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COMPARISON OF TRAMADOL AND OXACEPROL IN PATIENTS WITH OSTEOARTHRITIS

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Abstract

Introduction: Osteoarthritis (OA) is a chronic, degenerative disease of unknown origin which is characterised by gradual loss of articular cartilage. It is the most prevalent disease with a worldwide distribution. Earlier, osteoarthritis was seen as an inevitably progressive, degenerative disease process. Now it has been suggested that it is a dynamic process that may progress episodically. It is a heterogeneous group of diseases characterised by an adaptive response of synovial joints to a variety of genetic, environmental, aging and biomechanical stresses. NSAIDs intake increases the risk of gastritis and does not a have direct impact on the underlying pathogenesis of articular diseases. Tramadol augments serotonergic and noradrenergic neurotransmission, although it's main active metabolite, O-desmethyltramadol. Oxaceprol is an atypical inhibitor of inflammation, used as a drug for joint disease without less side-effects with better safety profile than non-steroidal anti-inflammatory drugs (NSAIDs).

Material and Methods: Participants were randomized in two study groups of 50 patients each sing computer generated random number list. Each group was given either oxaceprol 200 mg capsule or tramadol 50 mg capsule, thrice daily after food, for 12 weeks. The primary efficacy variable for this study was symptom relief stiffness, and physical function, measured on 100 mm Visual analogue scale (VAS) scale. Rescue medication used during the study period was also recorded. Complete blood count, blood glucose, liver function tests, and serum creatinine was recorded at the start of the study and. Vital signs were recorded at each visit and adverse events were reported.

Results: A total of 100 patients were included in the study of which 50 each were placed in tramadol group and oxaceprol group. No statistically significant difference was noted in both the group about baseline parameters about sex, age and blood pressure. Blood sugar was higher in Oxaceprol group as compared to tramadol group (P =0.0042) which was statistically significant. No statistically significant difference was observed between groups for WOMAC scores. Significant reduction in pain, stiffness and physical function was observed between oxaceprol and tramadol group at baseline and after 6 months follow-up. None of the adverse events were severe in nature in both the group commonest were dizziness and nausea.

Conclusion: Oxaceprol efficacy and tolerability was comparable with tramadol and the drug can be considered as an alternative to low-potency opioids in the management of knee osteoarthritis. Further studies are required to confirm the clinical utility of oxaceprol in osteoarthritis.

Keywords: OA, tramadol, oxaceprol, NSAID, WOMAC

Introduction

Osteoarthritis (OA) is a chronic, degenerative disease of unknown origin which is characterized by gradual loss of articular cartilage. It is the most prevalent disease with a worldwide distribution[i]. OA joints include progressive loss and destruction of articular cartilage, formation of osteophytes, variable degrees of inflammation of the synovium, thickening of the subchondral bone, degeneration of ligaments and menisci and hypertrophy of the joint capsule[ii].

Earlier, osteoarthritis was seen as an inevitably progressive, degenerative disease process. Now it has been suggested that it is a dynamic process that may progress episodically. It is a heterogeneous group of diseases characterized by an adaptive response of synovial joints to a variety of genetic, environmental, aging and biomechanical stresses[2],[iii].

The current treatment of OA is generally focused on symptomatic relief by use of rapid action drugs like analgesics and NSAIDs and newer cycloxygenase (COX-2) specific inhibitors. NSAIDs intake increases the risk of gastritis and does not have direct impact on the underlying pathogenesis of articular diseases, thus have minimal role in modifying disease course and improving quality of life. COX -2 inhibitors have less incidence of gastrointestinal adverse events but may have significant renal and cardiovascular toxicities. Hence, there is continuous search of new and better drug for OA[iv].

Tramadol augments serotonergic and noradrenergic neurotransmission, although it's main active metabolite, O-desmethyltramadol[v]. Guidelines suggest tramadol as the first-line drug for mild to moderate pain[vi]. Also it has been observed that tramadol is modestly effective for osteoarthritis-related pain in placebo-controlled trials[vii]. Tramadol abuse has been observed in some Middle Eastern countries[viii]. Generalized seizures can be seen with tramadol use, sometimes with modest doses, and particularly when the drug is combined with other serotonergic or proconvulsant agents such as antidepressants.

Oxaceprol (N-acetyl-L-hydroxyproline), is an atypical inhibitor of inflammation, used as a drug for joint disease without less side-effects with better safety profile than non-steroidal anti-inflammatory drugs (NSAIDs). [ix]. It is derived from L-proline, a DNA-encoded amino acid. The active effect of Oxaceprol is to inhibit the adhesion and migration of leucocytes[x].

Material and Methods:

This prospective, comparative study was carried out in the Dept. of Pharmacology at Vedanta Institute of Medical Sciences Palghar, Maharashtra; with Patients, diagnosed as Osteoarthritis. A total of 100 patients were included in the study with knee joint pain intensity of at least 35 mm on a 100 mm visual analog scale (VAS) present for at least preceding 3 months and with confirmed degenerative changes in knee skiagram. The primary efficacy variable for this study was symptom relief and was assessed by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain, stiffness, and physical function measured on a 100 mm visual analog scale (VAS). Patient's Clinical Global Impression (CGI) was reported on a 5 point Likert scale as much worsened, worsened, no change, improved and much improved.

Patients with morning stiffness of over 30 min, secondary osteoarthritis, knee injury or diagnostic arthroscopy of signal knee within 6 months advanced osteoarthritis, deformed joint, and any serious concomitant disease were excluded. Participants were randomized in two study groups of 50 patients each sing computer generated random number list. Each group was given either oxaceprol 200 mg capsule or tramadol 50 mg capsule, thrice daily after food, for 12 weeks. The primary efficacy variable for this study was symptom relief stiffness, and physical function, measured on 100 mm Visual analogue scale (VAS) scale. Rescue medication used during the study period was also recorded.

Complete blood count, blood glucose, liver function tests, and serum creatinine was recorded at the start of the study and. Vital signs were recorded at each visit and adverse events were reported.

Statistical analysis

In the present study the data have subjected to Paired and Independent t-test as applicable. P values less than 0.05, 0.01 and 0.001 were considered as significant, very significant and highly significant respectively.

Results:

A total of 100 patients were included in the study of which 50 each were placed in tramadol group and oxaceprol group.

Table 1: Baseline characteristics

parameters	Tramadol group (n=50)	Oxaceprol group (n=50)	P value
Male n (%)	22 (44%)	23 (46%)	0.8415
Female n (%)	28 (56%)	27 (54%)	0.8415
Age years (mean ± SD)	52.48±11.6	51.24±9.45	0.5592
Symptoms months (mean ± SD)	56.78± 15.87	54.89±12.47	0.5094
Systolic blood pressure mmHg (mean ± SD)	139.46±11.54	141.22±9.55	0.4081
diastolic blood pressure mmHg (mean ± SD)	81.23±5.44	82.78±6.47	0.1978
Blood sugar (mean ± SD)	128.41±12.77	136.74±15.49	0.0042

No statistically significant difference was noted in both the group about baseline parameters about sex, age and blood pressure. Blood sugar was higher in Oxaceprol group as compared to tramadol group (P =0.0042) which was statistically significant.

Table 2: Western Ontario and McMaster Universities Osteoarthritis Index score

		Baseline	After 6 months follow-up	P value
WOMAC Pain	Oxaceprol (mean ± SD)	318.01±55.78	200.8±55.74	0.0042
	Tramadol (mean ± SD)	322.14±66.51	199.24±99.51	< 0.0001
	P value	0.7373	0.9232	
WOMAC stiffness	Oxaceprol (mean ± SD)	31.22±10.44	20.47±6.82	< 0.0001
	Tramadol (mean ± SD)	32.55±9.46	22.44±5.49	< 0.0001
	P value	0.5060	0.1148	
WOMAC physical function	Oxaceprol (mean ± SD)	1045.4±201.8	759.8±278.11	< 0.0001
	Tramadol (mean ± SD)	1101.8±241.56	815.4±284.7	< 0.0001
	P value	0.2082	0.3257	

No statistically significant difference was observed between groups for WOMAC scores. Significant reduction in pain, stiffness and physical function was observed between oxaceprol and tramadol group at baseline and after 6 months follow-up. None of the adverse events were severe in nature in both the group commonest were dizziness and nausea.

Discussion

OA is the most common joint disease associated with pain stiffness and disability. About 25% of the adult population, or more than 50 million people in the US, will be affected by this disease by the year 2020 and that OA will be a major cause of morbidity and physical limitation among individuals over the age of 40 years[xi]. Pain management and end stage surgical intervention are available therapeutic treatments for OA. Thus, there is a clinical need for studies of the etiology and alternative treatments for OA. It has been seen that the chronic low-grade inflammation is found in OA which contributes to disease development and progression. During OA progression, the entire synovial joint, including cartilage, subchondral bone, and synovium, are involved in the inflammation process[xii].

In a study by Bauer et al. oxaceprol was compared with diclofenac in Germany. Joint function, evaluated by Lequesne's indices, improved clinically in both treatment groups. In both groups VAS score for pain was reduced nearly 50%, joint mobility improved nearly 60% and pain-free walking period more than doubled. Differences between groups were not significant[xiii]. Herrmann *et al*[xiv] also compared oxaceprol with diclofenac n knee and hip osteoarthritis, in this study oxaceprol was better tolerated.

In our study it is observed that oxaceprol may decrease pain, reduce stiffness, and improve function and overall well-being similar results were observed in other studies[xv],[xvi]. Our study also show that the efficacy and tolerability of oxaceprol are comparable to tramadol. The drugs were equivalent in improving pain, stiffness and physical function components of WOMAC at follow-up visits

Conclusion:

Oxaceprol efficacy and tolerability was comparable with tramadol and the drug can be considered as an alternative to low-potency opioids in the management of knee osteoarthritis. Further studies are required to confirm the clinical utility of oxaceprol in osteoarthritis.

References:

1. Murray CJL, Lopez AD. *The global burden of disease.* Geneva: World Health Organisation, 1996.
2. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. Arthritis Rheum. 2012 Jun; 64(6):1697-707.
3. Creamer P, Hochberg M. Osteoarthritis. Lancet 1997;350:503–8.
4. Annil Mahajan, Kulbir Singh, Vishal Tandon, Sudesh Kumar and Hardeep Kumar, "Diacerein: A New Symptomatic Slow Acting Drug for Osteoarthritis", JK Science. 2006, 8(3), 173-175.
5. Leppert W. YP2D6 in the metabolism of opioids for mild to moderate pain. Pharmacology. 2011; 87(5-6):274-85.
6. Kahan M, Mailis-Gagnon A, Wilson L, Srivastava A, National Opioid Use Guideline Group.Canadian guideline for safe and effective use of opioids for chronic noncancer pain: clinical summary for family physicians. Part 1: general population. Can Fam Physician. 2011 Nov; 57(11):1257-66, e407-18.
7. Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis. Cochrane Database Syst Rev. 2006 Jul 19; (3):CD005522.
8. Hassanian-Moghaddam H, Farajidana H, Sarjami S, Owliaey H.Tramadol-induced apnea. Am J Emerg Med. 2013 Jan; 31(1):26-31.
9. Bauer H W, Klasser M, von Hanstein K L, Kolinger H, Schladitz G, Henke H D, Gimbel W, Steinbach K. Oxaceprol is as effective as diclofenae in the thempy of osteoanthritis of the knee and hip. Clin Rheumatol 1999: 18: 4-9.
10. Herrmann G; Steeger D; Klasser M; et al. (2000). "Oxaceprol is a well-tolerated therapy for osteoarthritis with efficacy equivalent to diclofenac". Clin. Rheumatol. 19 (2): 99–104.
11. Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, Liang MH, Kremers HM, Mayes MD, Merkel PA, Pillemer SR, Reveille JD, Stone JH, National Arthritis Data Workgroup.Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. Arthritis Rheum. 2008 Jan; 58(1):15-25.
12. Malfait AM. Osteoarthritis year in review 2015: biology.Osteoarthritis Cartilage. 2016 Jan; 24(1):21-6.
13. Bauer HW, Klasser M, von Hanstein KL, Rolinger H, Schladitz G, Henke HD, et al. Oxaceprol is as effective as diclofenac in the therapy of osteoarthritis of the knee and hip. Clin Rheumatol 1999;18:4-9.
14. Herrmann G, Steeger D, Klasser M, Wirbitzky J, Fürst M, Venbrocks R, et al. Oxaceprol is a well-tolerated therapy for osteoarthritis with efficacy equivalent to diclofenac. Clin Rheumatol 2000;19:99-104.
15. Smith SR, Deshpande BR, Collins JE, Katz JN, Losina E. Comparative pain reduction of oral non-steroidal anti-inflammatory drugs and opioids for knee osteoarthritis: Systematic analytic review. Osteoarthritis Cartilage 2016;24:962-72.
16. ongtharvonskul J, Anothaisintawee T, McEvoy M, Attia J, Woratanarat P, Thakkinstian A. Efficacy and safety of glucosamine, diacerein, and NSAIDs in osteoarthritis knee: A systematic review and network meta-analysis. Eur J Med Res 2015;20:24.