Effects of anti-malarial prophylactic mefloquine on the light-dark test of anxiety
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Introduction

Mefloquine is an anti-malarial medication developed in 1970 by the Walter Reed Army Institute of Research. Not much is known about the drug’s mechanism of action in terms of preventing malaria, but it has been shown to successfully reduce the chance of contracting the disease when used preventively (Tioevo, 2009). It has been used in various different instances recently including U.S. troops and Japanese troops. Those who experience combat become more susceptible to many different psychiatric disorders such as PTSD, and major depression. It is speculated that taking mefloquine in addition to the major stressful events encountered during combat will in turn cause a more exacerbated reaction (Tioevo, 2009). Those who take mefloquine and have a neuropsychiatric disorder have been shown to have more exacerbated symptoms after taking mefloquine, and are at a greater risk for developing adverse effects to the drug (Office of Assistant Secretary of Defense, 2009).

Mefloquine has also been shown to increase acute depression after cessation of use. (Callon, et al., 1992). The number of exacerbated neuropsychiatric cases due to mefloquine use could be reduced if prescribed properly. One study showed that in US military troops deployed to Afghanistan, approximately one in seven individuals with neuropsychiatric contraindications to mefloquine received a prescription to it (Nevin et al., 2009). This led to an increased risk of an adverse event arising due to this drug. Due to the amount of adverse reactions seemingly caused by mefloquine, the United States Military dropped mefloquine as its primary antimalarial drug in 2009 (Office of Assistant Secretary of Defense, 2009).

Our experiment evaluates the impact of mefloquine given a similar psychiatric single dose on subjects’ performance in the light-dark test of anxiety.

Methods

Subjects

41 C57BL/6J male mice were maintained in groups of five animals in a reverse 12/12 h light/dark cycle in a temperature and humidity controlled vivarium with continual access to food and water. The subjects were randomly assigned to receive a 0, 2, or 5 mg/kg injection of mefloquine. A corn oil vehicle was used to inject the subjects. The light-dark avoidance test was used to measure anxiety 24 hours after injection.

Behavioral Testing and Analysis

The apparatus consisted of two chambers separated by a plastic door. The first chamber was a smaller, completely dark box. The second chamber was illuminated, separated by four quadrants and is where behaviors were videotaped and analyzed. At the beginning of the testing period, the subject is placed in the dark chamber. After 30 seconds, a door was opened providing access to the illuminated chamber. Subject is then allowed to freely explore the cage for 6 minutes. During this time the subject is videotaped. The purpose of this test is to measure locomotive and anxiety type behaviors. Analysis of the videotape was accomplished using a computer program to track the subject’s position in the apparatus. Subjects were tested 24 hours after the injection. Time in light, emergence latency number of rears, and amount of times groomed variables were all recorded.

Results

Subjects injected with 5 mg/kg reared significantly more compared to controls, t(39) = -2.92, p = 0.01 (see figure 1).

Subjects injected with 5 mg/kg spent significantly more time in the light compared to controls, t(39) = -1.66, p = 0.09 (see figure 3). There were no differences of emergence latency, t(39) = 0.07, p = 0.47 (see figure 2), or grooming variables, t(39) = -0.26, p = 0.40, between the two groups.

Discussion

The mice injected with a 5 mg/kg of mefloquine reared significantly more and longer than controls. This indicates that mefloquine had an anxiolytic effect as the animals were more explorative and thus the change in environment caused less anxiety compared to controls.

Mice injected with a 5 mg/kg dose of mefloquine spent more time in the light, again indicating that mefloquine had an anxiolytic effect, as the mice were less intimidated of the lighted area. However, there were no differences between the groups in the amount of time groomed or emergence latency. More subjects may have been needed to see an effect with these variables.

As stated, those who have taken mefloquine are susceptible to depression and agitation during withdrawal from the drug (Callon, et al., 2009). The anxiolytic effect observed here supports this idea as with anxiolytics, such as alcohol, a depressive withdrawal effect can be observed.

In order to get a better idea of mefloquine’s neuropsychiatric effects on those taking it, future studies should focus on using more subjects and administration of the drug over a longer period of time to replicate prophylactic use. A test for depression, such as the tail-suspension test, should also be administered to gauge if subjects are suffering from depression during the withdrawal period of the drug.

References


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