DRUGS IN CONTEXT
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REVIEW

Motion sickness: an overview

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Abstract

Background: Motion sickness is a common phenomenon that affects almost everybody at some point in their lifetime. Clinicians should be familiar with the proper management of this condition.

Objective: To provide an update on the current understanding of the pathophysiology and management of motion sickness.

Methods: A PubMed search was performed with Clinical Queries using the key term 'motion sickness.' The search strategy included meta-analyses, randomized controlled trials, clinical trials, observational studies, and reviews. The search was restricted to English literature. The information retrieved from the earlier search was used in the compilation of the present article.

Results: Motion sickness is typically triggered by low-frequency vertical, lateral, angular, rotary motion, or virtual stimulator motion, to which an individual has not adapted. *Sine qua non* for developing motion sickness is when the brain receives conflicting information from different sensors about real body movements or virtual environment. The principal sensors are the eyes, the vestibular apparatus, and proprioceptive receptors. The conflicting information is judged in relation to a pattern of expected associations formed under normal or experienced conditions stored in the brain. Motion sickness typically presents with malaise, anorexia, nausea, yawning, sighing, increased salivation, burping, headache, blurred vision, non-vertiginous dizziness, drowsiness, spatial disorientation, difficulty concentrating, and sometimes vomiting. Simple behavioral and environmental modifications can be effective in the prevention of motion sickness. Medications that are effective in the prophylaxis and/or treatment of motion sickness include anticholinergics, antihistamines, and sympathomimetics.

Conclusion: In most cases, motion sickness can be prevented by behavioral and environmental modifications (avoidance, habituation, and minimization of motion stimuli). Pharmacotherapy should be considered in the prevention and/or treatment of more severe motion sickness and for patients who do not respond to conservative measures. Medications are most effective when combined with behavioral and environmental modifications. Drugs that are effective in the prophylaxis and/or treatment of motion sickness include anticholinergic agents and antihistamines.

Keywords: antihistamines, nausea, neural mismatch, scopolamine, sensory conflict, sympathomimetics, vomiting.

Citation

Leung AKC, Hon KL. Motion sickness: an overview. Drugs in Context 2019; 8: 2019-9-4. DOI: 10.7573/dic.2019-9-4

Introduction

Motion sickness, also called kinetosis, was first described by the Greek physician Hippocrates who wrote: "sailing on the sea proves that motion disorders the body." The term 'motion sickness' was first used in 1881 by Irwin to describe a malady resulting from repeated oscillatory movement of the body. It includes a feeling of unwellness or sickness that develops during travel by air, sea, or land, and while riding in a car, train, elevator, amusement ride, swing, or, less commonly, on an animal such as a horse.[1–3] Similar symptoms also occur on entry and return from space. Motion sickness typically presents with malaise, non-vertiginous dizziness, nausea, and sometimes vomiting. However, real motion is not an absolute requirement for the disorder to manifest; perception of motion can also result in motion sickness.[4] Thus, one can experience the symptoms of motion sickness while viewing a large moving field or taking part in virtual reality rides in amusement parks, although the individuals affected are not physically in motion.[5] Some authors prefer the term 'pseudomotion sickness' or

'pseudokinetosis' to be used for those occasions.[6] Depending on the environment that it occurs, motion sickness is also called travel sickness, seasickness, car sickness, space sickness, and simulator sickness/cinerama sickness/cybersickness.[5]

A PubMed search was performed with Clinical Queries using the key term 'motion sickness.' The search strategy included meta-analyses, randomized controlled trials, clinical trials, observational studies, and reviews. The search was restricted to English literature. The information retrieved from the earlier search was used in the compilation of this article.

Epidemiology

Motion sickness is a common phenomenon. Almost everybody has experienced motion sickness at least once in his/her lifetime.[7] Seasickness is the most common and notorious form of motion sickness.[5] Indeed, nausea, the main symptom of motion sickness, is derived from the Greek word *naus*, hence 'nautical,' meaning a ship. Up to 25% of the passengers on a large ship will develop motion sickness within 2–3 days of the start of an ocean voyage.[2,3] The incidence is higher in smaller vessels and with adverse weather. In the extreme case, as many as 60% of passengers (even an experienced crew) may be affected.[5] In an extensive survey of 2366 passengers who had collectively traveled on 26 cruise trips for a total of 34,501 person-days, the incidence of motion sickness requiring physicians' consultations was 4.2 per 1000 person per day.[8] The incidence of car sickness is up to 4%, especially for those driving rally cars and those sitting in the back seats or reading a book during the journey.[2,3,5,9] Motion sickness occurs in approximately 0.13% of individuals who ride on trains. Less than 1% of travelers in pressurized commercial aircraft have motion sickness.[2,3,10] The incidence of motion sickness in student aviators is between 10% and 31%. The overall incidence decreases over time as these student aviators gain experience.[11] Space sickness affects up to 80% of astronauts during their first 3 days of their space mission.[12]

Motion sickness can develop in any individual if the movements applied to the body are significant enough. However, there is considerable individual susceptibility to motion sickness that might also be a result of gene–environment interaction.[13–15] Certain characteristics are correlated with this susceptibility. Females are more susceptible to motion sickness than males of the same age in terms of increased frequency and severity of symptoms, especially during menstruation.[1–3,5,6,16,17] In this regard, pregnant women are particularly susceptible to motion sickness, presumably because of the hormonal changes during pregnancy.[14,16] Motion sickness is rare in children under the age of two possibly because of the lack of sufficient visual input in the children of this age group.[4,6] In addition, young infants are often in a recumbent position and therefore less susceptible to motion sickness.[4] Children 6–12 years old are most susceptible, with a peak between 9 and 10 years old.[1,4,5,14] The susceptibility declines through puberty and thereafter perhaps because of habituation.[4,10,14,18] Motion sickness is less frequent in adults and rarely occurs after the age of 50 years.[2,3,6,17] In females, there is a transient increase in susceptibility at around menopause versus their age-matched male counterparts.[17]

Although motion sickness can occur in individuals of all races, race disparity is also significant.[19] It has been shown that Chinese are more susceptible to motion sickness than white people.[15,20,21]

Motion sickness may be familial.[18] If either parent has a childhood history of car sickness, the chances that their child will develop car sickness are twice as great as when neither parent has the problem.[2,3] Monozygotic twins are concordant for car sickness two and half times as often as dizygotic twins, suggesting the existence of a genetic background.[2,3] Heritability estimates are in the range of 55–70%.[10] Hromatka and colleagues conducted a genome-wide study on motion sickness in 80,494 individuals who were surveyed for car sickness.[22] The authors found 35 single-nucleotide polymorphisms associated with motion sickness. The genes for motion sickness have been mapped to chromosome 4.[23]

Motion sickness is more prevalent in individuals who suffer from migraine, vertigo, and Meniere disease.[14,17,24–28] Exposure to short-wavelength light increases the susceptibility to motion sickness.[29] Sleep deprivation can also increase susceptibility.[30,31] Blind individuals are as susceptible to motion sickness as normal sighted individuals with their eyes closed.[1,31,32] On the other hand, dancers, rope walkers, acrobats, and individuals with bilateral loss of labyrinthine function have a lower incidence of motion sickness. Lying supine may also decrease the susceptibility to motion sickness.[13]

Pathophysiology

Motion sickness is not a pathological condition in the strict sense. Rather, it is a normal physiological response to real or virtual motion stimuli that occur mostly in individuals with an intact vestibular system.[6,33] Patients in whom the labyrinthine function has been destroyed by disease or operation do not normally become motion sick,[33,34] although they are still partially susceptible to visually induced motion sickness.[10,35] Motion sickness is typically triggered by low-frequency vertical, lateral, angular, or rotary motion, to which an individual has not adapted, although it can also be triggered by virtual stimulator motion (e.g., playing complex video games on large screens, watching 3D stereoscopic movies, or using virtual reality headsets), to which an individual has not adapted.[3,6,13,14,24,36–38]

Sine qua non for developing motion sickness is when the brain receives conflicting or discrepant information from different sensors about real body movements or virtual environment.[15,24,39,40] The principal sensors are the eyes, the vestibular apparatus (semicircular canals, otolith organs, velocity storage integrator in the vestibular nuclei), and proprioceptive

receptors.[3,40–42] The conflicting or discrepant information is judged in relation to a pattern of expected associations formed under normal or experienced conditions stored in the brain.[15] Both the vestibular cortex and the hippocampus are areas where the 'internal model' is stored.[15] The severity and duration of motion sickness depend on the degree of mismatch of motion-sensitive input signals and on the ability of the individual to adapt to the abnormal environment.[24,42] As such, the intensity of the stimulus is not necessarily related to the severity of the motion sickness.[1] It should be noted that the level of impact varies with stimulus frequency, but in a nonlinear fashion. The most provocative movement frequency is 0.2 Hz. Motion sickness severity becomes lower in the ranges above and below 0.2 Hz. 1At each frequency, motion sickness severity is dependent on the stimulus intensity.[43]

Adaptation is presumed to occur if a susceptible individual learns to accept this conflicting sensory information without developing symptoms of motion sickness. This sensory conflict and neural mismatch theory are compatible with the observation that predictable voluntary movements do not normally result in motion sickness, regardless of the magnitude of the stimulus. The theory also explains why some individuals experience motion sickness while viewing a moving field even if they are still.[40] Thus far, the sensory conflict and neural mismatch theory is the most widely accepted theory on motion sickness.[15,24]

Motion sickness may also result from a 'spilling-over' or 'irradiation' from overexcited equilibratory centers to the vomiting center.[39] This theory is suggested by the observation that the incidence of motion sickness is usually related to the intensity of the stimulus.[40] This theory, however, does not explain why presumably weak stimuli such as slow ship movements often result in motion sickness while more powerful and active movements such as walking, jumping, and swimming do not usually cause motion sickness.

The vestibular cerebellum also plays an important role.[39] Patients with spinocerebellar degeneration or resection are not susceptible to motion sickness.[39]

Neurotransmitters such as acetylcholine, histamine, norepinephrine, dopamine, serotonin, γ-aminobutyric acid, glycine, and glutamate may be involved in the mechanism of motion sickness.[3,6,44–46] Enhanced cholinergic activity plays an important role in the production of complex autonomic manifestations of motion sickness.[45,46] This is suggested by the observation that parasympatholytic agents such as scopolamine (hyoscine) can prevent motion sickness.[2,3] Antihistamines, such as dimenhydrinate, which also have an anticholinergic property, can also prevent motion sickness.[2,3] In addition, sympathomimetic agents such as amphetamines can suppress motion sickness.[2,3]

There may be a psychological component to motion sickness.[6] Some individuals develop symptoms of motion sickness after boarding a ship even before sailing, while others have symptoms at sight of a ship. In addition, when one individual in a group develops motion sickness, similar symptoms in other individuals may be precipitated. In addition, approximately 45% of patients with motion sickness have been shown to benefit from placebo treatment.[6,47]

Clinical manifestations

The onset of symptoms is usually insidious and typically follows an inciting event or exposure to an unfamiliar motion.[3,14] Early symptoms of incipient motion sickness include general discomfort, malaise, reduced alertness, increasing lethargy, and apathy.[3] The earliest and hallmark symptom of motion sickness is nausea – an unpleasant feeling develops from a sense of epigastric discomfort to an awareness that vomiting is imminent.[37] Nausea may be aggravated by a full stomach, physical illness, a stuffy atmosphere, tobacco smoking, offensive odor (e.g., smell of emesis or hydrocarbon), the sight of vomiting, fear, or excitement. Other common symptoms include frequent yawning, sighing, anorexia, increased salivation, burping, headache, eye strain, blurred vision, non-vertiginous dizziness, drowsiness, spatial disorientation, difficulty focusing/concentrating, hyperventilation, and a desire to be left alone.[1,3,13,48,49] There is often a feeling of bodily warmth and increased sensitivity to offensive odors.[8,13] The individual may seek cool air to obtain symptomatic relief, although the improvement usually lasts only a short time. Cold sweating and facial/perioral pallor may ensue if the individual continues to be exposed to the precipitating motion or trigger.[3,24] Less commonly, flushing may occur due to vasodilatation in the skin.[1] Blood pressure is significantly lower at times of motion sickness and also significantly lower than those without motion sickness.[50] There is often an initial increase in heart rate followed by a rebound decrease.[1]

Unless the provocative motion or trigger stops, a sudden worsening of the symptoms may culminate in retching or vomiting. Some individuals have difficulties in vomiting and retch violently, while others vomit readily.[51] Temporary relief is often experienced after vomiting, although the symptoms may redevelop, resulting in repeated episodes of vomiting. In severe cases, intractable retching and vomiting, postural instability, inability to walk, incapacitation, dehydration, and electrolyte imbalance may result.[14]

Once the triggering factors are eliminated, the symptoms usually resolve completely within 24 hours.[3] Sopite syndrome is a constellation of symptoms including profound drowsiness, fatigue, apathy, depression, boredom, irritability, lethargy, disinclination for work, sleep disturbances, failure of initiative, desire to be left alone, and decreased participation in group activities that may persist for hours to days following exposure to the motion stimuli.[13,30,49] Yawning is a behavior marker for the onset of sopite syndrome.[31,48,49] Unfortunately, sopite syndrome is often missed because of its nonspecific symptoms and that the syndrome may occur independently of the vegetative

symptoms.[52,53] Symptoms are sometimes mild, which might lead to the syndrome being overlooked, while symptoms such as apathy and depression might lead to misdiagnosis of other conditions.[53]

With prolonged exposure to the same provocative motion, some individuals adapt and exhibit a reduction in symptoms. The course of this adaptation varies, but a few days are usually needed before a significant level of adaptation is achieved.[1]

Mal de debarquement syndrome (sometimes referred to as disembarkment syndrome) is a possibly related disorder. The syndrome is characterized by a continuous perception of self-motion and a conglomerate of symptoms lasting more than 1 month from the onset following disembarkment from a vehicle.[54]

Diagnosis

The diagnosis is mainly clinical, based on the history of a triggering situation (imposed or perceived motion) and typical symptoms and signs of motion sickness such as malaise, anorexia, nausea, yawning, sighing, increased salivation, burping, headache, blurred vision, non-vertiginous dizziness, drowsiness, spatial disorientation, difficulty concentrating, and sometimes vomiting. The diagnosis can be facilitated if there is a prior history of motion sickness, especially following the exposure to similar events. Laboratory testing is usually not necessary.

Motion Sickness Susceptibility Questionnaires (MSSQs: sometimes called Motion History Questionnaires) enable a rapid estimate to be made of an individual's susceptibility.[1] A typical questionnaire can be found on page 379 (Table 27.3) in the Handbook of Clinical Neurology published by Golding.[1] An overall indicator of susceptibility may be calculated as the MSSQ score = (total sickness score) × (18)/(18 – number of types not experienced). This formula corrects for the different extent of exposure to different motion stimuli in individuals.[1]

Differential diagnosis

Differential diagnosis of motion sickness includes migraine, pregnancy, concussion, intoxication, hangover, basilar artery occlusion, cerebral vascular accident, vestibulopathy, hypoglycemia, depression, and anxiety.

Complications

The most common complications include dehydration, electrolyte imbalance, anxiety, and depression.[13] Motion sickness reduces motivation and muscular coordination and has an adverse effect on the performance of the individual. It also impairs judgment and the ability to carry out allotted duties, especially for those duties that are complex and require sustained attention.[1] Patients with a history of high motion susceptibility are at risk of more prolonged vestibular dysfunction following sport/recreation-related concussion.[55] In addition, motion sickness has an adverse effect on the patient's recreation, employment, and quality of life.[37,56]

Prevention and treatment

Behavioral and environmental modifications

Motion sickness is easier to prevent than to cure. As such, emphasis should be placed on prevention.[10,13] Simple behavioral and environmental modification can be effective in the prevention of motion sickness. Susceptible individuals should avoid heavy meals, ingestion of caffeine, alcohol, foods high in histamine content (e.g., cheese, tuna, salami) or a large volume of liquid, before traveling.[3] A stuffy atmosphere while traveling may predispose an individual to motion sickness and should be avoided. For smokers, smoking should be avoided.[14] Susceptible individuals should travel when well rested, stop often for rest, and stay well hydrated. The importance of adequate sleep cannot be overemphasized. Susceptible individuals should select the proper means of transportation that produce a minimal amount of motion.

Reducing head and body movement can reduce motion sickness.[8,14] In one study, passive restraint of the head and body helped to reduce visually induced motion sickness.[57] Affected individuals should consider positioning themselves where there is less opportunity for head and body movement.[1,14] This will reduce the visual-inertia conflict.

Attenuating or eliminating visual input may reduce visual sensory conflict and therefore may delay the onset of motion sickness or weaken the severity of the symptoms.[58] Reading or watching a video screen while in a moving environment should be avoided.[14] Sitting in the front seat rather than the back seat may help to reduce motion sickness.[14] Focusing the eyes on a fixed spot such as the horizon or looking in a vehicle's direction of travel is helpful.[5,8,14,59,60] Actively steering a vehicle may also help in the prevention of motion sickness.[37,61] Sunglasses may reduce visual input and thus may be beneficial. If the above measures do not work, individuals with motion sickness may obtain relief by closing the eyes and lying supine where practical.[5,58]

In one study, visually induced motion sickness was alleviated by the smell of rose.[62] The authors of the study suggested that olfaction can modulate visually induced motion sickness and that a pleasant odor can potentially reduce visually induced motion sickness. Further studies are necessary to confirm or refute their findings.

It has been shown that controlled regular breathing can be used to suppress physiological responses associated with motion sickness.[63–65] Presumably, controlled breathing can activate the parasympathetic nervous system and the known inhibitory reflex between respiration and vomiting can be used

to suppress physiological responses associated with motion sickness.[1,64] Some authors suggest listening to pleasant music may help.[5,14] In one study, 24 healthy subjects were exposed to nauseogenic Coriolis stimulation on a rotating turntable under three conditions: while listening to a music audiotape, focusing on controlling breathing, or without any intervention.[66] The authors found that the mean motion exposure time in minutes tolerated before the onset of nausea was significantly longer for music (10.4 minutes; $p<0.01$) and for controlling breathing (10.7 minutes; $p<0.01$) compared with no intervention (9.2 minutes). Well-designed, large-scale, randomized, studies are necessary to evaluate the efficacy of controlled breathing and/or pleasant music in the prevention of motion sickness.

Reassurance about the temporary nature of the illness may alleviate the symptoms and every effort should be made to avoid suggesting the symptoms of motion sickness.

In situations when exposure to motion stimuli is inevitable and symptoms are incapacitating or severe enough to affect the ability of the individual to function, incremental exposure, progressive increasing the intensity of stimulation over multiple exposures, can be used to prevent motion sickness.[10,31,67] Continued exposure to motion stimuli leads to habituation. Presumably, the changes brought about by the habituation process are preserved in the central nervous system. Habituation/desensitization is an effective long-term countermeasure.[8,10,14] However, at least 5% of individuals with motion sickness show no signs of habituation.[6] In addition, such habituation is highly specific to the particular stimulus that is adapted.[6] In seasickness, approximately 50% of the population may succeed in habituating.[68]

Pharmacotherapy

Anti-motion sickness medications are helpful when given prophylactically. They are less effective for treatment because motion sickness may induce gastric stasis that interferes with the absorption of the medications given orally.[13] Anti-motion sickness medications may make the difference between an uncomfortable and an enjoyable trip. In general, medications may be considered for patients who are prone to significant motion sickness and for patients who do not respond to conservative measures.[13] The types of medication used should depend on the duration of exposure, the susceptibility of the individual to motion sickness and the severity of expected symptoms, the incidence and severity of adverse events, and the differences in the effectiveness of the medication.[13] Medications are most effective when combined with behavioral and environmental modifications.[37] Drugs that are effective and most commonly used in the prophylaxis or treatment of motion sickness are anticholinergic agents and antihistamines.[6] Because of the associated adverse events such as drowsiness and confusion, these medications may be used with sympathomimetics (catecholamine activators) to increase efficacy and to alleviate adverse events.[8,15]

Anticholinergics

It has been shown that scopolamine is effective in the prevention and treatment of motion sickness.[6,69,70] Scopolamine acts as a nonselective anticholinergic agent by inhibiting input to the vestibular nuclei and vomiting center in addition to its central anticholinergic properties.[6,14,71] Scopolamine is the drug of choice for individuals who wish to maintain wakefulness during travel.[37]

Scopolamine is most commonly used as a 1 mg transdermal patch applied behind the ear on the mastoid on a clean, hairless area.[13,14] The patch should be applied at least 4 hours, preferably 8 hours, before exposure to motion, with effects lasting for approximately 72 hours,[13–15,72] at which point the patch can be replaced if necessary.[13,73] Hands should be washed thoroughly both before and after touching the transdermal patch.[10] An advantage of the transdermal route is that it allows therapeutic blood levels of a drug with a short half-life to be maintained over long periods. In addition, gastric stasis is common with motion sickness. Therefore, nonoral routes of administration, such as transdermal route, are advantageous.[10] In general, transdermal scopolamine is well tolerated.[13] Performance is not usually affected for short-term use.[72] Adverse events include dry mouth, dry eyes, blurred vision, mydriasis, photosensitivity, and dermatitis at the site of application.[6,13,15,70] Less common adverse events include headache, drowsiness, confusion, palpitations, tachycardia, bloating, constipation, and urinary retention.[37] Restlessness, memory disturbances, hallucination, toxic psychosis, acute angle glaucoma, ipsilateral mydriasis, and cycloplegia have rarely been reported.[70,72] Transdermal scopolamine should not be used in children under 10 years old, as its safety in children in that age group has not been established and should be used with caution in the elderly.[14] The transdermal scopolamine should not be cut in half as this can affect the rate of release of the medication.[6] People who use scopolamine should not drive or engage in heavy machinery work. Scopolamine is contraindicated in patients with glaucoma or prostatic enlargement.[13] A randomized, double-blind, crossover study on 76 naval crew members showed that transdermal scopolamine is more effective than cinnarizine in the prevention of motion sickness and has fewer side effects than cinnarizine.[74]

When fast protection is needed, oral scopolamine is the most useful anti-motion sickness medicine.[6,69,70] Given orally, scopolamine is effective within 30 minutes for a period of 4–6 hours and is useful for short trips.[6,70] Nevertheless, it is advisable to take the medication 1 hour before traveling. The recommended oral dose for adults is 0.3–0.6 mg and that for children is 0.006 mg/kg. Drowsiness, blurred vision, and dry mouth are uncommon at these doses.[2,3] If the recommended dose does not adequately relieve the symptoms, the dose may be doubled.[37] Some authors prefer the combination of transdermal scopolamine and oral scopolamine for rapid onset of action and maintenance of the required plasma level to prevent motion sickness.[6,75]

In adults, intramuscular injection of 0.3–0.6 mg (children, 0.006 mg/kg) of scopolamine may be effective even if vomiting has developed.[2,3] The dose can be repeated every 6–8 hours if necessary.

Scopolamine can also be administered as a nasal spray.[6,10,15] The preparation has an onset within 30 minutes after administration and has a higher peak plasma concentration than oral scopolamine.[14,71,76] A randomized, double-blind, placebo-controlled, crossover study on 16 young adults showed that intranasal scopolamine to be efficacious for the treatment of motion sickness with no significant sedative or cognitive effects.[71]

Antihistamines

Many first-generation antihistamines have been shown to be effective in the prevention and treatment of motion sickness, including cinnarizine, promethazine, dimenhydrinate, diphenhydramine, cyclizine, and meclizine.[6,37,77–80] Their effectiveness is likely due to their antihistamine activity and, if applicable, their anticholinergic property.[2,3] The blockage of histamine receptors in the vomiting center may alleviate symptoms, and the anticholinergic effects may contribute to the prophylactic effect.[2,3] Although the onset of action of antihistamines may be longer than that of scopolamine and they must be taken 2 hours before traveling, their prolonged action makes them suitable for use on long trips.[2,3] Adverse events include drowsiness, sedation, agitation, nervousness, delirium, tremors, constipation, dry mouth, blurred vision, and, occasionally, palpitation, fainting, hypotension, and urinary retention.[13] As antihistamines can cause drowsiness and sedation more than scopolamine, they should not be used when decreased alertness may be harmful.[37,81–83] The sedative effect may be potentiated by alcohol and some central nervous system depressants. Used alone, antihistamines rarely have severe toxic effects. For patients with vomiting and those who cannot tolerate oral medications, intramuscular administration of antihistamines may be necessary.

In general, second-generation antihistamines (e.g., cetirizine, fexofenadine, astemizole, loratadine) are nonsedating and not effective in the prevention or treatment of motion sickness.[37,84,85]

Pregnant women are particularly susceptible to motion sickness.[14,16] If prevention and treatment of motion sickness are necessary, antihistamines such as dimenhydrinate and meclizine are safe to use.[13,14] These medications are listed as category B in pregnancy by the United States Food and Drug Administration.[13,14] On the other hand, promethazine and scopolamine are listed as category C in pregnancy by the United States Food and Drug Administration.[13,14]

Sympathomimetics (catecholamine activators)

Sympathomimetics (catecholamine activators) such as ephedrine and dextroamphetamine have not been shown to be superior to scopolamine and antihistamines in the prevention or treatment of motion sickness. Rather, they are often used in combination with scopolamine and antihistamines to overcome the drowsiness and impaired performance caused by these agents.[3,86,87] The addition of ephedrine to either scopolamine or chlorpheniramine, however, does not increase the effectiveness of either medication against motion sickness.[86] Dextroamphetamine is more effective than ephedrine.[88] Studies have shown that a combination of scopolamine and dextroamphetamine is highly effective because these two drugs combine their different anti-motion sickness properties and their respective side effects of sedation and stimulation cancel each other out.[1,8,88] However, because of the potential of dextroamphetamine for drug dependence and abuse, the addition of dextroamphetamine to scopolamine is unsuitable for general use and is mainly used during space flights and for specialized military purposes.[6,14] Data on the efficacy of modafinil or caffeine in combination with scopolamine or antihistamines in the management of motion sickness are limited.[10,15,77,89] Additional information is necessary before such a combination can be recommended. Generally, sympathomimetics should not be prescribed for patients who have or at risk for cardiovascular disease.

Complementary and alternative therapy

Several studies have shown that acupressure, acupuncture, and electroacupuncture on the P6 point (located on the anterior surface of the forearm, two inches proximal to the distal wrist crease and between the middle two tendons of the inside of the forearm) are effective in the treatment of motion sickness.[6,90–95] These measures, which are more popular in Asia than in the west, represent another therapeutic option. Presumably, the above measures work by activation of insulin receptors and extracellular regulated protein kinases in the dorsal motor nucleus of the vagus.[95] Other investigators did not find acupressure and acustimulation useful in the treatment of motion sickness.[96–98] Well-designed, large-scale, randomized, studies are necessary to confirm the efficacy of these treatments in order to make formal recommendations regarding their use in the management of motion sickness. Suffice to say, adequate blinding and allocation concealment are difficult to perform.

Some authors suggest the use of ginger (rhizomes of *Zingiber officinale*), such as sucking on hard ginger candies, in the prevention and treatment of motion sickness.[13,99] The exact mechanism of action is not known. Studies have shown that ginger might exert its effect on the gastric system and on the 5-hydroxytryptamine $(HT)_3$ receptor ion-channel complex.[100–102] In a blind placebo-controlled study, the effects of powdered rhizomes of *Zingiber officinale* (940 mg in two gelatin capsules) were compared with those of dimenhydrinate (100 mg) in reducing symptoms of motion sickness caused by a motor-driven revolving chair in

36 undergraduate men and women.[99] The authors found that powdered rhizomes of *Zingiber officinale* were more effective than dimenhydrinate. In a double-blind study, 80 naval cadets (mean age of 17 years), unaccustomed to sailing in heavy seas, were randomized to receive 1 g of powdered ginger root (n=40) or 1 g of lactose as placebo (n=40).[103] The cadets were monitored hourly for the next four consecutive hours for the symptoms of motion sickness and side effects. The authors noted that ginger root reduced the tendency to vomiting and cold sweating significantly better than the placebo did ($p < 0.05$). Fewer symptoms of nausea and vertigo were noted in the group with ginger root ingestion, but the difference did not achieve statistical significance. No side effects were reported in the two groups. It is hoped that future, well-designed, large-scale, randomized, double-blind, placebo-controlled trials will provide more information on the efficacy and safety profile of ginger root ingestion in the prevention of motion sickness.

A preliminary prospective, double-blind, placebo-controlled, crossover study (n=70) showed that 2 g of vitamin C is effective in suppressing symptoms of motion sickness, particularly in men and women below 27 years old.[104] Further studies are necessary to confirm or refute this finding.

Prognosis

In general, the prognosis is good. The symptoms usually resolve in 72 hours after the cessation of the provoking stimuli. Patients with a previous history of motion sickness are more likely to experience it again in the presence of the same or similar environment.

Conclusion

Motion sickness is a common problem during traveling and virtual reality immersion. It is believed that the condition results from sensory conflict and neural mismatch. The cardinal features are nausea and vomiting. Other associated features include yawning, sighing, anorexia, increased salivation, burping, headache, dizziness, drowsiness, spatial disorientation, difficulty concentrating, hyperventilation, pallor, and cold sweating. Motion sickness is unpleasant and has an adverse effect on the patient's recreation, employment, and quality of life. Motion sickness is easier to prevent than to cure. The importance of behavioral and environmental modification (avoidance, habituation, and minimization of motion stimuli) cannot be overemphasized. In general, medications may be considered for patients who are prone to significant motion sickness and are most effective when combined with behavioral and environmental modifications.

Contributions: Professor Alexander KC Leung is the principal author. Professor Kam Lun Hon is the co-author who contributed and helped with the drafting of this manuscript. Both named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosure and potential conflicts of interest: Professor Alexander KC Leung and Professor Kam Lun Hon are associate editors of Drugs in Context and confirm that this article has no conflicts of interest otherwise. This manuscript was sent out for independent external peer review by the editor-in-chief. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at http://www.drugsincontext.com/wp-content/uploads/2019/11/dic.2019-9-4-COI.pdf

Acknowledgments: None.

Funding declaration: Professor Leung and Professor Hon disclose no relevant financial relationship.

Article URL: https://www.drugsincontext.com/motion-sickness:-an-overview/

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Provenance: invited; externally peer reviewed.

Submitted: 25 September 2019; **Peer review comments to author:** 6 November 2019; **Revised manuscript received:** 8 November 2019; **Accepted:** 11 November 2019; **Publication date:** 13 December 2019.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: Plaza Building, Lee High Road, London, England, SE13 5PT.

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