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Elsevier Masson France EM|consulte www.em-consulte.com

Diabetes & Metabolism

Diabetes & Metabolism 36 (2010) S84–S87

Stroke in diabetic patients

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Abstract

Stroke is the leading cause of disability and the second most frequent cause of death worldwide. On the one hand, diabetic patients have a 1.5 to 3-times higher risk of stroke, especially cerebral infarction, than non-diabetic subjects. This excess risk, which is particularly pronounced in younger individuals and women, can be reduced by effective therapeutic strategies aimed at improving glycaemic control and the management of co-morbid conditions such as hypertension and dyslipidaemia. On the other hand, the prevalence of diabetes in stroke patients is between 10 and 20%, and has been increasing over the last 20 years, probably in response to rising rates of overweight and obesity in the general population and other factors such as a sedentary lifestyle. Even though diabetes has long been considered a specific risk factor of lacunar stroke, recent epidemiological studies have demonstrated that this risk factor was in fact not associated with any ischemic stroke subtype. Finally, it has been suggested that diabetic stroke patients have poorer motor and functional outcomes, and are at a higher risk of dementia, recurrent stroke and death.

Keywords: Stroke; Diabetes; Risk factors; Outcome; Review

Résumé

Accidents vasculaires cérébraux chez le patient diabétique

Les accidents vasculaires cérébraux représentent la première cause de handicap et la seconde cause de décès à travers le monde. Les patients diabétiques ont un risque 1,5 à 3 fois plus élevé d'accident vasculaire cérébral, et en particulier d'infarctus cérébral, que les non diabétiques. Cet excès de risque, qui est particulièrement marqué chez les sujets jeunes et les femmes, peut être réduit par des stratégies thérapeutiques efficaces qui visent au contrôle glycémique et à la prise en charge des co-morbidités telles que l'hypertension artérielle ou encore les dyslipidémies. D'autre part, la prévalence du diabète au sein des patients victimes d'un accident vasculaire cérébral est évaluée à 10 à 20%, et est en augmentation au cours des 20 dernières années, probablement du fait de l'accroissement de la prévalence du surpoids et de l'obésité dans la population générale, et en lien avec d'autres facteurs tels que la sédentarité. Alors que le diabète a longtemps été considéré comme un facteur de risque spécifique des infarctus cérébraux lacunaires, les études épidémiologiques récentes ont démontré que ce facteur de risque n'était en fait associé à aucun sous-type étiologique particulier d'infarctus cérébral. Enfin, les patients diabétiques qui présentent un accident vasculaire cérébral ont un pronostic moteur et fonctionnel moins bon, et sont à plus haut risque de démence, récidive ou décès.

Mots clés : Accidents vasculaires cérébraux ; Diabète ; Facteurs de risque ; Pronostic ; Revue générale

1. Introduction

Stroke is the leading cause of disability and the second most frequent cause of death worldwide. In France, both stroke and transient ischemic attack result in over 125,000 hospitalizations annually, and standardized mortality rates for stroke are estimated at approximately 25 to 30/100,000/year [1]. Diabetes mellitus (DM) is one of the major risk factors for stroke, as it contributes to the progression of atherothrombotic cerebrovascular lesions.

In this article, we review epidemiological data about stroke in diabetic patients by discussing: 1) the risk of stroke in individuals with diabetes, the influence of this risk and ways to reduce it; 2) the frequency of DM in stroke patients and

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the clinical characteristics of diabetic stroke patients; and 3) the prognosis of stroke patients with DM in terms of the risk of recurrence, mortality, disability, handicap, and cognitive impairment.

2. Risk of stroke in diabetic patients

Epidemiological studies have suggested that the overall relative risk of stroke is 1.5 to 3 times greater in patients with DM than in healthy controls [2-4]. This increase in risk is particularly pronounced in younger subjects as well as in women. Hence, compared with healthy controls, the risk of developing a stroke is 2 to 3 times higher in men with DM, and 3 to 6.5 greater in women with DM [2,5,6]. In a large cohort study in the UK, which included 41,799 type 2 diabetic subjects and 202,733 controls, the absolute rate of stroke was 11.9 per 1,000 person-years in people with DM, and 5.5 per 1,000 person-years in the control group. The maximum likelihood estimate of the hazard ratio for stroke was observed in the 35-54 year age group (4.66 in men, and 8.18 in women), and the risk decreased with age [7].

The risk of stroke is also influenced by other factors such as the severity of the diabetes. The Atherosclerosis Risk in Communities (ARIC) study, which included 15,792 people aged 45-64 years at baseline, with a mean follow-up of 8-10 years, showed a robust association between diabetes-specific HbA_{1C} tertiles and incident stroke risk, both in diabetic and non-diabetic subjects [8]. In diabetic patients, the adjusted relative risk of stroke was 2.33 (95% CI: 1.29-4.21) in the highest tertile of HbA_{1c} (HbA_{1c} > 6.8%) compared with the lowest one (HbA_{1C} < 4.7%). A high level of proteinuria, defined as over 300 mg/d, is also considered an independent and strong risk factor for stroke in type 2 diabetic patients, even though no correlation between proteinuria and stroke mortality has been established yet [9].

The other classical vascular risk factors, including hypertension, dyslipidaemia, smoking and atrial fibrillation, also contribute to the increase in the stroke risk in patients with DM. Hypertension is twice as prevalent in diabetic as in non-diabetic individuals and in patients with diabetes; it is associated with accelerated progression of both microvascular and macrovascular complications, leading to a greater risk of stroke. Several randomized clinical trials have demonstrated that antihypertensive treatment dramatically reduces this risk in diabetic patients [10,11]. Therefore, in the UK Prospective Diabetes Study (UKPDS), a 10 mmHg reduction in mean systolic blood pressure was associated with a 44% reduction in stroke incidence [10]. In the secondary prevention setting, the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) showed a 38% risk reduction in diabetic patients treated with the combination therapy perindopril plus indapamide [11]. A meta-analysis of 14 randomised trials on statin therapy conducted in over 18,000 diabetic patients reported a highly significant reduction in stroke risk in diabetic patients (21%; 95% CI: 7-33%); this reduction was more marked than in the non-diabetic group (16%; 95% CI: 7-24%) [12]. Finally, the cumulative effect of lifestyle risk factors, such as cigarette smoking, alcohol abuse, obesity, physical inactivity, poor diet and stress, could be greater in individuals with diabetes than in those without.

Contrasting with these data, which clearly demonstrate that the control of vascular risk factors in diabetic patients is associated with a reduction in the incidence of stroke, there is longstanding controversy about the efficacy of improving glycaemic control in the risk reduction of macrovascular complications, including stroke, in patients with DM. A recent systematic review and meta-analysis of all randomized controlled trials comparing interventions to improve glycaemic control with conventional treatment included 1800 patients with type 1 DM and 4472 patients with type 2 DM [13]. The author found clear evidence that glycaemic control is associated with a substantial decrease in macrovascular risk in diabetic patients. Interestingly, in type 1 DM, improved glycaemic control significantly reduced the risk of cardiac events and peripheral vascular disease, whereas it did not reduce the risk of stroke. In contrast, for type 2 DM, a significant 42% reduction in the risk of stroke was noted with active treatment and a similar reduction was observed for peripheral vascular disease, but not for cardiac events [13].

3. Prevalence of diabetes mellitus in stroke patients

DM is a frequent condition in stroke patients. Population-based registries of stroke have reported a global prevalence of DM ranging from 9.5% to 20% [14-16]. In France, based on the national database called "Hospital Discharge Diagnosis Records" (Programme de Médicalisation des Systèmes d'Information, PMSI), the prevalence of diabetes among all hospitalized patients from 2005 through 2008 with a diagnosis of stroke has been estimated at 15% (unpublished data). In addition, in a recent study 16% to 24% of patients with undiagnosed DM at admission for acute stroke were found to have DM according to an oral glucose tolerance test performed 12 weeks after the stroke [17]. The prevalence varied greatly according to the subtype of stroke considered. Hence, the prevalence of DM is lower in patients suffering from spontaneous intracerebral haemorrhage than in those with ischemic stroke. In the latter group, the prevalence is around 25% [18-22]. However, some variations have been noted according to the etiological subtype of ischemic stroke (lacunar, cardioembolic, or large vessel ischemic stroke). Several studies, most of which were hospital-based, have suggested that lacunar stroke is associated with a particular risk factor profile characterized by a higher frequency of hypertension and DM, both of which contribute to the development of lipohyalinosis involved in small vessel brain disease [23,24]. Contrasting with these results, in a previous study conducted on the population-based stroke registry of Dijon, France, we reported a DM prevalence of 19.1% in lacunar strokes, 21.9% in large vessel strokes, and 13.6% in cardioembolic