MINI REVIEW

CHLORPHENIRAMINE MALEATE: AN EFFECTIVE ANTIALLERGIC AGENT

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ABSTRACT
Chlorpheniramine maleate is H1 receptor antagonist and is useful in the management of allergic and nonallergic rhinitis. It is commonly used to treat different symptoms associated with rhino conjunctivitis and urticaria. This article briefly reviews the therapeutic uses, drug-drug interactions, incompatibilities and side effects of chlorpheniramine maleate.

Keywords: Chlorpheniramine maleate, antiallergic agent, first generation antihistamine.

1. INTRODUCTION
Chlorpheniramine maleate (CM) (C16H19ClN2, C4H4O2) belongs to the first generation of H1 receptor antagonists and is a propylamine derivative1. Its chemical name is γ-(4-chlorophenyl)-γ-cyano-N,N-dimethyl-2-pyridinepropanamine (Fig. 1) 2 and have a pKa value of 9.2 3. Being a halogenated pheniramine due to a chlorine moiety on para position, it is considered to be more effective (10 times) and have exhibited longer duration of action as compared to the parent pheniramine4. It is available alone as well as in combination with different classes of drugs5.

Fig. 1. Chemical structure of chlorpheniramine maleate.

2. MECHANISM OF ACTION
H1 receptors are particularly present on smooth muscles, central nervous system (CNS), vascular endothelial cells and heart. CM binds to these receptors and blocks the action of endogenous histamine. This subsequently results in the temporary relief of the negative symptoms brought on by histamine6,7.

3. DOSAGE AND ADMINISTRATION
CM is available in tablet and syrup dosage forms in a dose of 4-12 mg and 2 mg per 5 ml, respectively, for oral use. Its daily administration should not increase the dose of 24 mg / day8,8.

4. PHARMACOKINETICS
4.1. Absorption and Distribution
CM is absorbed rapidly from the gut after oral administration9. Its half life (plasma) is 12-15 hrs10. It has an absolute bioavailability of 34% and 25% obtained from oral solution and tablets, respectively10. Plasma protein binding of the drug is around 60-70%. It maintains 2.5-3.2 L/kg steady state volume of distribution following intravenous administration11,12.

4.2. Metabolism and Excretion
The compound is metabolized by demethylation and oxidative deamination in the liver13. N-desmonomethylchlorpheniramine and N-desdimethylchlorpheniramine are the reported metabolites of CM found in healthy male subjects14. Total body clearance of the drug in adults is 5-12 mL/min/kg9. It is mainly excreted from urine having a clearance rate of 4.4-7.92 mL/min/kg15.
5. THERAPEUTIC USES

5.1. Perennial and Seasonal Allergic Rhinitis
Main causes of seasonal and perennial rhinitis are due to the exposure to antigens like seasonal pollens, cat dander, cockroaches, dust miles, etc. CM is used in combination with sympathomimetic drugs in the treatment of allergic rhinitis.

5.2. Vasomotor Rhinitis
CM is also considered to be useful in non-allergic rhinitis. It is used in combination with phenylephrine hydrochloride and methscopolamine nitrate in the treatment of vasomotor rhinitis.

5.3. Allergic Conjunctivitis
Reddening of the eyes extends rapidly and is accompanied by itching and tearing during inflammation of the conjunctiva. CM can be used to treat different symptoms of rhino conjunctivitis.

5.4. Urticaria and Dermographism Urticaria
CM is usually prescribed to relieve various symptoms of urticaria and dermographism urticaria.

5.5. Anaphylactic Reactions and Angioedema
For the treatment of anaphylactic reactions and angioedema this compound is given through intravenous route usually in a dose of 10-20 mg.

5.6. Local Anesthetic
CM is also reported to produce local anesthetic effect but for a short duration of action.

5.7. Clopidogrel-Induced Adverse Skin Reactions
CM in combination with prednisolone is also known to be effective in the management of clopidogrel-induced skin reactions.

5.8. Itching in Late Pregnancy
CM has been found to be effective in overcoming the itching associated with rashes in late pregnancy.

5.9. Acute Side Effects of Irinotecan
Misumi et al. reported that pre-administration of CM developed defensive features which avoided different side effects that may appear in the initial phase of the treatment after administration of irinotecan i.e. drowsiness, abdominal discomfort, nasal discharge and soggy eyes.

6. DRUG-DRUG INTERACTIONS

6.1. Phenytoin
When CM interacts with phenytoin, it potentiates neurological signs and symptoms which indicate its toxicity.

6.2. Belladona
Interaction with belladona may initiate anti-cholinergic responses.

6.3. Amphetamines
Therapeutic response of CM can be altered when given with amphetamines.

6.4. Alcohol
Intake of alcohol with this compound enhances depressant effects in the patients.

6.5. Caffeine
Caffeine counteracts the sedative response and psychomotor impairments caused by CM.

6.6. Amodaquine
CM when administered along with amodaquine is known to increase the efficacy of amodaquine.

6.7. Ephedrine
Buckey et al. performed a randomized, double blind, crossover trial and found that ephedrine counteracts sedative and performance effects of CM.

6.8. Chloroquine
Okonkwo et al. reported that CM enhanced the therapeutic activity of chloroquine in acute malaria (uncomplicated) by increasing the uptake / concentration of chloroquine in resistant parasites.

7. INCOMPATIBILITIES
Various studies have been performed related to the compatibility of CM. It is found to be incompatible with phenobarbitone sodium, kanamycin sulphate,
Heinemann, Elsevier Inc., St. Louis, Missouri, USA, 2008; p. 561.