

High Dose Ondansetron for Reducing Motion Sickness in Highly Susceptible Subjects

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Background: Ondansetron is currently being explored as a treatment for motion sickness due to its proven prophylactic effect on post-operative nausea, the nausea and vomiting associated with chemotherapy, and its lack of side effects. This study sought to compare the effectiveness of placebo, dimenhydrinate, and ondansetron for preventing motion sickness in highly susceptible subjects. **Methods:** A total of 63 subjects with a history of frequent motion sickness and positive report of self-treatment of motion sickness with over-the-counter medications were divided into 3 groups of 20 (3 were disqualified). Depending on their group assignment, subjects were given placebo, dimenhydrinate, or ondansetron 1 h before being rotated at 20 rpm while making head movements. Symptoms of motion sickness and electrogastrogram (EGG) data were collected prior to and during rotation. **Results:** There were no differences between the groups in number of head movements tolerated, time rotating, or symptom questionnaire scores. All groups showed a marginally significant decrease in normal 3 cycle per minute activity [$F(1,45) = 3.04, p = 0.088$] and a significant increase in gastric tachyarrhythmia [$F(1,45) = 9.71, p = 0.003$], a pattern typically associated with motion sickness development. **Conclusion:** Neither ondansetron or dimenhydrinate prevented motion sickness in groups of highly susceptible people. Continued development of new treatments is necessary.

Keywords: electrogastrography, gastric tachyarrhythmia, nausea, anti-emetics.

MOTION SICKNESS, which refers to a collection of symptoms that occur after exposure to real or illusory motion, affects an estimated 90% of U.S. adults at some point in their lives (12). Symptoms can include dizziness, headache, sweating, nausea, drowsiness, and vomiting (17). The debilitating symptoms are an annoyance at best for most people; however, for some people, symptoms are so unbearable that the individual avoids the stimulus (e.g., a ship) altogether. The purpose of this study was to examine the efficacy of ondansetron, a possible drug remedy for motion sickness, on inhibiting the symptoms of motion sickness and nausea in subjects with a history of severe motion sickness.

The efficacy of available drug remedies for reducing motion sickness symptoms is somewhat constrained. Drugs such as dimenhydrinate (which is the most common motion sickness prophylactic) and scopolamine perform well when it comes to the reduction of nausea and other incapacitating motion sickness symptoms (4). Many studies support the efficacy of these options. On the other hand, most of these anti-motion sickness drugs also have unwanted side effects such as drowsiness, dizziness, blurred vision, decreased performance,

and slowed reaction time. For example, in a previous study using replicated naval crew tasks, it was found that 100 mg of dimenhydrinate significantly slowed decision reaction time (7). Another study focusing on motion sickness found that the ingestion of 100 mg of dimenhydrinate resulted in significantly greater drowsiness reports when compared with subjects who received placebo (17). In doses as small as 0.6 mg, scopolamine has been associated with a significant increase in the number of errors on visual attention and mental arithmetic concentration tasks (2). Many other studies have found similar results regarding the side effects of current anti-motion sickness drugs (24). In the military, increased operator drowsiness is thought to be the underlying factor in many serious accidents and incidents that are attributed to insufficient operator attention (3). Other treatments for motion sickness without these incapacitating side effects include ginger, acupressure bracelets, and countless other methods. However, many of these alternatives seem to have limited efficacy (16). An alternative motion sickness treatment is needed that will prevent symptoms without producing undesired side effects and be effective in individuals with a history of severe motion sickness.

Ondansetron is currently being explored as a treatment for motion sickness due to its proven prophylactic effect on post-operative and chemotherapy-induced nausea and vomiting and relative lack of side effects. It has been found that 4 mg of ondansetron significantly reduced post-operative nausea and vomiting in patients recovering from general anesthesia (13,15). Ondansetron also produces satisfactory anti-emetic effects when given 1 h before cisplatin (a cancer treatment drug) (19). Several other studies have also shown ondansetron to be effective in reducing nausea and emesis due to cytotoxic drugs used in chemotherapy (4). Overall, ondansetron has been repeatedly shown to inhibit nausea and vomiting due to chemotherapy and anesthesia (10).

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Although ondansetron is associated with inhibiting gastric tachyarrhythmia (an increased frequency of pacemaker potentials in the stomach which disrupt gastric contractions that has been linked with nausea and motion sickness), previous studies have failed to show ondansetron as effective in reducing motion sickness and its accompanying symptoms (14,23). The lack of effect on motion sickness could be due to the fact that each of these studies had particular weaknesses such as small dosages, lack of screening for susceptible subjects, or using a stimulus that was too mild to evoke the needed response. If a study compensating for these weaknesses found that it is in fact effective against motion sickness, ondansetron could provide relief from motion sickness symptoms without the undesired side effects. Thus, it was hypothesized that ondansetron would differ significantly from placebo and dimenhydrinate in preventing motion sickness in highly susceptible subjects. Furthermore, it was also hypothesized that dimenhydrinate would perform significantly better than placebo in preventing the onset of motion sickness.

METHOD

Subjects

After screening, 72 possible subjects were identified. Of these, 63 (23 men and 40 women) healthy college student volunteers from Clemson University with an age range of 18 to 25 (mean = 19.5, SD = 1.6) agreed to participate. Note that three subjects were disqualified: two for apparent adverse reactions to the test medication before exposure to chair motion; and one for mechanical failure of the rotating chair during the motion. All three subjects were replaced with a same condition subject by the pharmacy while maintaining the double-blind procedure. A motion sickness history questionnaire (MSHQ) (21) and demographic questionnaire were distributed to 750 volunteers in order to identify eligible subjects. Volunteers filling out screening questionnaires were compensated. In order to be eligible to participate in the actual study, subjects were required to be highly susceptible to motion sickness and have had a history of use of over-the-counter treatments for motion sickness. Those with a score of at least 45 on the MSHQ and who self-reported using over-the-counter motion sickness medications were considered highly susceptible. The subjects were also screened for neurological, gastrointestinal, and cardiovascular disorders that could interfere with the experiment. The subjects were compensated at the end of the study. The Greenville Hospital System Institutional Review Committee approved the study. All subjects provided written informed consent.

Design

This study was a randomized, double-blind, placebo-controlled between-subjects design. The independent variable was the type of drug given to each subject. The dependent variables were number of head movements tolerated, scores on the Motion Sickness Assessment Questionnaire (MSAQ) (6), and scores on the Nausea Profile (18).

Apparatus

The Visual-Vestibular Device (VVD) from the Clemson University Human Stress and Motion Science Laboratory was used in this study. A Biolog physiological recording device was used along with Fetrodes to obtain respiration, heart rate, and electrogastrogram (EGG) data (UFI, Morrow Bay, CA). Questionnaires were also used to assess motion sickness. These included the MSHQ, the MSAQ, and the Nausea Profile. These questionnaires provided verbal and written self-reports from the subjects about their feelings of motion sickness before, during, and after the study.

VVD: The VVD is a cylinder-shaped room which contains a rotating chair and an optokinetic projection drum (5). The room is 2.4 m tall with a diameter of 2.2 m. The optokinetic projection drum is capable of projecting a stripe pattern or random dot pattern onto the wall of the room. However, the optokinetic projection drum was not used during this study, as subjects were in complete darkness. The chair and drum are designed to rotate in clockwise and counter-clockwise directions from 0–40 rpm. The chair was rotated counter-clockwise at 20 rpm in this study.

Measures

MSHQ: The MSHQ questionnaire was used to collect pre-study information on the motion sickness susceptibility of subjects (21). It inquires about past experiences with motion and feelings of motion sickness and then assigns a score to the subject using their answers and a standard scoring method. Previous research indicates that scores on this questionnaire correlate significantly tovection-induced motion sickness (11). The minimum and maximum scores possible are 0 and 180, respectively. The MSHQ form used in this study did not differentiate between childhood and adulthood since subjects were between the ages of 18 and 26. Using this questionnaire allowed those who were highly susceptible to motion sickness and those who were not susceptible at all to be identified.

MSAQ: The MSAQ was used to assess 16 symptoms of motion sickness before, after, and while the subject was in the VVD. It was developed for the subjective assessment of motion sickness (6). By basing scores on symptoms such as sweatiness, queasiness, drowsiness, nausea, fatigue, and lightheadedness, it allows researchers to differentiate between different dimensions of motion sickness such as gastrointestinal distress, emotional distress, and somatic distress. In this experiment, the MSAQ was administered verbally every 5 min. The subjects indicated their feelings of each motion sickness symptom on a 0 to 10 scale. The minimum and maximum scores possible are 0 and 160, respectively. These answers provided an assessment of the progression of motion sickness symptoms over time.

Nausea profile: The Nausea Profile consists of 17 items and was administered both before and after the experiment. This questionnaire rates aspects such as shakiness, lightheadedness, hopelessness, and queasiness. The Nausea Profile was developed to give researchers a way to differentiate between different types of nausea

and it has been shown to be reliable (18). The minimum and maximum points possible are 0 and 153, respectively, from which a percentage of the maximum score is derived.

EGG: The lack of 3 cycles per minute activity (cpm) and the increase of 4–9 cpm activity (also known as tachyarrhythmia) have been repeatedly linked withvection-induced nausea (22). Therefore, a decline in 3 cpm activity and an increase in tachyarrhythmia were used as a physiologic nausea indicator. EGG data were collected using the Biolog and EGG electrodes were positioned with one on the midline of the abdomen (at the lower third of the distance between the umbilicus and sternum) and one on the left side of the subject at the level of the lower rib. A reference electrode was placed on the right side of the subject at the level of the lower rib. Electrode sites were prepared using gauze pads and an abrasive gel to clean the area.

Procedure

Screening phase: Due to the fact that individuals differ in susceptibility to motion sickness, a rigorous screening process took place to find highly susceptible subjects. During the screening phase, subjects were recruited through on and off campus advertisements. The ads posted several sessions at which subjects were able to show up to complete the MSHQ, several questions regarding their use of over-the-counter (OTC) motion sickness medications, and several demographic questionnaires to further assess their eligibility for participating. There were 750 subjects who were targeted and were paid for completing the questionnaire. Note that this recruiting questionnaire was linked to the study, but did not involve the full consent for participation in the study. It contained a brief statement of consent for completing the questionnaire and stated that subjects completing the questionnaire might be contacted to ask their willingness to participate in further research. Subjects who scored greater than 45 on the questionnaire were considered highly susceptible to motion sickness. Those who had high susceptibility and a positive history for OTC use of motion sickness medication were recruited to participate in the motion phase and contacted via phone or e-mail.

Randomization: Subjects were randomized in blocks of six. The pharmacy associated with the project handled the treatment randomization so that the experimenters were blinded to the treatment condition. The experimenter was given the appropriate drug or placebo combination prior to the subject's arrival. If a scheduled subject did not show for an appointment, the next subject filled that randomized subject slot so that no subject slots went empty.

Motion phase: Subjects arrived at the laboratory fasted for 4 h and having abstained from nicotine, alcohol, and caffeine for 8 h. After being briefed on the study they were asked to read and sign an informed consent form. Subjects were then asked to ingest either: 1) three 8-mg orally disintegrating ondansetron tablets + a tablet placebo; 2) one 100-mg dimenhydrinate tablet + three orally disintegrating placebo tablets; or 3) one placebo tablet + three orally disintegrating placebo tablets. All

test medications were ingested with 8 oz of water. Subjects' heart rates and BPs were taken prior to the medication and before and after exposure to the VVD to screen for any adverse BP reactions. Following ingestion of the test medication, subjects were prepared for physiological recordings including heart rate, stomach activity, and respiration. Subjects then completed a "pre-baseline" measurement on the MSAQ and the Nausea Profile. Subjects then were seated in a rotating chair and a 20-min baseline physiological recording was taken. Following the baseline, the head movement profile was demonstrated. At least 1 h elapsed between ingesting the test medication and chair rotation. Just before rotation subjects completed a "post-baseline" measurement on the MSAQ and the Nausea Profile.

During chair rotation at 20 rpm, subjects completed a series of roll and pitch head movements timed to an audio tape. They started with their head centered, then rolled their head right, back to center, rolled their head left, back to center, and then pitched their head forward and then back to center. Head movements were guided using an audiotape and executed smoothly during a 1-s period and held for a 1-s pause. After a series of three head movements there was an 18-s pause, making the total duration of a head movement series 30 s. Subjects continued to make the head movements for up to 20 min while they were rotated at 20 rpm. Once before and every 5 min during rotation, subjects were asked to verbally complete the MSAQ. While completing the questionnaire, the head movements momentarily stopped. Subjects were informed that they could request termination of rotation at any time. If they could not continue the head movements, rotation was terminated. Duration of the chair rotation was the earlier of: 1) exposure to 20 min of rotation; or 2) the subject requesting termination because they could not tolerate any more head movements.

After rotation, subjects were asked to again complete the Nausea Profile and MSAQ. They were then disconnected from all devices and asked to remain in the lab until nausea and dizziness symptoms returned to baseline. The subjects were then compensated before leaving.

Data Reduction and Statistical Analyses

MSHQ: The MSHQ was analyzed using standard formulas that assigned weight and values to subject responses (21). A post hoc one-way ANOVA was later used for comparing conditions.

MSAQ: The MSAQ scores were analyzed using standard weighted formulas. The total score of responses was divided by the total points possible (144) and multiplied by 100 to obtain a percent value (6). When performing studies dealing with motion sickness and nausea, it is inevitable that, as time goes on, subjects from each group will withdraw from the experiment (16). Data replacement for these subjects is not recommended because the reason for quitting the study could range from sickness to boredom. For this reason, a data reduction method was used to assess the data from the MSAQ. Instead of overall averages of symptoms, the

peak symptom score (maximum total symptom score among the multiple MSAQs that were completed) was used for analysis. The MSAQ was administered at 0, 4, 9, 14, and 19 min while the subject was inside the VVD. The peak scores and time to peak scores (which could range from 0–19 min) were analyzed separately using one-way ANOVAs.

Nausea profile: The Nausea Profile was analyzed using standard weighted formulas (18). The total score of responses was divided by the total points possible (153) and the multiplied by 100 to obtain a percent value. A two-way mixed-measures ANOVA was later used for comparing conditions.

EKG: EKG data were analyzed using a Fast Fourier Transform in order to obtain power values of cycle frequencies. A running spectral analysis was performed with 4-min, 75% overlapping windows and the results were averaged across the windows for the entire period—baseline and rotation. Spectral density estimates were derived at a bandwidth of 0.25 cpm and summed for 3 cpm (2.75–3.75 cpm), tachyarrhythmia (4–9 cpm), and total power (0.75–15 cpm). Percent of total power in the 3-cpm and tachyarrhythmia bandwidths were calculated for baseline and rotation by dividing each bandwidth by total power and multiplying by 100%. Between-subjects repeated measures ANOVAs were used for comparison of the EKG data.

RESULTS

A one-way ANOVA between the mean MSHQ scores of each group showed a significant difference [F (2,57) = 3.53, p = 0.036]. Follow-up tests revealed a statistically significant difference of 10.94 between the ondansetron group (mean = 73.9, SD = 21.5) and the placebo group (mean = 63.0, SD = 15.6) (p = 0.048), and a statistically significant difference of 13.53 between the dimenhydrinate (mean = 60.4, SD = 13.1) and the ondansetron group (p = 0.015). It is worth noting that the ondansetron group had a standard deviation several steps higher than the other groups.

Subjects could choose to stop the rotation stimulus at any time; however, only one subject from the ondansetron group requested an early stop. A Chi-square test revealed no significant difference between any of the groups [χ^2 (2) = 2.03, p = 0.362]. A one-way ANOVA between the mean rotation duration times of each group showed no statistically significant difference between the placebo (mean = 3.7 min, SD = 2.1), dimenhydrinate (mean = 4.4 min, SD = 3.6), or ondansetron groups (mean = 4.6 min, SD = 4.6) [F (2,57) = 0.36, p = 0.697].

A one-way ANOVA between the mean number of head movements tolerated for each group revealed no significant difference between the placebo (mean = 17.5, SD = 9.9), dimenhydrinate (mean = 22.1, SD = 17), or ondansetron groups (mean = 22.3, SD = 18.4) [F (2,57) = 0.49, p = 0.612]. Fig. 1 illustrates the mean symptom scores of each group over time (MSAQ scores). A two-way, mixed-measures ANOVA could not be run on mean MSAQ scores over time due to subject dropouts over time; therefore, a different method was needed.

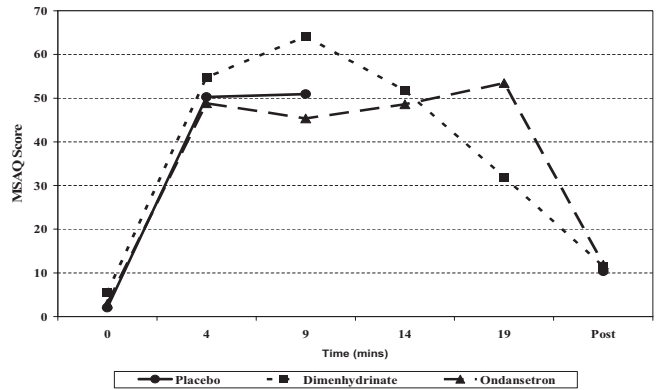


Fig. 1. Mean MSAQ symptom scores over time.

Because of the decreasing number of subjects over time, it was also important to look at the peak symptoms and the time to peak symptoms to give a better look at the raw symptom data. A one-way ANOVA revealed that there were no statistically significant differences between the peak MSAQ scores of the placebo (mean = 51.4, SD = 17.8), dimenhydrinate (mean = 60.3, SD = 20.8), or ondansetron groups (mean = 55.5, SD = 15.5) [F (2,57) = 1.2, p = 0.310]. Another one-way ANOVA revealed that there were no statistically significant differences between group peak times of the placebo (mean = 4.5, SD = 0.3), dimenhydrinate (mean = 5.3, SD = 0.7), or ondansetron groups (mean = 5.6, SD = 0.9) [F (2,57) = 0.31, p = 0.732].

Mean Nausea Profile pre-baseline, post-baseline, and post-rotation scores for each group are illustrated in Fig. 2. A 3 × 3 mixed measures ANOVA revealed a main effect of time [F (2,57) = 51.03, p = 0.00], but no main effect of condition [F (2,57) = 1.28, p = 0.285]. The ANOVA also revealed no significant interaction of group and time [F (4,57) = 0.27, p = 0.898].

For EKG data, the change in 3-cpm activity from baseline to rotation period is shown in Table I. All groups showed a marginally significant decrease in normal 3-cpm activity [F (1,45) = 3.04, p = 0.088]. There were no significant differences between the groups and no significant interactions of time (baseline vs. rotation).

Table I illustrates the change in gastric tachyarrhythmia activity between the baseline and rotation periods. All groups showed a significant increase in tachyarrhythmia [F (1,45) = 9.71, p < 0.003]. There were no significant differences between the groups and no significant interactions of time (baseline vs. rotation).

DISCUSSION

The main purpose of this study was to examine the efficacy of high dose ondansetron in preventing motion sickness. This study also aimed to improve on previous research by correcting possible weaknesses in previous studies such as screening, small dosages, or mildness of the stimuli. In order to conclude that ondansetron was a successful motion sickness preventative in this study, it was necessary to observe a reduction in peak symptoms, an increase in time to peak symptoms, an increase in rotation duration, or a greater number of tolerated head movements. However, the results fail to support

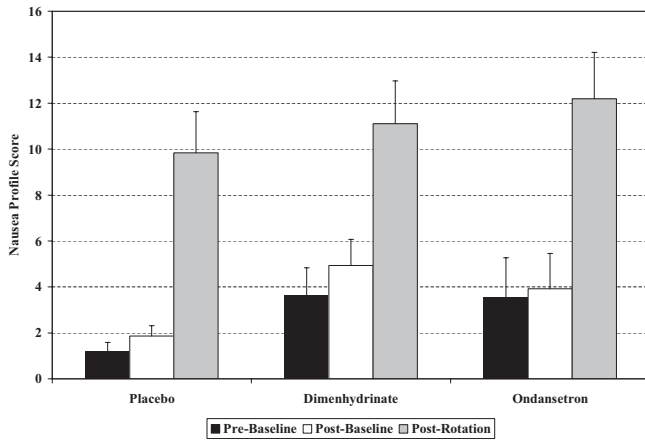


Fig. 2. Nausea Profile pre-baseline, post-baseline, and post-rotation scores plus standard errors.

that ondansetron successfully prevented motion sickness in this highly susceptible group of subjects on any of these measures. The standard drug treatment, dimenhydrinate, also failed to prevent motion sickness in this group. Both groups showed similar subjective and objective (physiological) responses to the motion stimulus compared with placebo. They both had increased symptoms, similar durations of motion tolerance, and changes in the EGG consistent with the development of motion sickness. This failure of even the standard dimenhydrinate treatment merits further discussion for possible explanations.

First of all, this study was conducted between subjects. Although this was an advantage in solving the possible problem of adaptation issues, it also opened the door for other problems. Not only did the between-subjects design provide less statistical power in analyses, it also allowed for individual differences in susceptibilities to motion sickness between the groups. Overall, it is possible that significance may have been achieved with more statistical power and less individual variability. To quantify the individual susceptibilities, the MSHQ was used. The fact that there was a significant difference in motion sickness history between the groups must be acknowledged. Nevertheless, this difference does not explain the current ineffectiveness of dimenhydrinate since the dimenhydrinate group had the lowest motion sickness history mean, which should have been an advantage.

It is also possible that the failure of the treatments is simply due to the high level of motion sickness susceptibility of subjects resulting from the strict screening process. In an effort to ensure that subjects would be susceptible to motion sickness, only those with high motion sickness history scores and a history of self-

treatment of motion sickness were allowed to participate. The overwhelming majority of studies before this did not screen so intensely. For example, a previous study tested several motion sickness drug remedies including dimenhydrinate, but did not allow subjects with exceptionally high motion sickness history scores (9).

An additional justification of these results could be attributed to the highly sickening nature of the stimulus used. In previous studies, the stimulus was thought to be too weak, so this study sought to counter that problem. It is possible that the stimulus was so sickening that not even those with dimenhydrinate could stay in long enough to produce a significant difference, especially since subjects were already highly susceptible to motion sickness. Most subjects tolerated only a low dose of the stimulus before quitting. Furthermore, part of the stimulus included sitting in complete darkness to make sure the subject remained disoriented. However, according to other research findings, this could have inhibited the possible effects of dimenhydrinate. In at least one previous study, using 100 mg of transdermally administered dimenhydrinate caused a significant decrease in nystagmus (20). These results led to supposition that dimenhydrinate, along with other anti-motion sickness drugs, may work partially by reducing visual-vestibular senses, which would suggest that dimenhydrinate would be less effective when a visual stimulus is removed. This theory coincides with the current study results. The subjects were in complete darkness, therefore taking away all visual cues, and possibly inhibiting the mechanics of dimenhydrinate at the same time.

It is also plausible that the non-significant results could be due to the procedures for termination. All subjects were allowed to terminate the study before any emetic episodes. This prevented the experimenters from being able to tell if there would have been a significant difference in emetic episodes if the subjects had been told to continue.

Dimenhydrinate could have been ineffective due to the dosage or the timing of the dosage. The 100-mg dosage and timing used in this study were based on a previous study where dimenhydrinate was found effective (17). However, in other studies with a similar dosage, dimenhydrinate has been found ineffective. One previous study used a 50-mg liquid solution of dimenhydrinate to prevent motion sickness caused by watching a film taken from an automobile driven through mountainous roads at high speeds in 15 susceptible subjects (1). This study found that dimenhydrinate was not significantly different from placebo or control. An additional study also found that 50-mg injections of dimenhydrinate did not prove

TABLE I. MEANS AND SDs FOR PERCENT OF CORRECTED TOTAL POWER IN THE ELECTROGASTROGRAM FOR 3 CPM AND TACHYARRHYTHMIA (TACHY) DURING BASELINE AND ROTATION FOR THE THREE CONDITIONS.

Condition	Baseline 3 cpm	Rotation 3 cpm	Baseline Tachy	Rotation Tachy
Placebo	56.66% ± 13.77%	40.54% ± 15.56%	43.34% ± 13.77%	60.29% ± 15.39%
Dimenhydrinate	58.52% ± 13.35%	41.91% ± 15.72%	41.48% ± 13.35%	58.09% ± 15.72%
Ondansetron	58.58% ± 15.77%	46.48% ± 10.37%	41.417% ± 15.77%	53.53% ± 10.37%

beneficial to subjects as a rescue drug in a parabolic flight experiment (8). A more recent study found that dimenhydrinate did not help at least 3 of their 20 subjects even when using a 100-mg dose (17). Hence, it is difficult to rule out whether dimenhydrinate may have been effective at a different dose or timing of dose.

While several possibilities as to the cause of the results have been discussed, it is also possible that the results are accurate and that ondansetron simply is not effective in preventing motion sickness. When motion sickness is induced by an optokinetic drum, ondansetron has been shown to inhibit the development of tachyarrhythmia in subjects, but have no effect on the prevention of nausea or other motion sickness symptoms (14). It was also found that ondansetron in 4-mg and 8-mg doses was ineffective in reducing post-operative nausea and vomiting after middle ear surgery in patients with a history of motion sickness (10). The lack of an anti-emetic effect of ondansetron, which is effective in the treatment of nausea induced by chemotherapy, on motion sickness further highlights that there are different neural mechanisms involved in the development of motion sickness (23). Previous evidence suggests that ondansetron may be ineffective for motion sickness due to the fact that it operates in the gastric system without inhibiting the neural aspects that also contribute to motion sickness.

Conclusion

The fact that there is not yet a certain explanation for why anti-motion sickness medications are not 100% effective all the time is testament that there is still much to learn about motion sickness and its remedies. Future studies on the effectiveness of anti-emetic drugs should perhaps focus on a more intermediate group of susceptible subjects as well as a more intermediate stimulus. Also, future studies should compare the efficacy of dimenhydrinate with and without visual cues available to further investigate the possible effect of a decrease in visual cues. Furthermore, the lack of an anti-emetic effect of ondansetron on motion sickness indicates a need for further research on the neural aspects of motion sickness.

Nonetheless, the purpose of this study was to determine if ondansetron is an effective motion sickness preventative for highly susceptible people and if so, what its efficacy relative to dimenhydrinate was. The conclusion of this study is that neither ondansetron nor dimenhydrinate was effective in preventing motion sickness in this highly susceptible population. However, the high level of individual differences in responding to motion sickness treatments and the past research reporting successful treatment of motion sickness using dimenhydrinate warrants additional studies with a more moderately susceptible group of subjects. In addition, there may be some degree of stimulus specificity, i.e., medications may be more effective against some stimuli than others. Finally, this study points to an ongoing need for effective treatments of motion sickness in highly susceptible individuals.

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