



Effect of Single Dose 10 mg Cetirizine on Visual Processing Speed for low and high intensity stimuli in Healthy Human Volunteers

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Abstract

Objective: This study was designed to assess the effect of a second generation antihistaminic (H-1 blocker) namely Cetirizine on the visual processing speed for low and high intensity stimuli in healthy human volunteers at one and three hour after Cetirizine consumption.

Methods: It was a single dose, prospective interventional study held in BJGMC, Pune. 50 healthy human volunteers were enrolled and baseline readings for all volunteers were noted. After recording baseline 10 mg single, oral dose of Cetirizine was administered. The visual processing speed was tested on Flicker –fusion apparatus (visual acuity in flickering frequency per second). Baseline was compared with one hour and three hour respectively.

Results: The visual processing speed did not show any significant changes when readings at one hour and three hours, each were compared to baseline readings ($p > 0.05$).

Conclusion: Single dose 10 oral Cetirizine does not significantly alter the visual processing speed for low or high intensity stimuli at one or three hour after administration.

Keywords: visual processing speed, Cetirizine, Critical Flicker Fusion Apparatus.

INTRODUCTION

The term “visual processing speed” can be defined as, “the amount of time needed to make a correct judgment about a visual stimulus.”^[1] These responses are crucial for visual tasks which include detecting the presence of a target, distinguishing between targets, identifying what a target is and its recognizing its familiarity. Most important is indicating its spatial location then subsequently making other types of decisions about visually complex events. Humans can process visual stimuli

at extremely rapid presentation durations, as short as 14 ms. ^[2] A studies have concluded that visual processing impairment has an association with motor vehicle crashes and injury but most of these studies were conducted among the elderly. ^{[3][4][5]} A Road Traffic Accident (RTA) can be defined as, ‘An event that occurs on a way or street open to public traffic; resulting in one or more persons being injured or killed, where at least one moving vehicle is involved. According to the World Health Organization (WHO), road traffic injuries are the

sixth leading cause of death in India with a greater contribution of hospitalization, deaths, disabilities and socio-economic losses in the young and middle-aged population. Road traffic injuries also place an enormous burden on the health sector in terms of pre-hospital and trauma care and rehabilitation.^[6] There are multiple causes of RTA traffic followed by drinking and driving, drugs like antihistamines, cellular mobile phone use while driving, etc. Widespread use of antihistamines present a particular concern since the antihistamines are recognized for causing sedation and central nervous system (CNS) hypofunction that can jeopardize safe driving.^[7] There are many studies which have delved in the controversial issue that cetirizine although is classified as second generation non-sedative anti-histaminic yet is associated with the liability of causing sedation^{[8][9][10]} Reports have suggested that Cetirizine tends to affect psychomotor performance^[11]. There is significant relationship between Visual Acuity impairment and road accidents^[12] In the brain, antihistamines block histamine receptors. Histamine is associated with arousal, attention and processing speed of basic but important information. Antihistamines have a wide pharmacologic profile: they easily cross the blood-brain barrier and bind non-selectively to H-receptors, but they also interact with adrenergic, serotonergic, and cholinergic neurons. A variety of adverse effects may come with their use, including sedation, reduced alertness, and anticholinergic effects (e.g. blurred vision). The critical flicker/fusion frequency is a sensitive measure used to detect sedation caused by centrally active antihistamines.^[13] These unwanted effects may affect performance of routine activity such as driving.^[14] Critical flicker fusion (CFFF)^[15] non invasive and of good reliability in cortical arousal as well as a good marker of cortical alteration to physical workload, drug administration, alcohol intoxication, anaesthesia hypoxia or in case of encephalopathy. The current study was designed to assess the changes in visual processing speed associated the use of second generation anti-H1 anti-histaminic –Cetirizine using CFFF as the parameter.

AIM AND OBJECTIVES

This study was designed to assess the effect of a second generation antihistaminic (H-1 blocker) namely Cetirizine on the visual processing speed for low and high intensity stimuli in healthy human volunteers at one and three hour after Cetirizine consumption.

METHODS

It was single dose, interventional pilot study; conducted in a tertiary care teaching Government Hospital, Pune. Study was conducted after obtaining approval from Ethics committee. It was conducted over 1 month. The Critical Flicker Fusion Frequency (CFFF) was measured using Flicker – fusion apparatus (Medicraft Manufacturer, Model And Serial No. 715/FF-008).

Flicker fusion Apparatus

Instrument: The device consists of a rotating ring, surrounding a short cylindrical waterproof housing of 8 cm diameter containing the numeric (digital) frequency indicator. Attached to this housing is a flexible cable, on the end of which a single red LED (Light Emitting Diode) RED colour is enclosed in a smaller cylindrical container (to shield it from stray light and reflections). The subject to be tested was instructed to look straight at the LED light at a distance.

Individually adapted to his personal vision (generally around 50 cm), the investigator turned the dial slowly clockwise in order to increase the flickering frequency of the LED. As there are no markings on the dial, nor a visible “starting position”, the test subject had no indication whatsoever of the actual flicker frequency. When the subject sees a change from flicker to fusion, he signals this to the investigator, who notes the actual frequency—which is the definition of CFFF.^[15]

This test was carried out systematically three times in order to check its reproducibility. Baseline CFFF values were noted initially for each volunteer. The average of the three measurements was noted as the actual individual CFFF. Both Low frequency and high intensity stimuli were tested.

INCLUSION CRITERIA

1. Healthy human volunteers of age should be between 18-55 years,
2. Healthy subjects with no pathology or injury that will interfere with visual acuity.
3. Subjects with no history of drug consumption that might affect visual acuity. Eg: sedatives, atropine derivatives, etc
4. Subjects with no history of drug abuse of any kind.
5. Subjects with vision 6/6 or corrected vision 6/6 were included.

EXCLUSION CRITERIA

1. Volunteers <18 yrs and > 55yrs
2. Volunteers consuming alcohol, smoking and drug abuser were excluded.
3. Patients of any psychiatric disorder both were excluded as there might be an error in reporting fusion values.
4. Patient who is suffering from other central nervous diseases like epilepsy, sleep-disorders- narcolepsy, insomnia etc. that will affect the study outcome were excluded.
5. Volunteer not signing the consent form or not willing participate in the study.

SCREENING AND SELECTION

The 50 healthy human volunteers were screened and included for the study as per the inclusion criteria. Those who do not fulfill the above inclusion criteria or having any one of the exclusion criteria were excluded. Written informed consent was obtained from these eligible and willing volunteers.

Baseline reading on Flicker –fusion apparatus was taken for each participant from each group which acted as the control baseline value. No other group was used as control but the baseline values were used as control so to minimize person to person variation in CFFF values and hence to obtain reliable results.

Tests were repeated one hour and three hours later after drug administration -Tab. Cetirizine 10 mg oral stat (Film coated tablet contain Cetirizine Hydrochloride IP 10 mg, Titanium Dioxide IP) the

investigator to the volunteer for the study duration. Parameters of distractions which could affect the outcome of the study – like sitting position of the volunteers were maintained uniformly for all participants. Other parameters like ambient noise distractions were minimized as well as luminosity of the study room was standardized and maintained throughout the project.

STATISTICAL ANALYSIS

Student's paired t-test was applied to calculate change from baseline reading each as compared to one hour and three hours respectively. The statistical analysis was done using software Graph pad prism 6.0 version.

RESULTS AND DISCUSSION

The study group included 50 volunteers out of which 24 were males and 26 were females. 44 volunteers belonged to the age group of 18 to 40 years whereas only 6 volunteers belonged to age group more than 40 years. Table No.1 shows that the baseline CFFF values were 40.30 ± 1.677 and 40.76 ± 1.316 hertz for low and high intensity. The values for low and high intensity respectively at one hour after 10 mg single dose Cetirizine administration values were 40.06 ± 1.445 and 39.59 ± 1.474 hertz. The CFFF values at three hours post-drug administration were 41.26 ± 1.318 and 41.39 ± 1.334 hertz for low and high intensity respectively. On comparison of one hour values with baseline CFFF values the p-value was 0.9137 ($p > 0.05$) for low intensity and 0.3020 ($p > 0.05$) on high intensity. (On comparison of both the group p-value of post test is 0.5389. Therefore there was a no statistically significant change in critical flicker fusion (low intensity and high intensity) from baseline as compared to one hour when the three hour reading was taken after single oral dose of 10 mg Cetirizine. Similarly no significant difference was observed on comparison of three hour values with baseline CFFF values as the p-value was 0.9956 ($p > 0.05$) for low intensity and 0.1553 ($p > 0.05$) on high intensity.

Table No.1: Critical Flicker Fusion Frequency at 1 hour and 3hours:

	CETIRIZINE (low intensity) (Hertz)	CETIRIZINE (high intensity) (Hertz)
Base(SEM)	40.30±1.677	40.76±1.316
Post Drug (SEM)1 hr	40.06±1.445	39.59±1.474
P Value#	0.9137#	0.3020#
Post Drug (SEM) 3 hrs	41.26±1.318	41.39±1.334
P Value \$	0.9956 \$	0.1553 \$

Values are presented as mean ±SEM .# p> 0.05 by Student's Paired t Test when baseline values compared with post-drug values at 1 hours.\$ p> 0.05 by Student's Paired t Test when baseline values compared with post-drug values at 3 hours

DISCUSSION

The grey area of research of refers to certain second generation antihistamines (viz. Cetirizine) that are not free from limitations of varying degrees of sedation. ^{[16][17]} There are several studies showing effects of Cetirizine on performance and measures of alertness. ^{[18][19]} On the other hand, there are also studies that did not find behavioral effects of Cetirizine. ^{[20][21]} The 2nd-generation antihistamines represent a major triumph for the pharmaceutical industry in reducing potential side effects; there still remains some evidence that all antihistamines, even the 2nd- generation drugs, can have objective skills impairment consequences at least in some cases. ^[22]

The present study included 50 healthy volunteers where males and females had equal representation. The age group 18 to 44 years included maximum number of volunteers whereas only 6 volunteers belonged more than 40 years. The age discrimination of groups was set 18 to 40 years and more than 40 years as studies suggest that there is a significant alteration in age-related visual processing speed. ^[1] The flicker fusion frequency is directly proportional to the logarithm of light intensity (Ferry-Porter law) up to 90-95 flashes/sec. With an increase in light intensity above 2,500 lux, the flicker fusion frequency once more diminishes. ^[23] Different points in the visual system have very different critical flicker fusion rate (CFF) sensitivities. Cones function best at higher intensity of light. ^[24] Therefore two intensities - low and high intensity stimuli were used.

The baseline CFFF values were 40.30±1.677 and 40.76±1.316 hertz for low and high intensity which were in accordance with finding another study who

reported a finding of 38.74±0.56 hertz; but intensity details of CFFF stimuli were not mentioned and that study was done in only ten normal healthy adult volunteers aged 21 to 39 years. ^[9] The same study had reported a CFFF value of 38.74±0.56 at 1 hr after Cetirizine (10 mg oral) administration which was in accordance with results of present study .Another study reported lower values of CFFF (29.2 ± 0.8) after Cetirizine (10 mg and 20 mg dose level) which included subject aged 23 years maximum. ^[25] Probably the age variation translated as an impact on the outcome values. In the present study comparison of one hour values with baseline CFFF values showed no statistically significant change in critical flicker fusion ,both for ,low intensity and high intensity, after a single oral dose of 10 mg Cetirizine, the p-value was 0.9137 (p> 0.05) for low intensity and 0.3020 (p> 0.05) on high intensity. Similar results were obtained at three hours after Cetirizine (10mg) administration (p> 0.05) for both the intensities of light.Certain studies are in agreement with this finding. ^{[9][25]} But the studies had tested CFFF only for one intensity in a smaller group of volunteers (10-12) .Whereas the present study further evaluated CFFF at low as well as high intensities to study the effect of the drug on photo-receptor cells as cones and rods separately. Although reports about sedation due to Cetirizine as controversial but the effects on visual processing speed in a dose 10 mg orally are statically insignificant for both low and high intensity light stimuli.

CONCLUSION

The mystery of sedative effect of Cetirizine remains elusive and debatable. Cetirizine at commonly used single therapeutic dose i.e. 10 mg orally does not produce alterations in visual processing speed at one or not even at three hours. The degree of drowsiness is not severe to affect these parameters. These results hold true for both the intensity of light tested concluding that both color vision and light vision processing are intact with that single dose of Cetirizine.

LIMITATION**INDIVIDUAL VARIABILITY**

The studies are done on healthy volunteers, not on patients, whose conditions in themselves (allergic rhinitis) could be causes of somnolence.

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