Challenges in Vascular Dementia Research

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Summary

Vascular disease affects not only the peripheral and cardiac circulations, but also the cerebral circulation, thus leading to impaired cognition. The term vascular dementia (VaD) is now generally used to describe this condition. VaD is the second most common dementia, affecting between 1.2% and 4.2% of the population aged more than 65 years, and up to 16.3% of males over 80 years. The major risk factors for VaD are hypertension, diabetes mellitus, heart disease and stroke. The selective diagnosis of VaD requires confirmation by a computed tomography scan or by magnetic resonance imaging. As dementia affects not only cognitive function, but also other abilities such as emotional control, motivation and social behaviour, outcomes research should comprise 3 levels of assessment: global clinical impression, cognitive function and activities of daily living. Published studies with naftidrofuryl, an agent with a pharmacological profile suggesting it could provide some benefit in this condition, have demonstrated a beneficial effect in patients with dementia of varying aetiologies. A double-blind placebo-controlled study of naftidrofuryl in patients with vascular dementia is now in progress.

1. Dementia

1.1 Clinical Symptoms

The term ‘dementia’ describes a psychopathological syndrome predominantly, but not exclusively, presenting as a cognitive deficit. Dementia may be secondary to a chronic medical condition (e.g. HIV infection, metabolic disorders, head trauma) or chronic intoxication (e.g. alcohol) and, as such, the treatment of the underlying disease or state should be given priority. In contrast, primary dementia, such as Alzheimer’s disease (AD) and vascular dementia (VaD), is a direct manifestation of the disease itself. Despite its multiple aetiologies, the diagnosis of dementia is always established clinically. Different diagnostic manuals have been published in the past, the two most established being the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) and the International Classification of Diseases, 10th edition (ICD-10). For the diagnosis of dementia, the ICD-10 requires a decline in memory, which is most evident in the learning of new information. A decline in other cognitive abilities characterised by a deterioration in judgement and thinking, e.g. in planning and organising and in the general processing of information, should also be present. Deterioration from a previously higher level of performance should be established. Since dementia also affects emotional control, motivation and social behaviour, at least one of the symptoms of emotional lability, irritability, apathy and coarsening of
social behaviour, should be manifest. The diagnosis of dementia cannot be established unless these symptoms have been present for at least 6 months.

1.2 Vascular Dementia

While a number of different terms have been used to describe this disease, the term vascular dementia is currently recommended by both the DSM-IV and the ICD-10. The term ‘multi-infarct dementia’ (MID), which was widely used during the last 2 decades, reflects the fact that vascular lesions evoking a chronic ischaemia are involved in the pathophysiology of VaD. The term MID is, however, now considered misleading when used as a synonym for VaD, since multiple brain infarcts are only one of several causes of the disease. Senile leucoencephalopathy and multiple lacunar strokes (lacunes), as observed in Binswanger’s dementia, are even more important possible causes of VaD. In addition, single strategic infarcts, hypoperfusion of the brain because of extracranial reasons and other mechanisms (e.g. combinations of different lesions, sequelae of subarachnoid haemorrhage) may play a role in the pathogenesis of VaD.[3-5]

1.3 Epidemiology

Although prevalence figures vary greatly in different studies, the evidence generally indicates that up to 8.4% of persons aged more than 65 years suffer from dementia of varying types. Prevalence increases with age and reaches 10.5 to 16% in the population aged more than 75 years, and is as high as 38.9% in those older than 85 years.[6] The prevalence of AD is reported to be 1.6 to 15.3% in those aged between 65 and 74 years, 4.1 to 7.9% in the 75- to 84-year-old age group and between 7.1 and 47.2% in the population aged more than 85 years. Despite the fact that in the past scientific interest has mainly focused on AD, VaD is the second most common type of dementia; prevalence figures of 0.8 to 8.0%[7] are reported (table I). Although the AD/VaD ratio is markedly affected by geographical variations, it is usually found to be >1, e.g. being 1.36 in Finland and 3.25 in England.[7] In only a few studies, particularly in Japanese populations, have figures shown a higher proportion of patients with VaD. Hence, the relative prevalence of VaD, calculated as a percentage of all types of dementia, varies between 30% in Canada and 48% in Japan.[10] Whether the AD/VaD ratio is dependent on age does not seem to be completely clear; some studies reported that the ratio increased in higher age groups, whereas others noted constant AD/VaD ratios. Despite some variations, both genders seem to be similarly affected by VaD (male/female ratios 0.75 to 1.38).

1.4 Risk Factors

There is strong evidence for the role of certain risk factors in VaD, despite methodological problems. These problems arise, at least in part, from the inclusion of certain risk factors, such as atherosclerosis and stroke history, in clinical scores designed for the diagnosis of vascular dementia [e.g. the Hachinski-score (HIS)].[11] In addition to age, heart disease, hypertension, haematocrit level and diabetes mellitus have been shown to be related to VaD.[7] In a case-control study, odds ratios of 3.09 (95% CI: 1.24 to 7.73), 3.11 (1.23 to 7.88) and 4.88 (1.55 to 15.53) were calculated for hypertension, pathological ECG and haematocrit >45%, respectively.[10] More importantly, these factors were independently related to VaD. In contrast, hyperlipidaemia, smoking, alcohol consumption and glucose intolerance were not identified as independent risk factors, although each was highly correlated with VaD. Because of the aetiopathology of VaD, a relationship to stroke is clear. Hence, risk