Can J Diabetes 40 (2016) 12–16

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

Original Research

Influence of Blood Pressure and Other Clinical Variables on Long-Term Mortality in a Cohort of Elderly Subjects with Type 2 Diabetes

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ARTICLE INFO

Article history:
Received 14 August 2015
Received in revised form
24 September 2015
Accepted 25 September 2015

Keywords:
Ambulatory blood pressure monitoring
Diabetes mellitus
Elderly
High blood pressure, mortality

ABSTRACT

Background: Diabetes mellitus and high blood pressure (HBP) are commonly associated conditions in the elderly population. An effect of treatments, biologic and anthropometric variables on long-term mortality is unknown in this population.
Objectives: To determine the prevalence of HBP control in a sample of elderly patients with type 2 diabetes with office blood pressure (BP) readings and ambulatory blood pressure monitoring (ABPM) and evaluate the influence of BP, anthropometric and laboratory variables on long term mortality.
Methods: Cohort study in patients living at home in the area of Sherbrooke, ≥65 years old, receiving reimbursement for antidiabetic medication. The study included medical history, 2 sets of BP measurements, 2 24-hour urinary collections for microalbuminuria, 1 24-hour ABPM, blood level of creatinine and glycosylated hemoglobin. Charts were reanalyzed 8 years later for analysis of cardiovascular and total mortality cases.
Results: 198 patients were initially recruited. By history, 83% of the subjects had diagnoses and treatments for high blood pressure. In multivariate analysis, factors associated with an 8-year increased risk for cardiovascular mortality were creatinine ≥84 µmol/L, office seated systolic blood pressure ≤130 and diastolic BP ≤67.6 over 24 hours. Factors associated with total mortality were lower waist circumference, serum creatinine ≥84 and diastolic BP ≤67.6 over 24 hours.
Conclusions: Lower systolic and diastolic BP (office and ABPM), lower waist circumference and higher creatinine values are associated with an increased mortality risk. This suggests that a lower BP, declining kidney function and frailty are factors associated with this observation.

Mots clés :
Monitorage ambulatoire de la pression artérielle
Diabète sucré
Âgé/personnes âgées
Hypertension artérielle
Mortalité

RÉSUMÉ

Introduction : Le diabète sucré et l'hypertension artérielle (HTA) sont des maladies fréquemment associées qui touchent la population âgée. Les effets des traitements, des variables biologiques et anthropométriques sur la mortalité à long terme sont inconnus dans cette population.
Objectifs : Déterminer la prévalence de la HTA dans un échantillon de patients âgés souffrant du diabète de type 2 par des lectures de pression artérielle (PA) en cabinet et un monitorage ambulatoire de la pression artérielle (MAPA), et évaluer l'influence de la PA, des variables anthropométriques et biologiques sur la mortalité à long terme.
Méthodes : L'étude de cohorte portait sur des patients≥65 ans qui vivent à domicile dans la région de Sherbrooke et qui reçoivent un remboursement pour les médicaments antidiabétiques. L'étude comprenait les antécédents médicaux, 2 séries de mesures de la PA, 2 recueils des urines des 24 heures, 1 MAPA des 24 heures, la concentration de créatinine et d'hémoglobine glyquée dans le sang. Huit ans plus tard, nous avons analysé les dossiers en ce qui trait aux cas de mortalité cardiovasculaire et totale.
Résultats : Nous avons initialement recruté 198 patients. Selon l'interrogatoire, 83 % des sujets recevaient un diagnostic et un traitement de HTA. À l'analyse multivariée, les facteurs associés à l'augmentation du risque de mortalité cardiovasculaire après 8 ans étaient une créatinine≥84 µmol/l, une PA systolique en

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1499-2671
http://dx.doi.org/10.1016/j.jcjd.2015.09.089

cabinet réalisée en position assise≤130 et une PA diastolique≤67.6 sur 24 heures. Les facteurs associés à la mortalité totale étaient un périmètre abdominal plus petit, une créatinémie≥84 µmol/l et une PA diastolique≤67.6 sur 24 heures.
Conclusions : Des valeurs de PA systolique et diastolique plus basses (en cabinet et au MAPA), de périmètre abdominal plus petites et de créatinémie plus élevées sont associées à une augmentation du risque de mortalité. Cela suggère qu'une PA plus basse, le déclin du fonctionnement rénal et la fragilité sont des facteurs associés à cette observation.

Introduction

Diabetes mellitus is common in elderly people, and the presence of diabetes approximately doubles the risk for having concomitantly high blood pressure (HBP) (1). At the time when the blood pressure (BP) measurements were initially done, the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure recommended that when treating HBP, the office measurements should be less than 140/90 mm Hg in the general population and less than 130/80 mm Hg in the presence of diabetes (2). The Canadian recommendations are similar (3). Nevertheless, these BP targets are reached in less than 40% of patients in the general population, with aging further decreasing the odds of achieving a target BP lower than 140/90 (4). Furthermore, there are no clear recommendations as to whether the target BP in the elderly population with diabetes should be lower than 140/90 mm Hg or lower than 130/80 mm Hg.

Office BP readings may be higher than measures done at home or by ambulatory blood pressure monitoring (ABPM) in the elderly (5). With the onset and progression of diabetic nephropathy, BP values tend to remain in the higher range over 24 hours (6).

In normal individuals, BP declines by at least 10% during sleep and this is called the nocturnal dipping phenomenon. When this physiologic drop does not occur, these patients are referred to as "nondippers" (NDs). In a mixed population, the combination of type 2 diabetes and nondipping is associated with a higher risk for death (7). Consequently, it has been proposed that in certain clinical situations, the total BP burden should be evaluated over 24 hours by ABPM (8–10).

Frailty has been associated with type 2 diabetes in elderly patients. The presence of the frailty phenotype increases the mortality rate (11). Both cardiovascular problems and frailty contribute to increase the mortality rate, but the contribution of each factor remains uncertain, with the duration of the disease increasing and the subjects' getting older.

Methods

The current protocol was approved by the Ethics Committee of the Research Center on Aging of the Centre Intégré Universitaire de Soins et Services en Santé de L'Estrie.

The initial part of this study (in 2002) was to evaluate the prevalence of HBP in an elderly population with type 2 diabetes living in the community. With a prevalence of HBP around 50%, to achieve a 2-sided 95% confidence interval of and precision of 0.073, the sample size was estimated at n=180. The study subjects were identified through a list of patients from the Régie de l'Assurance Maladie du Québec, Quebec's public health insurance agency. A letter of invitation to participate was sent by mail to potential study subjects if they had received reimbursement for any oral antidiabetic agent (insulin secretagogues, metformin, thiazolidinediones) or insulin for at least 3 months. Candidates with known renovascular hypertension, on prednisone>10 mg per day, known to have active neoplasia, undergoing hemodialysis or unable to give informed consent were excluded.

After subjects read and signed the consent form, medical histories were taken (including review of charts from our hospital, other hospitals and private clinics). A registered nurse obtained the first set of 2 BP measurements with the study subject in the lying, sitting and standing positions, according to recommended procedures (3). A sphygmomanometer with mercury column was used in all study subjects. A blood test was performed for glycolated hemoglobin (A1C) (HPLC Tosoh G7; Tosoh Bioscience, South San Francisco, California, USA) and for creatinine (Vitros 950 chemistry analyzer; Ortho-Clinical Diagnostic, Markham, Ontario, Canada). Each study subject was requested to complete 2 consecutive 24-hour urine collections for microalbuminuria (CX5; Beckman Coulter, Fullerton, California, USA).

We used the ABPM Spacelabs 90207 device for a 24-hour recording of BP, which provides automatic sphygmomanometer BP readings at 30-minute intervals during the day and every hour during the night (9). To be valid, the ABPM had to have a BP measurement success equal to or more than 70% of readings done over 24 hours (10). The daytime period was set from 6 AM to 10 PM, and the night-time period, from 10 PM to 6 AM. A second set of manual BP measurements were done the next morning after removing the ABPM device. The initial evaluation of the cohort was made between March and November of 2002.

From September through November of 2010 (approximately 8 years later), charts of the subjects who were enrolled in the first part of this study were studied at the Centre Hospitalier Universitaire de Sherbrooke and the Centre de Santé et des Services Sociaux-Centre de Recherche sur le Vieillissement, Sherbrooke, Canada, to identify the candidates who died in the interval. Mortality was classified as cardiovascular, including fatal myocardial infarction, fatal stroke, sudden death and fatal heart failure, and total mortality, including death from any cause.

All BP reading are expressed in mm Hg. Data are presented as means±1 standard deviation (SD). We used the Cox regression model to evaluate mortality risk. For cardiovascular mortality, the following variables with statistical significance in univariate analysis were used for multivariate analysis: seated office BP ≤130, creatinine and diastolic blood pressure over 24 hours. For total mortality, the variables significant in univariate analysis used for multivariate analysis were waist circumference, creatinine and diastolic BP measured during 24 hours. For certain variables, such as A1C and systolic blood pressure, we used traditional cut-off points, but when the numbers of groups were too unequal (such as diastolic BP), we used the median so as to have comparable numbers among groups.

All analyses were done using alpha levels of 0.05.

Results

After the postal invitations, 198 subjects were eligible to participate in the study and completed the protocol. Characteristics of the study population are shown in Table 1. After review of hospital and private clinic medical charts, 83% of the subjects had diagnoses of HBP. In this group, the pharmacologic interventions for HBP treatment were as follows (in percentages), with various combinations: diuretics (32%), angiotensin converting