Tidsskriftet Tidsskrift for Den norske legeforening

Dizzy and female – could there be a hormonal explanation?

PERSPECTIVES

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Several studies suggest that hormonal factors play a key role in the development of dizziness. This ought to have an impact on the treatment.

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Dizziness most commonly affects women, and it has recently been pointed out by the Women's Health Commission that sex is of relevance in respect of several disorders (1). There are complex reasons why there are differences between the sexes in respect of vestibular dysfunction, but a number of studies suggest that hormonal factors are key, including the identification of sex hormone receptors in the inner ear and parts of the central nervous system that affect the sense of equilibrium (2–5).

Vestibular dysfunction is one of several causes of dizziness. This affects the sense of equilibrium in various ways and can cause nausea and an unsteady gait in addition to dizziness (6). At the heart of it all are the organs of balance, found in the inner ear, where signals from sensory hair cells are received based on the position of the head. The signals are sent through the balance nerve to the brainstem and the vestibular nuclei, where they are processed and further relayed to other parts of the central nervous system, like the cerebellum, the oculomotor nuclei, the reticular formation and the spinal cord (7).

Most common in women

Vestibular disorders are most common in women, and as with other types of dizziness, psychosocial factors have been assumed to play a significant role. However, recent studies have found a link between the presentation of vestibular disorders and hormonal fluctuations associated with puberty, the menstrual cycle, pregnancy, use of hormonal contraception and the menopause (5). This is linked to the recently identified oestrogen and progesterone receptors in the inner ear, where oestrogen receptors alpha and beta and progesterone receptors dominate (5, 8).

> ***«We need to learn more about the effects of hormones on the inner ear, with a view to future prevention and personalised treatment of vestibular disorders»***

In several studies, hormonal factors have therefore been introduced as contributors to the pathophysiology found in benign paroxysmal positional vertigo (BPPV) and Ménière's disease (5, 8–11), and in some studies, hormone therapy has been found to alleviate the symptoms of these disorders (9, 12–15). Similar connections between disease presentation and hormonal factors have also been observed in central vestibular disorders like vestibular migraine and Mal de Debarquement syndrome (5). Both conditions are more common in women, which is probably due to central nervous mechanisms (16). Fluctuations in oestradiol levels throughout life are likely to affect the development and incidence of vestibular disorder (5). We need to learn more about the effects of hormones on the inner ear, with a view to future prevention and personalised treatment of vestibular disorders.

Benign paroxysmal positional vertigo

Benign paroxysmal positional vertigo is a common cause of dizziness and accounts for 8 % of moderate to severe dizziness complaints (2). A population study from Germany showed a lifetime prevalence of 2.4 % (3). Women make up 65 % of the patient group with an average age of 50–70 years (3). The disorder tends to have idiopathic causes and involves the degeneration of structures in the inner ear and otolith displacement into the semicircular canals (2). Symptoms occur when the head moves, resulting in episodes of rotational dizziness, unstable gait, nausea or vomiting (2).

Many women experience the onset of benign paroxysmal positional vertigo, or worsening of episodes, in connection with the menopause and the physiological decrease in oestradiol (5). The hypothesis is that not only direct changes in oestradiol levels can trigger benign paroxysmal positional vertigo, but also other physiological mechanisms affected by low levels of oestradiol, such as calcium metabolism, can contribute (17). Patients with benign paroxysmal

positional vertigo have been found to have a higher prevalence of osteopenia or osteoporosis (5, 18). Low levels of serum oestradiol, calcium and vitamin D appear to be predisposing factors for recurrence of the disorder in post-menopausal women (17). Otoliths are synthetised from the crystallisation of calcium carbonate, and it is a likely assumption that this synthesis is affected by disruptions to the calcium homeostasis, as seen in osteoporosis (19).

Animal studies have shown that low levels of oestradiol contribute to the pathophysiology evidenced in otolith vertigo (9). Beta oestrogen receptors in the utricle and saccule have been shown to have significant impact on the morphology, adherence and maintenance of otoliths in the inner ear (9, 17). Changes to hormone receptor stimulation can therefore be central to the pathogenesis of benign paroxysmal positional vertigo (5, 8, 9, 17). The oestrogen receptor alpha, which is thought to have a regulating function in the inner ear's calcium and carbonate homeostasis, is assumed to play a role. Low expression of this receptor may disrupt the otolith synthesis and disturb the endolymph composition (10). (Table 1)

Table 1

Benign paroxysmal positional vertigo (2, 3)

Epidemiology	Pathophysiology	Possible hormonal risk factors in women
Liefetime prevalence: 2.4 % 65 % women Average age at onset: 50–70 years	Degeneration of structures in the inner ear and otoliths that cause displacement to the semicircular canals.	Oestradiol deficiency may affect the synthesis, maintenance and adherence of otoliths in the inner ear.

Ménière's disease

Ménière's disease is assumed to be caused by an increased volume of endolymph and expansion of the labyrinth in the inner ear, most probably due to an obstruction in the endolymphatic system (20). Based on a population study from England, the condition has an incidence of 13 per 100 000, and women make up 65.4 % (4). Clinically, Ménière's disease is characterised by episodic attacks of dizziness, hearing loss, tinnitus, and a sense of pressure in the affected ear (20).

It has been observed in women of reproductive age that attacks often occur in connection with ovulation and decreased oestradiol concentration (11). Women with Ménière's disease who were prescribed hormonal contraception, have been observed to have fewer and less intense attacks (21).

«The women who received menopausal hormone therapy had less intense attacks, and they generally reported fewer problems with dizziness than the control group»

Several women experience exacerbation of symptoms in connection with the menopause (5). One study investigated the correlation between the functioning of the inner ear and oestradiol levels in postmenopausal women with Ménière's disease versus healthy postmenopausal women (14). In general, the women with the disease had lower levels of oestradiol in serum and abnormal latency in brainstem audiometry compared to the control group. The study concluded that reduced levels of oestradiol can contribute to the worsening of symptoms in postmenopausal women, and the functioning became increasingly worse with falling serum oestradiol (14). The women who received menopausal hormone therapy had less intense attacks, and they generally reported fewer problems with dizziness than the control group. The study concluded that reduced levels of oestradiol can exacerbate symptoms in postmenopausal women with Ménière's disease.

Little research has been conducted on the pathophysiological mechanism behind the impact of oestradiol and progesterone. The hypothesis is that low levels of oestradiol and progesterone affect the micro-circulation in the inner ear. This can lead to endolymph disturbances and cause an accumulation of fluid. As previously mentioned, menopausal hormone therapy (MHT) and hormonal contraception have a potential alleviating effect, but the existing body of research and trials is insufficient to draw these conclusions (9, 15, 21). (Table 2)

Table 2

Ménière's disease (4, 9)

Epidemiology	Pathophysiology	Possible hormonal risk factors in women
Lifetime prevalence: 0.1–0.2 % 65.4 % women Average age at onset: 30–50 years	Accumulation of endolymphatic fluid and expansion of the labyrinth. Most likely caused by obstruction of the endolymphatic system.	Fluctuations in oestradiol and progesterone levels can cause changes to the microcirculation in the inner ear, leading to alterations in the composition of the endolymph and an accumulation of fluid.

Clinical implications

There are many causes of dizziness. Once the most obvious ones have been ruled out, such as neurological disorder, cardiovascular disease and orthostatic hypotension, we tend to look to psychosocial factors for an explanation. Both

patients and doctors can find this unsatisfactory, and frustrated patients may well start looking for answers wherever they can. It is therefore an important finding that hormonal factors potentially trigger or exacerbate the cause of vestibular disorder in women, primarily because it may help patients cope and boost their confidence. Women's lives are often impacted by periodic hormonal fluctuations, and learning that this may be the cause of dizziness can give hope of improvement. This should also lead to the recording of a more targeted medical history in relation to hormonal issues. Secondly, the finding supports a multidisciplinary approach for the worst affected patients and opens the door to potential new therapies.

Hormone therapy has a well-documented efficacy against vasomotor symptoms and osteoporosis associated with the menopause. In animal studies, oestradiol treatment has been shown to reverse degenerative changes in the composition of the otolith, and in a similar study, oestradiol treatment was found to have a preventive effect against otolith degeneration after oopherectomy (9, 12). Postmenopausal women who received hormone therapy, had a lower incidence of benign paroxysmal positional vertigo than the group not in receipt of treatment (13). It has also been found that postmenopausal women with Ménière's disease who received hormone therapy had less intense attacks and were less impacted by dizziness.

Hormone therapy appears to have the potential to ease symptoms and reduce attacks in women of near-menopausal age who suffer from vestibular disorder. This would be a useful addition to the clinical toolbox. However, further research is needed before it is possible to draw these conclusions, and individual assessments must be made in relation to adverse effects and the risk involved with hormone therapy. For some women, knowing that their disorder is linked to a certain phase of life, and that there is a definite hope of getting better at the end of that phase, will in itself be sufficiently therapeutic.

Multidisciplinary approach

Recent research shows a connection between vestibular disorders and hormonal factors in women. Local oestrogen receptors appear to be important for the homeostasis of otoliths, calcium concentration, and endolymph composition in the inner ear. Several studies have shown that hormone therapy reduces symptoms of benign paroxysmal positional vertigo and Ménière's disease, but this must be balanced against risk factors and adverse effects in the individual women. We believe that the findings we present show the need for a broader and more multidisciplinary approach to women who struggle with dizziness as a symptom. An explanatory model of how hormonal fluctuations in different life phases contribute to troublesome symptoms can, in itself, give patients reassurance and strengthen their belief that they will improve over time. Collaboration across disciplines such as general medicine, neurology, otolaryngology and gynaecology appears to be conducive to providing optimal treatment. More research is needed into dizziness as a condition, including when linked to vestibular disorder, and into the effect that a patient's sex may have on incidence and presentation.

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Publisert: 18 March 2024. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.23.0838
Received 10.12.2023, first revision submitted 30.1.2024, accepted 2.2.2024.