years significantly difference between the VAS score of the first and second group, as the t-test is significantly different from each other. Hence in the light of above results it was observed that there was significant difference in the total volunteers of group 1 and group 2. Hence it was concluded that 38-58 years age people showed a good effect than the other age groups. It was observed that the treatment with fentanyl therapy is recommended compared to ketoprofen therapy to avoid any further side effects to be caused to patients.

The study was done with VAS and WOMAC scale to measure the intensity of the pain, however patient response for the WOMAC scale is not encouraged as they were not able to differentiate the questionnaire of WOMAC scale hence further use of WOMAC scale was not used in the present study thus intensity of pain was measured with VAS scale.

Table.1: VAS score of group 1 treated with the ketoprofen therapy

Subject	Age& Sex	Ketoprofen Dose	Baseline	Day Wise VAS Score of each subject		
				Day 1	Day 3	Day 6
P1	38-M	20mg	9	7.3	6	4
P3	22-M	20mg	9	7.1	6	3.5
P5	65-M	20mg	8.5	7.6	6	5
P7	18-M	20mg	9	7.9	6	5.5
P9	32-M	20mg	8.5	6.8	5	4.5
P11	50-M	20mg	8	7	6.5	5
P13	45-F	20mg	9.5	8.2	6	4

UNDER PEER REVIEW

P15	41-M	20mg	9	7.8	6	5
P17	18-F	20mg	9	7	6	4.3
P19	22-F	20mg	9	7	6	4
P21	54-F	20mg	9	8	7.6	5
P23	31-M	20mg	8	6	4.5	2.9
P25	27-M	20mg	9	8	7	5
P27	35-M	20mg	9	8.5	7	6
P29	45-M	20mg	8	7	6	5
P31	36-M	20mg	8	7	6	4.5
P33	24-M	20mg	8.8	6.8	5.8	3.9
P35	60-F	20mg	8.5	8	7	6
P37	32-M	20mg	6.5	6	5	3.4
P39	42-M	20mg	7	6	5	3
P41	29-M	20mg	7	6	6	5.1
P43	45-M	20mg	9	8	7	6
P45	53-M	20mg	9.5	8	7.5	5
P47	60-F	20mg	7	6	5	4
P49	28-M	20mg	8	7	6	6
P51	21-M	20mg	8	7.5	7	6.5
P53	18-M	20mg	9	8	7	4.5
P55	22-M	20mg	7	6	4	3
P57	27-M	20mg	9	7.5	6	5
P59	48-M	20mg	8	75	6.5	5.5
Mean ± Standard deviation				6.59 ± 1.6214		

Table. 2: VAS scores of group 2 treated with fentanyl therapy

Subject	Age & Sex	Fentanyl Dose	Base line	Day wise VAS score of each subject		
				Day 1	Day 3	Day 6
P2	44-M	1.25mg	9	6	3	1.5
P4	18-M	1.25mg	7	6	5.5	3.2
P6	40-F	1.25mg	8.7	6	4	2
P8	42-M	1.25mg	9	7.5	5	3
P10	35-M	1.25mg	9	6.8	4	2
P12	36-M	1.25mg	8	5.5	3	1
P14	42-M	1.25mg	9.5	7	3	2
P16	63-F	1.25mg	8	6	4	2.5
P18	42-M	1.25mg	9	7	3.5	1
P20	20-M	1.25mg	9.5	7	5	1
P22	25-M	1.25mg	8.5	7	6	3
P24	29-M	1.25mg	9	6	4	2
P26	38-M	1.25mg	9.5	6	4	2
P28	20-M	1.25mg	9	7	4	1
P30	34-M	1.25mg	9	6	4.5	2

UNDER PEER REVIEW

P32	30-M	1.25mg	8	6	5	1.5
P34	42-M	1.25mg	9	8	5	2
P36	24-M	1.25mg	8.5	7	4	2
P38	30-M	1.25mg	9	8	6.5	2.4
P40	22-M	1.25mg	9	8	5	3
P42	40-M	1.25mg	9	6	4	3
P44	45-M	1.25mg	8.5	7.5	4	2
P46	33-M	1.25mg	8	6.4	4	3
P48	27-M	1.25mg	9	4.5	3	1.5
P50	45-M	1.25mg	9	7.5	6	4
P52	20-M	1.25mg	8	7	6	2.5
P54	65-F	1.25mg	7.7	6	4	2
P56	26-F	1.25mg	6.5	5	3	1
P58	36-F	1.25mg	7.5	6	4	2
P60	23-F	1.25mg	8	6.5	6	3
Mean ± Standard deviation				5.4142 ± 2.5311		

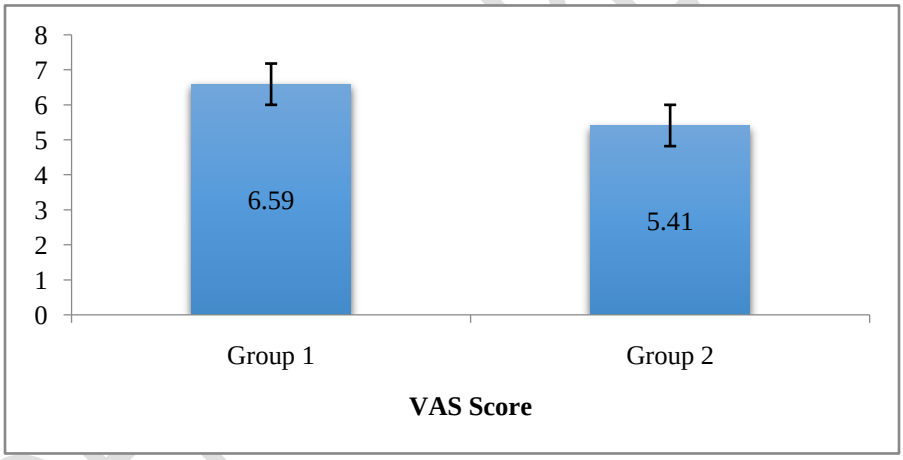

Figure .1: Histograms of average VAS scores of subjects of group 1 and group 2

From the above graph, decrease in VAS score observed in group 2 subjects. Therefore the pain control was more effective in group-2 subjects than in group-1.

Table.3: T-test for VAS score of subjects who had participated in the study

Statistical parameter	Group 1	Group 2
Mean ± Standard deviation	6.59 ± 1.6214	5.4142 ± 2.5311
Standard error of mean	0.295953	0.462095
N	30	30

Table.4: Represents that the two values of VAS score were significantly different (p = 0.0363)

UNDER PEER REVIEW

t-Value	2.1427
Degree of Freedom	58
Standard error of difference	0.549
Two tailed p value	=0.0363
Alpha (α)	0.05

Table. 5: Average VAS score of subjects of various age groups in group 1 and group 2

Age group	Group 1	Group 2
18-38	6.38	5.05
39-58	6.83	5.5
59-78	6.52	5.025

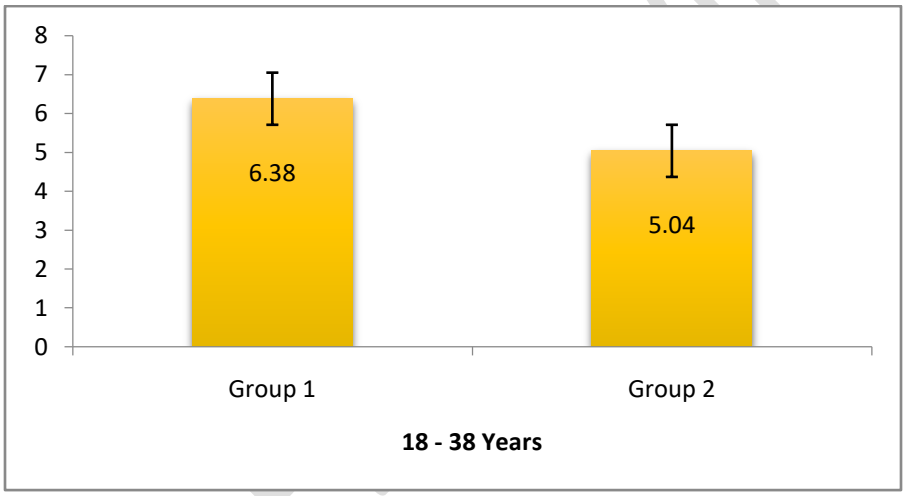

Figure. 2: Histograms of average VAS score of subjects of age group 18-38 years in group 1 and group 2

The above graph shows that there was decrease in VAS score in group-2 subjects. Therefore, the pain control was more effective in group-2 subjects than in group-1 in 18-38 years age group.

UNDER PEER REVIEW

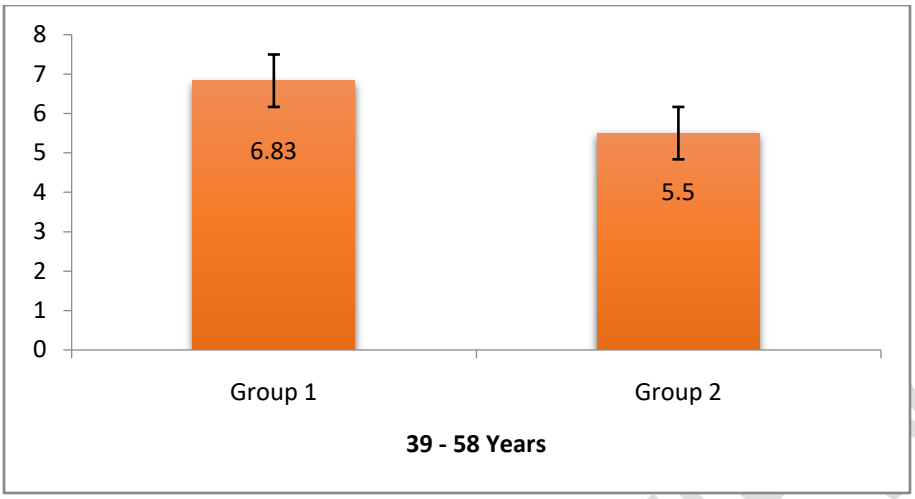

Figure.3: Histogram of average VAS scores of subjects of age group 39-58 years in group 1 and group 2

This graph shows that there was decrease in VAS score in group-2 subjects. Therefore, the pain control was more effective in group-2 subjects than in Group-1 in 39-58 years age group.

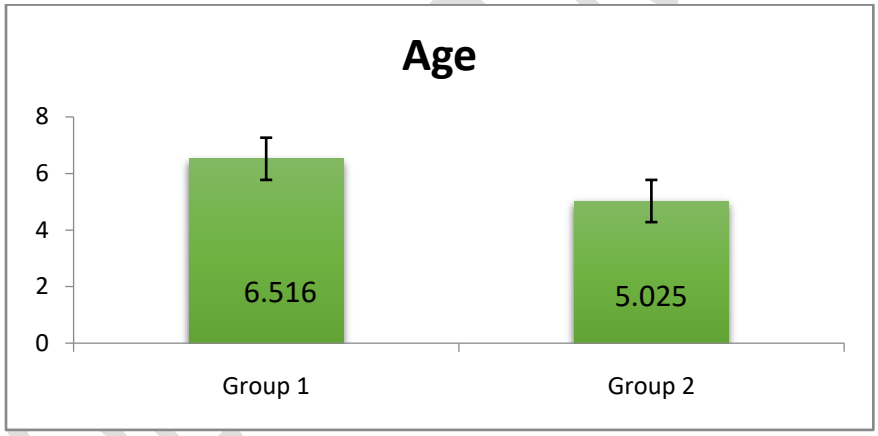

Figure.4: Histogram of average VAS score of subjects of age group 59-78 years in group 1 and group 2

This shows that there was decrease in VAS score in group-2 subjects. Therefore, the pain control was more effective in group-2 subjects than in group-1 in 59-78 years age group.

Table.6: t-test for VAS scores: t-test for the VAS scores of subjects of various age groups

Statistical parameter	Group 1	Group 2
Mean ± Standard deviation	6.57±0.2302	6.86±2.79
Standard error of mean	0.1329	1.6116
N	3	3

Table.7: The two values of VAS scores were significantly different (p=0.0005)

t-Value	0.1793
Degree of Freedom	4
Standard error of difference	1.617
Two tailed p value	0.8664
Alpha (α)	0.5

It shows that the pain control was more effective in group-2 subjects than in group-1 in various age groups. The study was done with VAS and WOMAC scale to measure the intensity of the pain, however patient response for the WOMAC scale is not encouraged as they were not able to differentiate the questionnaire of WOMAC scale and hence further use of WOMAC scale was not used in the present study. Thus, intensity of pain was measured with VAS scale.

Conclusion:

The current case report concluded that fentanyl transdermal patches show better therapeutic efficacy than ketoprofen transdermal patch. This difference in comparison of two drugs means VAS scores between ketoprofen and fentanyl also are statistically significant. The significant of change in VAS score between the two transdermal patches separately in different age groups; it was found that the difference is statistically significant. The result showed that the pain control was more effective in group -2 subjects (those in fentanyl patch) than in group 1 subjects (those on ketoprofen patches) in age group 18-35, 36-45 and 46-55years. The clinical significance of these results may be established by further work on post-operative orthopaedic patients receiving ketoprofen and fentanyl transdermal patches. Finally, our report has been proved that fentanyl transdermal patches show better therapeutic efficacy than ketoprofen transdermal patch by knowing their VAS scores.

Ethical Approval:

The present study was carried out for a period of six months after obtaining approval from Institutional Ethics Committee (IEC) of our study site. The approval for the study was obtained from IEC on 18- Dec- 2017.

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

Reference:

UNDER PEER REVIEW

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