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**Falls and medications in the elderly**

J.O. Daal1\*, J.J. van Lieshout2 1 Westfries Gasthuis, PO Box 600, 1620 AR Hoorn, the Netherlands, 2 Academic Medical Centre, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands, \* corresponding author

**INTRODUCTION**

Falls are common in the elderly and contribute to morbidity and mortality. Elderly people are often on a variety of medications as well, and this suggests a causative relation between use of medicine and falls. However, the evidence available to support this assumed relationship is not very robust. In this article, we will discuss specifically the medications that are presumed to be associated with falls. Falls in older people are a major public health problem with significant consequences for individuals, their families, and healthcare providers. The incidence of hip fractures increases with age. In the over 65 year olds, the rate of hospital admissions due to fractures from falls is increasing.1 There has been a doubling of the hospital admission rate for patients >65 years with a hip fracture in the Netherlands during the last 20 years.2-4 This has resulted in an enormous increase in the costs of intramural and extramural healthcare. In addition to an influence on morbidity and mortality, falls have a negative effect on daily life activities and quality of life. This is especially so when the fear of falling leads to avoidance behavior, which promotes inactivity with a further deconditioning of musculoskeletal function, propensity to inactivity and social isolation, all facilitating new falls.5 In the elderly, falls represent a multifactorial problem which should be regarded as the result of complex interactions between intrinsic factors and factors relating to environment and the specific situation. Judicious application of medications that enhance the likelihood of falling probably contributes to prevention of an important cause of morbidity in the elderly.6 Recent data from the Dutch Foundation for Pharmaceutical Statistics (SFK) have revealed that salicylates used as an antiplatelet agent, temazepam, furosemide and oxazepam (also see: www.sfk.nl) are among the medicines most frequently taken by elderly patients (>65 years). Pathophysiology of orthostatic hypotension is discussed and changes in the pharmacokinetics and pharmacodynamics due to ageing are addressed. A focus will be on the evidence currently available on medication as a risk factor for the occurrence of dizziness and falls. Osteoporosis and effects of medications on reaction time are beyond the scope of this review.

**DEFINING THE PROBLEM**

For elderly people aged >65 years who live in the community, the risk of falling varies from 25 to 40% a year,2,3,7,8 while for the institutionalized elderly this can be as high as 70%.9 The incidence of falls increases with age and is greater in women.10-12 At least 5% of community-dwelling elderly >65 years will suffer from a fracture related to a fall. Especially fractures of the hip result in hospital admission4 with a death rate within the following year of 20 to 30%.13,15 The same percentage of elderly people is admitted to a nursing home because of remaining disability.13,14

**PATHOPHYSIOLOGY OF ORTHOSTASIS**

Normovolaemia may be defined as the effectively circulating volume of a healthy person in the supine position.17 A change in posture to the upright position elicits a shift of © 2005 Van Zuiden Communications B.V. All rights reserved. MARCH 2005, VOL. 63, NO. 3 91

**REVIEW**

*J.O. Daal1\*, J.J. van Lieshout2 1 Westfries Gasthuis, PO Box 600, 1620 AR Hoorn, the Netherlands, 2 Academic Medical Centre, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands, \* corresponding author* Falls and medications in the elderly ~300 to 800 ml of blood from the chest to the lower parts of the body. To maintain cardiac output, the consequent fall in ventricular filling volume must be met by continuous adjustment of arterial and vasomotor tone and by regulating cardiac contractility and chronotropy.18 Humans can stand upright for long periods of time. Their orthostatic circulatory adaptation is provided by the evolution of an effective set of neuromuscular and circulatory mechanisms that are largely involuntary or autonomic, aiming to preserve arterial pressure as the controlled variable, independent of gravity. The arterial baroreflex is the well-known example of short-term control acting within the single heartbeat, while the more slowly acting but extremely powerful humoral-cardiovascular-renal system secures body fluid control, provided the fluid intake is normal.19,20 Orthostatic stress affects cerebral perfusion pressure and the cerebral autoregulatory system aims to limit the postural reduction in perfusion of the brain. Nevertheless assumption of the sitting or standing position affects cerebral perfusion and regional cerebral oxygenation in healthy humans.21-23 Age-related changes Although function and efficacy of cardiovascular reflex activity change with increasing age,24,25 arterial pressure in the upright position is usually well maintained.26 In addition, the magnitude of the blood volume declines with age but its possibly disadvantageous effects are offset at least in part by the concurrent decline in venous compliance limiting the volume of blood pooled. This explains the increased susceptibility of elderly patients for diuretic treatment interfering with the maintenance of blood volume and thus orthostatic tolerance.27,28 Postural stress affects cerebral oxygenation in the elderly29 but it is as yet uncertain whether this is related to a decline in autoregulatory capacity.30 Orthostatic tolerance in the elderly is reduced,31 and blood pressure and cerebral perfusion are affected further for at least for ~45 to 60 minutes following a meal.32-36 Postprandial hypotension is defined as a >20 mmHg postural drop in systolic blood pressure but this cut-off point should be regarded as less relevant with respect to the development of orthostatic symptoms.16 Especially in elderly people with hypertension a limited reduction in blood pressure may already elicit symptoms of cerebral incompetence.37 Following a meal, instead of resting, walking may benefit postprandial blood pressure and development of symptoms.38 *Moderate exercise training expands plasma volume and enhances leg muscle tone limiting orthostatic venous pooling and supporting orthostatic tolerance.*39 In the elderly the use of medicines and time of a meal may interfere with orthostatic tolerance in a complex way.

**AGE-RELATED CHANGES OF PHARMACOKINETICS AND PHARMACODYNAMICS**

In the elderly, the rate of absorption of most drugs administered orally is almost identical to that of younger people, but with ageing marked changes in body components affect the distribution. Body fat as a proportion of body weight increases by over 35% from the age of 20 to 70 years. There is a concurrent decrease in plasma volume of 8% with normal ageing; lean body mass and total body water decrease approximately 17%40 with an increased rate of adverse effects of both lipophilic (for example diazepam: large volume of distribution) and hydrophilic medications (high plasma concentration). Also, the metabolism of many medicines’ changes with ageing. Hepatic biotransformation is a prerequisite for drugs with limited renal clearance. There is a modest decrease in the efficiency of phase I reactions (oxidative and hydroxylation processes), reactions generally mediated by the mixed-function monooxygenase system (cytochrome P-450 system). In contrast, phase II reactions (by conjugation enzymes and transferases) are generally unaffected and in older vs younger patients’ drugs metabolized by phase II processes only are preferable. Drugs known to have a strong ‘first pass’ effect, such as metoclopramide and opiates, should be used in low doses. Renal drug excretion includes glomerular filtration, tubular secretion, and in a varying degree, tubular reabsorption as well. The half-life of a drug is directly related to the volume of distribution and inversely related to its clearance (metabolism and excretion). In the majority of elderly people renal function is diminished due to a reduction in both renal blood flow and number of functional nephrons with an increased half-life for drugs that depend on renal function for elimination.41 Insight into the effects of ageing on pharmacodynamics, probably through disease-related changes in target organs, diminished reserve capacity and changes in receptor function of end organs, is limited.42 As an example, the plasma concentration of diazepam required to achieve a certain level of sedation is much lower in the elderly than in subjects aged 30 to 50 years. An increased sensitivity has also been shown for opiates, anticholinergic and antihypertensive drugs and dopamine agonists. In contrast, the susceptibility of older vs younger patients for -blockade and insulin40 is reduced. From this viewpoint, data from literature concerning antipsychotics, (tri)cyclic antidepressants, anticonvulsive and cardiovascular medications are discussed.

**MEDICAL CAUSES AND RISK FACTORS FOR DIZZINESS AND FALLS**

Theoretically, randomized controlled trials are likely to provide the evidence to prove the causal relationship between medication use and falls. When addressing the MARCH 2005, VOL. 63, NO. 3 Daal, et al. Falls and medications in the elderly. 92 - **SOURCE: Page 19:** [**https://www.njmonline.nl/getpdf.php?t=i&id=67#page=19**](https://www.njmonline.nl/getpdf.php?t=i&id=67#page=19)