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REVIEW

Meclizine: Safety and Efficacy in the Treatment and Prevention of Motion Sickness

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Abstract: Motion sickness is a self-limiting but uncomfortable phenomenon experienced by many people. It is common during civilian travel and also among professionals during travel or military manoeuvres. Meclizine is a piperzine antihistamine that is effective for the prevention and treatment of motion sickness, particularly during mild civilian travel. It is well tolerated with few adverse effects and its oral dosage form is convenient for patients to take prior to exposure to motion as a preventative measure.

Keywords: meclizine, motion sickness, antihistamine, motion sickness prevention, motion sickness treatment

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Introduction

Motion sickness is a common phenomenon that is usually self-limiting but may cause great discomfort. Everyone will experience motion sickness at some time during their life, although sensitivity varies tremendously among individuals.[1,2] It is very difficult to predict who will experience this syndrome when travelling on any moving vehicle or exposure to visual moving scenes, although it has been indicated that normal vestibular function is a necessary requirement for the development of motion sickness.[3,4] In addition, individual responses during motion sickness will vary due to stimulus conditions and duration of exposure.[4] Other factors include gender and age; females and children between the ages of 2 and 12 experience an increased incidence.[5–7]

Motion sickness is characterized by a combination of signs and symptoms, including nausea, vomiting, stomach awareness, pallor, cold sweats, and dizziness.[4,8] The exact mechanism of motion sickness still remains a mystery.[8] One of the most widely accepted theories describes the mismatch or confusion between the vestibular, visual and proprioceptive systems.[1,2,9] Vestibular receptors are found in each inner ear. These receptors communicate with the vestibulocochlear nerve, which is responsible for balance and spatial orientation. Visual information is relayed to the brain by the optic nerve. The proprioceptive system provides information to the brain concerning the body's movement and position. When visual and/or proprioceptive input does not match what the vestibular receptors are sensing, there is a great mismatch, resulting in homeostasis upset.[1]

The most common treatments for motion sickness include antihistamines and anticholinergics. Most of the research regarding treatment has been funded by the National Aeronautics and Space Administration (NASA) and by navies worldwide, since this is the population most greatly affected.[1] The majority of research conducted in the area of motion sickness occurred during the mid to late 1900s. This paper will review the available literature and discuss the use of meclizine in the treatment and prevention of motion sickness.

Mechanism of Action, Metabolism and Pharmacokinetics

Meclizine is an antihistamine, reversibly inhibiting the interaction of histamine at the H1 receptors; it is a member of the piperazine class of H1 antagonists.[10,11] Antihistamines decrease the incidence of motion sickness by blocking H1 receptors in the emetic center and decreasing sensitivity of the vestibular apparatus within the inner ear.[1] In addition to antihistaminic activity, these compounds possess anticholinergic activity; since scopolamine, an anticholinergic agent, is very effective in preventing motion sickness, it has been thought that the anti-motion sickness activity of antihistamines is due to their anticholinergic actions.[10,12–14]

Human data regarding the pharmacokinetics of meclizine are lacking.[15] Meclizine has an onset of action of about one hour with a prolonged duration of action; drug effects can last anywhere between 8 to 24 hours following oral administration with a half life of 6 hours.[16] Based on studies conducted on rats, meclizine is metabolized to an inactive metabolite, norchlorcyclizine, most likely by the liver.[17] Norchlorcyclizine distributes throughout all body tissues of the rat, as well as penetrating the placental barrier. Meclizine is found unchanged in the feces, but was eliminated as norchlorcyclizine in the urine.

Clinical Studies and Efficacy

A study of 12 United States Navy personnel onboard a sailing naval ship examined the efficacy of meclizine 50 mg 1 hour prior to departure then daily for the first 8 days of the trip.[18] Six subjects reported regular symptoms of seasickness upon travel, while the other 6 subjects reported occasional symptoms. After meclizine was started, among those experiencing regular symptoms, one reported mild, transient nausea on day 2, while the remaining 5 experienced no symptoms. Among the occasional symptom subjects, none reported symptoms of seasickness after taking meclizine. The authors concluded that meclizine is an effective anti-motion sickness drug.

The National Aeronautics and Space Administration studied the efficacy of several motion sickness drugs including meclizine.[19] The authors concluded that meclizine 50 mg may be sufficient to treat motion sickness due to mild conditions, such as car travel, but that other agents might be required to treat moderate and severe motion conditions.

The efficacy of meclizine and transdermal scopolamine were compared to placebo in a double blind, double-dummy, placebo-controlled crossover

study.[20] Thirty-six healthy subjects were randomized to meclizine 25 mg taken 2 hours before motion exposure, scopolamine 1.5 mg transdermal patch (0.5 mg/hr for 72 hrs) applied 12 hours before motion exposure, or placebo; as this was a crossover study, each patient received each treatment once. A ship movement simulator was used for a 90 minute experiment to create motion sickness symptoms. Subjects rated their nausea every 3 minutes on a scale from 0 (no symptoms) to 5 (retching or vomiting). The lowest mean symptom scores occurred during scopolamine use, followed by meclizine and then placebo. Scopolamine produced the greatest efficacy in protecting 60% of subjects from motion sickness, as compared to meclizine at 20%. The authors concluded that transdermal scopolamine provides better protection against motion sickness than meclizine or placebo.

A more recent study examined the efficacy of various motion sickness medications in helicopter passengers.[21] A total of 64 subjects were randomly assigned to one of the following treatments: promethazine 25 mg + caffeine 200 mg; meclizine 25 mg; scopolamine 1.5 mg transdermal patch; or a stimulation wristband. Each patient was subjected once to a 30 minute helicopter ride after taking the active drug, and then to another ride 7 days later after receiving a matching placebo. Symptoms of motion sickness were rated using the Motion Sickness Questionnaire (MSQ). Subjects were also tested for balance, reaction time and cognitive performance. When compared to placebo, the promethazine + caffeine combination was the only one that produced statistically significant improvement on the MSQ for nausea ($P = 0.019$) and symptom severity ($P = 0.041$). Promethazine + caffeine also significantly improved (decreased) reaction time as compared to placebo ($P = 0.050$). The wristband increased reaction time ($P = 0.007$). Meclizine did not show any statistical significance on the MSQ or tests for balance, reaction time or cognitive performance. There were no between-group differences in any of the measures of efficacy or safety. The authors concluded that promethazine + caffeine was the only treatment that improved motion sickness symptoms when compared to placebo.

The above literature reports on the efficacy of meclizine for the prevention and treatment of motion sickness are conflicting; however, the data are overall difficult to interpret. One reason for this is that much of the data were published prior to 1990; the quality of reporting of this data is questionable since many of the reports failed to include specific data needed to adequately assess the study and its results, *P*-values and/or other statistical analysis, or both and offered qualitative summaries instead. Regardless, meclizine is likely to be an effective prevention and treatment of motion sickness caused by mild to moderate motion experienced during civilian travel.

Safety

Overall, meclizine appears to be generaly well tolerated. The most common adverse effect associated with meclizine use is drowsiness, although it appears to produce less drowsiness then dimenhydrinate and diphenhydramine.[15,22,23] In one study comparing meclizine with transdermal scopolamine, drowsiness was significantly greater ($P < 0.001$).[24] Another frequently reported adverse effect is dryness of the mouth.[15] When compared to transdermal scopolamine, the incidence of dry mouth is less.[20] Blurred vision is a rare occurrence associated with meclizine use; when compared with transdermal scopolamine, there was no significant difference between rates of occurrence.[20,24]

A study evaluated the effects of meclizine 50 mg and hyoscine 1 mg on memory and perceptual efficiency (vigilance).[25] Meclizine or hyoscine alone, meclizine or hyoscine with alcohol, alcohol taken 24 hours after meclizine or hyoscine were tested. The study found that meclizine had no significant effect on vigilance, but the addition of alcohol did decrease vigilance scores. The combination of meclizine with alcohol had additive effects of impaired vigilance that were beyond just the effects of meclizine alone plus the effects of alcohol alone. Meclizine alone and meclizine plus alcohol also decreased the speed of work, however this did not reach statistical significance. The authors concluded that meclizine may be preferred over hyoscine due to its lesser effects on performance.

A study of 24 healthy male volunteers examined the central nervous system effects of meclizine 50 mg to dimenhydrinate 100 mg.[26] This study found that meclizine significantly increased recognition and reaction time 9 hours after the dose ($P < 0.05$ for

both). Dimenhydrinate increased recognition time starting 1 hour after the dose ($P < 0.05$) and continued, with the maximal difference from placebo at 3 hours. Dimenhydrinate also increased reaction time starting 3 hours after the dose ($P < 0.05$). Sleepiness as rated on a visual analog scale was rated higher with both meclizine and dimenhydrinate as compared to placebo; however, this did not achieve statistical significance. Maximal sleepiness as rated by the Standford Sleepiness Scale was found to be higher in the dimenhydrinate group vs. placebo ($P < 0.05$). The authors concluded that both meclizine and dimenhydrinate produce CNS impairment; however, dimenhydrinate effects manifest 2–3 hours after dosing, while meclizine effects are delayed for up to 6 hours after that.

A study evaluated the memory effects of meclizine 25 mg, lorazepam 1 mg, promethazine 25 mg, scopolamine 0.4 mg and placebo in 67 healthy adults.[27] Subjects had to perform memory tests both before and after spinning in a rotary chair with no study drug, and both before and after spinning in a rotary chair with study drug. The authors found that meclizine produced the least amount of detrimental memory effects in that it did not significantly decrease overall accuracy of answer choices or increase the time to make a choice, followed by scopolamine, promethazine and lorazepam. However, the authors also said that only scopolamine improved motion sickness, as rated by the number of chair rotations tolerated by study subjects, and therefore, scopolamine may be preferred as the agent of choice in the treatment of motion sickness.

The US Food and Drug Administration (FDA) has rated meclizine as pregnancy category B. In 1962, it was thought that meclizine could possibly cause fetal abnormalities.[28] However, after reviewing data concerning meclizine use in pregnancy, the FDA determined that there was not enough evidence to support a restriction on the use of this drug in pregnancy.[15] Since 1962, there have been several trials demonstrating meclizine's safety in pregnancy.[29,30] One study evaluated a total of 50,282 mother-child pairs.[30] Of these, 1,014 mothers had taken meclizine during the first four months of pregnancy. The rate of all malformations combined among those not exposed to meclizine was similar to that in the exposed group (relative risk 1.13; 95% confidence interval 0.88–1.46). However, the rate of eye and ear malformations was higher in the exposed group (relative risk 2.79; 95% confidence interval 1.12–5.73; $P < 0.05$) but the authors did not identify a specific type of ocular abnormality to be higher in either group.

Patient Preference

Studies specifically evaluating patient preference for motion sickness treatments have not been conducted. As an oral agent, meclizine, which is approved for both the prevention and treatment of motion sickness, provides a convenient over-the-counter dosage form that is portable and easy to administer. Patients need to take meclizine one hour prior to exposure to motion; that one dose can last up to 12–24 hours.

Like meclizine, dimenhydrinate is also used for both prevention and treatment of motion sickness; however, it must be taken every 4–6 hours. Also of note, it is likely that dimenhydrinate causes adverse effects such as drowsiness more frequently than meclizine.[16]

Transdermal scopolamine is only approved as prevention of motion sickness and must be applied to the postaural area at least 4 hours prior to motion exposure; however, the patch remains effective for 72 hours, eliminating the patient's need to take frequent doses of medication. As a prescription-only product, a patient must visit a physician or other prescriber in order to obtain this drug.

Place in Therapy

Meclizine is an effective agent in the prevention and treatment of mild to moderate motion sickness, although promethazine and dimenhydrinate are more effective.[10] Although meclizine is slightly less effective, it may be the preferred agent; promethazine is only available with a prescription and dimenhydrinate is associated with more drowsiness. It also has the longest duration of action (up to 24 hours) compared to other antihistamines available for the treatment of motion sickness. Meclizine is better at preventing motion sickness when taken at least one hour prior to travel; promethazine is more effective once motion sickness has occurred.[15]

Conclusions

Motion sickness is a common ailment and one that is often self-treated by patients. Meclizine offers an effective and convenient option for motion sickness

caused by mild motion disturbances. While more severe conditions presented by military or other professional transport may warrant other agents, meclizine is likely effective for most types of civilian travel.

Disclosures

This manuscript has been read and approved by all authors. This paper is unique and not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

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