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Evaluation Of The Psychopharmacological Effects Of Loratadine With Concomitant Adminstration Of Erythromycin

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الخلاصة

استقصت هذه الدراسة التأثير النفسحركي للوراتادين وهو من الجيل الثاني لمضادات الهستامين باعطائه كجرعة مفردة او مع مثبط الايض ارثرومايسين. تم قياس وقت رد فعل حركه طرف الاصبع قبل اعطاء الادوية ثم كل ساعة بعد ذلك لمدة ثلاث ساعات ٠اوضح التحليل الأحصائي للنتائج ان الأرثرومايسين له تاثير معتد احصائيا على تحفيز التاثير المثبط للوراتادين على الاداء النفسحركي٠ تمثل ذلك باطالة الوقت اللازم لرد فعل الحركة٠

Abstract

In this study, the effect of a single oral dose (10 mg) of a 2nd generation antihistaminic agent – loratadine - administered alone or with a metabolic inhibitor – erythromycin - on psychomotor performance was investigated on 6 healthy volunteers.

Recording of movement reaction time and assessment of subjective feeling of sedation was done before medication and hourly afterward for 3 hours.

The results were analyzed statically by using "student's t test" which showed that loratadine erythromycin combination induced a statically significant impairment of psychomotor performance demonstrated by prolongation of finger tip reaction time.

Introduction

Loratadine is a long acting 2nd generation tricyclic antihistamine. It is a piperidine derivative that antagonizes selectively histamine H□ receptors. Loratadine is used in clinical practice to control symptoms of allergic rhinitis.(1)

Like the other 2nd generation antihistamines, it is claimed that loratadine has low sedation potential with no effect on cognitive and psychomotor performance.(2-4)

Loratadine is metabolized by hepatic CYP□A isoform of CYP□□□ to a biologically active metabolite desloratadine.(6,7)

Several studies indicated that desloratadine possesses anti-inflammatory as well as antiallergic activity.(8,9)

Several drugs including erythromycin inhibit CYP□A isoform of CYP□□□ and may interfere with loratadine metabolism.(1)

It is possible in clinical practice to co-administer erythromycin together with loratadine to treat symptoms of allergic rhinitis associated with respiratory tract infection. This stimulate us to determine the pharmacodynamic consequence of such combination regarding the central depressant psychopharmacological effects of loratadine.

Subjects and method

This study was conducted on apparently healthy six volunteers, two females and four males, with age ranging from 32-47 years.

It was randomized single blind placebo controlled cross-over study. Volunteers were assigned to receive treatment in sequence separated by seven days wash-out period. The treatment sequence was as follows:

1.Three days course of erythromycin capsules (500 mg) twelve hourly followed by placebo (glugose powder) or single dose of loratadine (10 mg) tablet (Lorasam SDI) on day four ,or three day course of placebo followed by single dose of loratadine.
2. Single dose of loratadine tablet(10 mg) alone.
Drugs were put in identical opaque capsules. All subjects were requested to avoid taking drugs or foods that have central depressant or hepatic enzymes inhibition actions. The effect of loratadine on psychomotor performance was assessed using finger tip reaction time. [5]Calculation of reaction time was performed before medication and hourly afterward for three hours, by dropping aruler between the out stretched fingers of subject without warning. Reaction time is calculated given the distance subject catch ruler and that the ruler was released from.

Results:

Results were expressed as mean ±SEM.The data were analyzed using student's t test considering $p \leq 0.05$ as lowest limit of significance. Loratadine exerts insignificant effects on reaction time throughout the three hours study period. However co-administration of loratadine with erythromycin shows statistically significant prolongation of reaction time in (respect to placebo and loratadine results) three hours post dosing. (Table 1).Subjects claimed that they felt drowsiness and lightheadedness after one hour of loratadine ingestion.

Table (1) : Values of Finger Tip Movement Reaction Time in Seconds
Values are Expressed as Mean ± SEM

Treatment	Time			
	0 hr	1 hr	2 hr	3 hr
Placebo	0.128 ± 0.0069	0.127 ± 0.0068	0.128 ± 0.0065	0.129 ± 0.0037
Loratadine	0.122 ± 0.0105	0.12 ± 0.0078	0.129 ± 0.0075	0.125 ± 0.0067
Loratadine plus Erythromycin	0.125 ± 0.0099	0.129 ± 0.0078	0.134 ± 0.0084	*0.143 ± 0.0079
Erythromycin plus Placebo	0.127 ± 0.0096	0.123 ± 0.018	0.129 ± 0.0079	0.125 ± 0.0084

***P<0.05**

Discussion

Tests of the effects of drugs on psychomotor performance are important regarding the safety of patients using medications on day-to-day basis. Different psychometric measures are available for psychopharmacological testing of drugs. Critical flicker fusion test and choice reaction time are an important psychometric measures which form the basis of assessment in human psychopharmacology[2,3,15,16]Choice reaction time with its two components recognition reaction time and movement reaction time reflects the rate at which the eye and eye and hand are coordinated [13,14]. Reaction time is sensitive to the sedative effect of drugs including antihistamines.[15-18]Finger tip

reaction time reflects the time the brain needs to recognize aruler being dropped between subject's out stretched fingers without warning[5].The results of this study showed that a single therapeutic dose of loratadine devoid of significant impairment of psychomotor performance as indicated by assessment of finger tip reaction time. This is in agreement with several studies that conluded that loratadine did not impair performance.[2, ,8))

The second observation in the present study that the CP_3A inhibitor (erythromycin) precipitates the central depressant effect of loratadine, as indicated by longer time subjects required to respond and catch the dropped ruler. The felling of drowsiness which the subjects described could be attributed to central anticholinergic effect of the antihistamine [1,19,20) . It is possible that erythromycin inhibits metabolism of loratadin and so exposes the central nervous system to its central depressant effect. Several studies demonstrated that administration of loratadin with enzyme inhibitor drug s as cimetidin or ketokonazole increased the plasma concentration and area under the curve of loratadin[10-12].1n contrary to our finding those studies did not demonstrate a change in pharmacodynamic profile of loratadine regarding its effect on ECG parameters. However administration of double therapeutic dose of loratadine with CYP3A inhibitor nefazodon enhanced the arrhythmogenic potential of loratadine

In conclusion administration of loratadin with erythromycin can interfere with performance of day time activates and place patient at an increased risk of accidents in situations as driving or operating machinery, where high level of alertness is required This also reduces compliance with treatment regimen due to excessive fatigue and drowsiness.

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