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KETOPROFEN;
AN EFFECTIVE AGENT AGAINST RHEUMATOID ARTHRITIS

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ABSTRACT… Ketoprofen is effectively useful in managing arthritis, rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. This article covers the pharmacological uses, toxicology, contraindications, food – drug, drug-drug interactions and associated side effects of Ketoprofen that have been reported in literature in earlier years.

Key words: Ketoprofen, Rheumatoid arthritis, Ankylosing spondylitis, Toxicology, and Contraindications.

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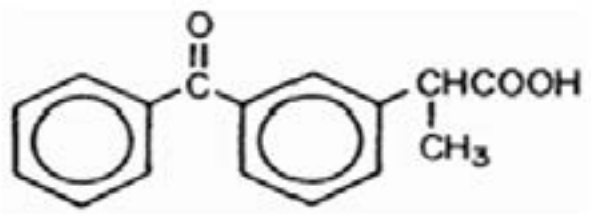
KETOPROFEN

Ketoprofen shares the therapeutic features of different other propionic acid derivatives. Ketoprofen facilitate COX inhibition which helps to antagonize the functions of bradykinin.[1]

Chemistry of Ketoprofen

Ketoprofen ($C_{16}H_{14}O_3$) is a (RS)-2-(3-Benzoylphenyl) propionic acid. Its molecular weight is 254.3 and pKa is 4.55.



Clinical Aspects of Ketoprofen

Ketoprofen reduces joint swelling and is helpful in the managing the incidences of arthritis and rheumatoid arthritis. It do not effects on the normal renal functions in individuals. It may facilitate gastrointestinal erosions by reducing the production of cytoprotective prostaglandins.[2]

Drug Metabolism and Pharmacokinetics

Ketoprofen metabolism is carried out in the liver. It is washed out through urine and in bile approximately 1% and 10 - 20%.[3] Ketoprofen particularly binds with plasma albumin, in a stereo selective manner.[4] Its half-life is about 2 hrs.[3]

Adverse Effects of Ketoprofen

Common adverse events which are reported in 30 % individuals are mild gastrointestinal, the ratio of the events are substantially decreased if it is taken with meal. Other most common problem associated with Ketoprofen is that it can cause liquid retention. This problem is mostly found in patients who are taking diuretics.[5]

Toxicology

Toxicological studies have been previously conducted on animals. Studies indicated that the major targeted organ is the GI mucosa particularly

in ulceration also different other organs (kidneys and testes) were also targeted.[2]

THERAPEUTIC USES

Pharmacological Equivalence Studies

Kantor in 1986[6] reported that double blind clinical trials have showed its pharmacological equivalence studies with different drugs particularly in osteoarthritis with aspirin and in managing rheumatoid arthritis with aspirin, indomethacin, and ibuprofen. Similarly, Mehlisch et al.,[7] found that Ketoprofen (50 and 100 mg) exhibits comparable analgesic characteristics with Codeine (90 mg) in individuals with postoperative dental pain and in postpartum women.[8] It exhibits similar therapeutic activity to different other non-steroidal anti-inflammatory drugs (NSAID's) in managing dysmenorrhoea.[9]

Permanent Focal Brain Ischemia

Silva et al.,[10] found that no neuroprotective response on the histopathological features or behavioural aspects of focal permanent brain ischemia during the study.

Adjunct use of Ketoprofen in Heel Pain:

White in 2006[11] reported a case study that child having heel pain had returned to his normal activities after few (18) days of intervention with ketoprofen gel.

Rheumatoid arthritis, Ankylosing spondylitis and Osteoarthritis:

Authors have reported that Ketoprofen showed better results in clinical trials in managing osteoarthritis, rheumatoid arthritis and ankylosing spondylitis; also in the studies it was found that Ketoprofen is equivalent with different drugs i.e. Ibuprofen and Indomethacin.[12-13]

Other Features

Ketoprofen was significantly effective in different conditions i.e. in tendonitis, frozen shoulder[12], headache[14], managing a rise in temperature after surgery.[15] Scientists also reported that Ketoprofen assist in the prevention different cancers of colorectal and lung as well as helps to treat neurodegenerative disorders i.e. Alzheimer's and Parkinson's disease.[16-17]

ADVERSE REACTIONS

1. Common adverse effects which were reported are hypersensitivity, drowsiness, gastrointestinal pain and vomiting mainly due to bronchospasm.
2. Authors reported acute intestinal nephritis after the administration of Ketoprofen.[18] Individuals with renal insufficiency, cardiac failure or liver cirrhosis showed a rapid decrease in renal function due to decrease prostaglandin synthesis.[19]
3. Different haematological adverse events were also found i.e. neutropenia, anaemia, eosinophilia, thrombocytopenia and agranulocytosis.[20]
4. Other adverse events include retention of fluid, pancreatitis, photosensitivity, eczema and alveolitis.[20]
5. Kokki et al., 2010[21] determined that mild to moderate adverse events were found in children.

Use of ketoprofen in pregnancy

No controlled data in pregnancy has yet been reported. When use in late pregnancy it may facilitate early closure of the ductus arteriosus and may extend delivery.[22-23]

CONTRAINDICATIONS

Cross sensitivity has been reported in patients of rhinitis and asthma ingesting Ketoprofen.[2]

FOOD INTERACTIONS WITH KETOPROFEN

NSAIDs (ibuprofen, ketoprofen and naproxen can induce irritation of stomach, thus NSAIDs should be ingested with food or milk.[24]

DRUG INTERACTIONS

1. Perrin et al., 1990[25] reported the decline in the plasma binding of methotrexate in vivo when ingested with ketoprofen.
2. Ketoprofen when ingesting with paracetamol it may results in reduction in morphine requirement.
3. Simultaneous adminstration of Ketoprofen

with Aspirin results in reduction in serum Ketoprofen levels.
4. Simultaneous adminstration of Ketoprofen with hydrochlorothiazide decreases urinary chloride and potassium emission.
5. This drug does not alter the prothrombin times after adminstration of Warfarin.
6. Ketoprofen raises the levels of lithium in plasma and decreasing the lithium renal clearance.
7. Ketoprofen when administered with furosemide and angiotensin converting enzyme (ACE) inhibitors risk associated with hyperkalaemia is increases.[20]

CONCLUSION

This review article has presented the therapeutic uses, interaction with food and drug and also sum up the side effects of Ketoprofen which will the practitioners, doctors and pharmacists in their work.

REFERENCES

1. Veys E.M. **20 years' experience with Ketoprofen.** Scand J Rheumat Suppl 1991;90:1-44.
2. Dollery SC. **Therapeutic Drugs.** 2nd vol. Churchill living stone, 1991;pp 25-26.
3. Delbarre F, Roucayrol JC, Amor B, Ingrand J, Bourat G, Fournel J, Courjaret J. **Pharmacokinetic study of Ketoprofen in man using the tritiated compound.** Scand J Rheumatol 1976;(suppl 14): 45-52.
4. Jamali F, Brocks DR. **Clinical Pharmacokinetics of Ketoprofen and Its Enantiomers.** Clin Pharmacokinet 1990;19 (3): 197-217.
5. Burke A, Smyth E, FitzGerald GA. **Goodman and Gilman's The Pharmacological Basis of therapeutics.** Brunton LL, Lazo JS, Parker KL (Eds.) 11th Edition, 26th Chapter, McGraw-Hill Medical publishing division, 2006;pp 700.
6. Kantor TG. **Ketoprofen: a review of its pharmacologic and clinical properties.** Pharmacotherapy 1986;6 (3):93-103.
7. Mehlisch D, Frakes L, Cavaliere MB, Felman M. **A double blind parallel comparison of Ketoprofen, Codeine and placebo in-patients with moderate to severe dental pain.** J Clin Pharmacol 1984;24: 486-492.
8. Sunshine A, Zighelboim I, Laska E, Siegel C, Olson NZ, De CA. **A double blind parallel comparison of Ketoprofen, Aspirin and placebo in-patients with postpartum pain.** J Clin Pharmacol 1986;26:706-711.
9. Glleeson S, Sobie J. **Efficacy of Ketoprofen in treating primary dysmenorrhoea.** CMAJ 1983;129: 842-843.
10. Silva MN, Colli BO, Coimbra NC, Coutinho Netto J. **Evaluation of the neuroprotective effect of ketoprofen on rats submitted to permanent focal brain ischemia.** Arq Neuropsiquiatr 2007;65(4A):978-84.
11. White RL. **Ketoprofen Gel as an Adjunct to Physical Therapist, Management of a Child With Sever Disease.** Phys ther 2006;86:424-433.
12. Fossgreen J. **Ketoprofen: a survey of current publications.** Scand J Rheumatol 1976;5 (suppl 14): 7-32.
13. Caldwell JR, Germain BF, Lourie SH. **Ketoprofen versus Indomethacin in patients with rheumatoid arthritis: a multicenter double blind comparative study.** J. Rheumatol 1988;15: 1476-1479.
14. Stensrud P, Sjaastad O (1974) **Clinical trial of a new antibradykinin, anti-inflammatory drug, Ketoprofen (19.583 R.P.) in migraine prophylaxis**. Headache 14:96.
15. Keinnannen-Kiukaanniemi S, Simila S, Kouvalainen K. **Oral antipyretic therapy evaluation of the propionic acid derivatives, Ibuprofen, Ketoprofen, Fenoprofen and Naproxen.** Padiatr Padol 1980;15:239-244.
16. Weder, JE, Dillon, CT, Hambley, TW, Kennedy, BJ, Lay, PA, Biffin, JR, Regtop, HL, Davies, NM. **Copper complexes of non-steroidal anti-inflammatory drugs: an opportunity yet to be realized.** Coordin Chem Rev 232: 95-126, 2002.
17. Hirohata, M, Ono, K, Morinaga, A, Yamada, M. **Non-steroidal anti-inflammatory drugs have potent anti-fibrillogenic and fibril-destabilizing effects for a-synuclein fibrils in vitro.** Neuropharmacology 2008;54: 620-627.
18. Ducret F, Poinlet P, Martin D, Villermet B **Insuffisance renale induite par le ketoprofene.** Nephrologie 1982;3:105-106.
19. Toto RD, Anderson SA, Brown – Cartwright D, Kokko JP, Brater DC. **Effects of acute and chronic dosing of NSAIDs in patients with renal insufficiency.** KI 1986;30:760-768.
20. Rençber S, Karavana SY, Özyazici M. **Bioavailability**

File: Ketoprofen. Fabad J Pharm Sci 2009; 34: 203-216.

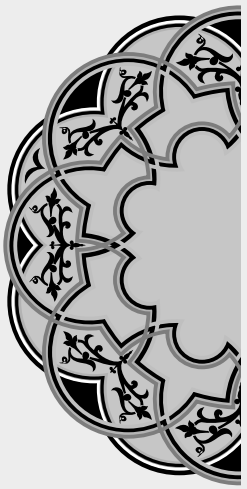
21. Kokki H. **Ketoprofen pharmacokinetics, efficacy, and tolerability in pediatric patients.** Paediatr Drugs 2010;12:313-29.

22. Chambers C, Tutuncu Z, Johnson D, Jones K. **Human pregnancy safety for agents used to treat rheumatoid arthritis: Adequacy of available information and strategies for developing post-marketing data.** Arthritis Res Ther 2006;8:215-25.

23. Awan AF, Nazir T, Ashraf M, Umer O, Rehman H. **Studies of ketoprofen toxicity in avian species.** J Basic Appl Sci 2011;7:127-31.

24. Størmer FC, Reistad R, Alexander J. **Glycyrrhizic acid in liquorice–evaluation of health hazard.** Food Chem Toxicol 1993;31(4):303-312.

25. 25. Perrin A, Milano G, Thyss A, Cambon P and Schneider M. **Biochemical and pharmacological consequences of the interaction between methotrexate and ketoprofen in the rabbit.** Br J Cancer 1990;62(5): 736– 741.



"Keep thinking;
It leads to progress."

Shuja Tahir

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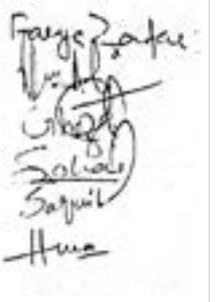
1	Dr. Farya Zafar	Equal contribution by all authros	
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