

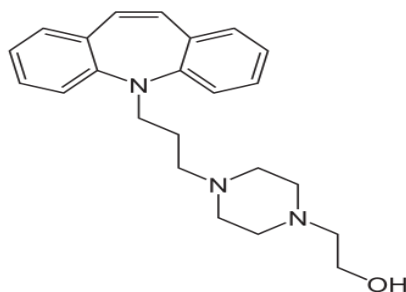
Opipramol

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Composition: Opipramol Hydrochloride

Strengths: 50 and 100mg tablets.



Class

It is an iminostilbene derivative, belonging to the dibenzazepine group. Opipramol was developed by Schindler and Blattner in 1961. Due to its structural similarities with tricyclic antidepressants and pharmacological profiles it was initially expected to be tricyclic antidepressant. However it is rather a potent sigma ligand.

Pharmacodynamic properties

Opipramol acts as a high affinity sigma receptor agonist, primarily at the σ_1 subtype, but also at the σ_2 subtype with somewhat lower affinity. Sigma receptors are a unique set of proteins located in the endoplasmic reticulum, σ_1 receptors play a key role in potentiating intracellular calcium mobilization thereby acting as a sensor or modulator of calcium signaling. Occupancy of σ_1 receptors by agonists causes translocation of the receptor from the endoplasmic reticulum to peripheral areas (membranes) where the σ_1 receptors may regulate ion channels, neurotransmitter receptors and neurotransmitter release. It is this property which is responsible for its therapeutic benefits against anxiety and depression. The biphasic action initially makes prompt improvement of tension, anxiety and insomnia. Opipramol is a tranquilizer with a thymoleptic component. After sub-chronic treatment, opipramol is significantly down-regulated to σ_2 but not σ_1 sites. Opipramol also acts as a low to moderate affinity antagonist for the D₂, 5-HT₂, H₁, H₂, and muscarinic acetylcholine receptors. H₁ and H₂ receptor antagonism account for its antihistamine effects, and muscarinic acetylcholine receptor antagonism is responsible for its anticholinergic properties.

Pharmacokinetic properties

Opipramol is rapidly and completely absorbed by the gastrointestinal tract. Its terminal plasma half-life is 6–11 hours. After single oral administration of 50 mg, the peak plasma concentration of the drug is reached after 3.3 hours and amounts to 15.6ng/ml. After single oral administration of 100 mg the maximum plasma concentration is reached after 3 hours and amounts to 33.2 ng/ml. The bioavailability of opipramol amounts to 94%. The plasma protein binding amounts to approximately 91% and the volume distribution is approximately 10 L/kg. Opipramol is partially metabolized in liver as deshydroxyethyl-opipramol. Metabolization occurs through CYP2D6-isoenzyme. Elimination is 70% renal and 10% unaltered. Remaining portion is eliminated through faeces.

Tolerability

The frequently ($\geq 1\%$ to $< 10\%$) reported adverse reactions with opipramol especially at the beginning of the treatment includes fatigue, dry mouth, blocked nose, hypotension and orthostatic dysregulation. The adverse reactions reported occasionally ($\geq 0.1\%$ to $< 1\%$) includes dizziness, stupor, micturition disturbances, accommodation disturbances, tremor, weight gain, thirst, allergic skin reactions (rash, urticaria), abnormal ejaculation, erectile impotence, constipation, transient increase in liver enzyme activities, tachycardia and palpitations. Rarely ($\geq 0.01\%$ to $< 0.1\%$) reported adverse reaction includes excitation, headache, paresthesia especially in elderly patients, restlessness, sweating, sleep disturbances, oedema, galactorrhea, urine blockage, nausea and vomiting, collapse conditions, stimulation conducting disturbances, intensification of present heart insufficiency, blood profile changes particularly leukopenia, confusion, delirium, stomach complaints, taste disturbance and paralytic ileus especially with sudden discontinuation of a longer term high dose therapy. Very rarely ($< 0.01\%$) adverse reaction includes seizures, motor disorder, (akathisia, dyskinesia), ataxia, polyneuropathy, glaucoma, anxiety, hairfall, agranulocytosis, severe liver dysfunction after long term treatment, jaundice and chronic liver damage.

Indications

Opipramol is typically used in the treatment of generalized anxiety disorder (GAD) and somatoform disorders. Its anxiolytic effect becomes prominent after only one to two weeks of chronic administration. Upon first commencing treatment, opipramol is rather sedating in nature due to its antihistamine properties, but this effect becomes less prominent with time.

Contradictions

In patients with hypersensitivity to opipramol dihydrochloride or another component of the formulation, Acute alcohol, analgesics and antidepressant intoxications, acute urinary retention, acute delirium. Untreated narrow-angle glaucoma, Prostate hypertrophy with residual urinary retention.

Pregnancy and lactation

Experimental animal studies did not indicate injurious effects of opipramol on the embryonic development or the fertility. Opipramol should be prescribed during pregnancy, particularly in the first trimester, only for compelling indication. Opipramol should not be used during lactation period, since the active ingredient passes into the milk in small quantities.

Drug Interactions

The therapy with Opipramol indicates an additional therapy with neuroleptics, hypnotics and tranquilizers (e.g. Barbiturates, Benzodiazepines). Therefore, it should be noted that some specific reactions, particularly CNS depressant effects could be intensified and an intensification of common side effects may occur. If necessary the dosage may be reduced. Co-administration with alcohol can cause stupor. MAO Inhibitors should be discontinued at least 14 days before the treatment with Opipramol. Concomitant use of Opipramol with β -blockers, antiarrhythmics (of class 1c), as well as drugs from tricyclic antidepressant group and preparations which influence the microsomal enzyme system, can lead to change in plasma concentration of these drugs. Co-administration of neuroleptics (example- haloperidol, risperidone) can increase the plasma concentration. Barbiturates and anticonvulsants can reduce the plasma concentration of Opipramol and thereby weaken the therapeutic effect.

Dosage and Administration

The usual dosage is 50mg in morning, 50mg in evening and 100 mg in the night. The dose can be reduced to 50-100 mg and increased upto 100mg three times a day depending on efficacy and tolerability. It can be taken before or after meals. In children and adolescents its use is not proved. A reduction in dose with patients of impaired renal function is necessary as 70% of drug is excreted through kidney.

Suggested References and Further Reading

1. Mohapatra S, Rath NM, Agrawal A, Verma J. Opipramol : a novel drug. Delhi Psychiatry Journal 2014;16 (2):409-11.
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