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Oral glucose tolerance test in the assessment of glucose-tolerance in the elderly people

SIR—Assessment of glucose tolerance in the elderly has been in the focus of research due to the increased incidence of diabetes type 2 in this population. Approximately 13% of adults older than 70 years have diabetes, and 11% of adults between the ages of 60 and 74 years remain undiagnosed [1]. Factors that may predispose to glucose intolerance in the aged are weight gain, decreased physical fitness, decreased insulin secretion and lack of glucagon suppression. The Baltimore Longitudinal Study of Aging documented a prominent decline in glucose tolerance after the age of 60 years with both fasting and postprandial concentrations being higher in elderly compared to younger subjects [2]. Although the prevalence of diabetes is highest among people

older than 65 years of age, the prevalence of obesity in this age group is only 14%, compared to 24% for men and women in their fifties [3]. Obesity is a marker of insulin resistance. However, it appears that ageing may be associated with dissociation between obesity and glucose intolerance. Senescence, *per se*, is associated with a progressive decline in insulin clearance and a subtle decrease in insulin secretion [4]. It appears that older individuals do not have the ability to increase insulin secretion to the degree necessary to prevent glucose intolerance. Insulin-mediated glucose disposal also decreases with age and correlates significantly with the decreased physical activity in the elderly. Finally, irregularities in glucagon secretion may initiate glucose intolerance. Lack of suppression of glucagon secretion in the elderly may cause hyperglycaemia by increasing hepatic glucose release [5]. Therefore, the aim of the present study was to assess glucose tolerance in healthy, non-obese, moderately active elderly subjects.

Methods

Forty-eight subjects aged 60–90 years, were recruited from the outpatient geriatric clinic of the ‘Zvezdara’ University Hospital during their regular annual visit. All subjects underwent a medical evaluation which included a medical history. Subjects with cardiovascular, renal or hepatic disease, diabetes, endocrine disorders, or those on medication that could influence carbohydrate metabolism were excluded from the study. All participants were moderately active, meaning that they had two exercise sessions of 30 min/week or walked at least 1 km daily. They were non-obese, according to the body mass index (BMI) with less than 25 kg/m². All subjects had their waist circumference measured. A greater waist circumference, a marker of metabolic syndrome, was not an exclusion criterion. All participants were non-smokers and consumed alcohol moderately (less than 2 alcohol units/day). The control group consisted of 45 non-obese healthy health care workers in the age group 30–45 years. Each participant gave an informed consent for participating in the study. The study was approved by the ethical committee of the ‘Zvezdara’ University Hospital.

A 75-g oral glucose tolerance test (OGTT) was performed in the morning after an overnight fast. Blood samples were collected from the venous catheter placed in the antecubital vein at 0, 60 and 120 min for glucose, insulin, c-peptide and glucagon levels. Participants remained seated for the entire testing period. Plasma glucose was measured using an automated glucose oxidase reaction (Glucose Analyser, Ames). Plasma samples were centrifuged at 4°C, separated and stored at –20°C until assay. Plasma insulin was determined by a commercially available radioimmuno-assay (RIA) kit (Pharmacia, Uppsala, Sweden, normal reference range 0–20 mU/l). Plasma c-peptide was measured by RIA kit provided by Behring (normal reference range 0.3–0.9 nmol/l). Plasma glucagon concentrations were measured by RIA by use of reagents purchased from Novo Nordisk (normal reference range 50–220 pgr/ml).

Table 1. Physical characteristics of the participants with values of glucose, insulin, c-peptide and glucagon during the 75-g oral glucose tolerance test

	Elderly <i>N</i> = 48	Control <i>N</i> = 45	<i>P</i>
Age (years)	77.4 ± 6.32	34.2 ± 5.6	<i>P</i> < 0.01
Body weight (kg)	75.65 ± 3.81	74.2 ± 2.32	NS
BMI (kg/m ²)	23.91 ± 3.81	23.8 ± 1.2	NS
Waist (cm)	96.26 ± 4.95	90.1 ± 5.32	<i>P</i> < 0.05
Fasting blood glucose (mmol/l)	5.05 ± 1.60	4.76 ± 0.90	NS
Blood glucose at 60 min (mmol/l)	9.04 ± 1.85	8.4 ± 1.60	NS
Blood glucose at 120 min (mmol/l)	6.34 ± 1.20	5.3 ± 1.15	<i>P</i> < 0.01
Fasting serum insulin (mmol/l)	12.6 ± 4.21	12.6 ± 5.58	NS
Serum insulin at 60 min (mmol/l)	76.86 ± 4.1	111.06 ± 9.36	<i>P</i> < 0.01
Serum insulin at 120 min (mmol/l)	52.66 ± 4.97	33.65 ± 3.98	<i>P</i> < 0.05
Fasting serum c-peptide (nmol/l)	0.72 ± 0.23	0.70 ± 0.30	NS
Serum c-peptide at 60 min (nmol/l)	2.08 ± 0.50	2.61 ± 0.43	<i>P</i> < 0.01
Serum c-peptide at 120 min (nmol/l)	1.85 ± 0.62	1.81 ± 0.12	NS
Fasting serum glucagon (pg/ml)	161.76 ± 3.84	145.07 ± 6.16	<i>P</i> < 0.05
Serum glucagon at 60 min (pg/ml)	150.38 ± 3.87	127.55 ± 5.90	<i>P</i> < 0.01
Serum glucagon at 120 min (pg/ml)	148.72 ± 4.95	127.70 ± 3.40	<i>P</i> < 0.05

Statistical Analysis

All analyses were done with the use of the statistical software package SPSS, version 10.0. Differences in baseline characteristics between elderly and control subjects were tested by Student's *t*-test. Pearson's correlation coefficients were calculated to evaluate the relation between age or waist circumference and glucose or hormone levels during OGTT. Linear regression analysis was performed for variables with significant relationship. Data were presented as mean ± SD; a *P* value < 0.05 was considered statistically significant.

Results

Physical characteristics of subjects are presented in Table 1. A significant difference was observed in the waist circumference between the elderly and younger subjects, although BMI and weight were not significantly different. The rise in blood glucose levels following an OGTT was not significantly different in the 1st hour, but was significantly higher in the 2nd hour in the group of elderly subjects. The response was, however, within normal limits according to the WHO criteria [6] indicating normal glucose tolerance in both elderly and control subjects. Insulin response during OGTT was significantly lower in elderly subjects in the 1st hour. During the 2nd hour, insulin levels declined significantly in both groups, but less so in the group of control subjects (Table 1). Hence, insulin levels were significantly lower in the 1st hour and significantly higher in the 2nd hour of OGTT in elderly subjects. C-peptide levels increased significantly in both groups, but less so in the elderly in the 1st hour of OGTT. C-peptide levels were similar in elderly and younger subjects at 120 min, but the fall in c-peptide levels from 60 to 120 min was greater in younger subjects, again, maybe indirectly indicating insulin resistance. Fasting serum

glucagon levels were significantly higher in the elderly. They remained significantly higher and unsuppressed during the OGTT in the group of elderly subjects.

A significant correlation was observed between waist circumference and insulin level at 60 min ($R = 0.301$; $P = 0.013$), age and glucose level at 120 min ($R = 0.403$; $P = 0.001$), age and insulin level at 60 ($R = -0.339$; $P = 0.005$) and 120 min ($R = 0.341$; $P = 0.004$), age and c-peptide level at 60 min ($R = -0.378$; $P = 0.001$), and age and glucagon level at 60 ($R = 0.345$; $P = 0.004$) and 120 min ($R = 0.257$; $P = 0.034$). Linear regression analysis revealed a strong relation of waist circumference with insulin level at 60 min, age with glucose level at 120 min, age with insulin level at 60 and 120 min, age with c-peptide level at 60 min, and age with glucagon level at 60 and 120 min.

Discussion

Our study has shown that maintenance of glucose tolerance in non-obese healthy elderly subjects differs from that in non-obese younger subjects. Higher fasting and stimulated glucose levels during OGTT may be the consequence of abdominal obesity or hormonal changes: lack of suppression of glucagon in the presence of relative insulin insufficiency.

Age-related increase in adiposity and decrease in physical activity are related to decreased insulin action with ageing [7]. Elderly participants in our study were moderately physically active, but had a significantly greater waist circumference than younger subjects. This may indicate greater visceral obesity, in spite of normal weight. Goodpaster *et al.* [8] have shown in the Pittsburgh Study that regional adipose tissue distribution is the key determinant of insulin resistance. That visceral obesity, more than age, *per se*, correlates with glucose intolerance, has also been shown in the study of Imbeault *et al.* [9]. Hence, normal weight elderly with abdominal

obesity, such as our group, may still be at an increased risk for developing diabetes. Higher fasting and stimulated glucose values could indicate insulin resistance, which was not evaluated in our study. Imbeault *et al.* [9] also noted higher fasting plasma glucose levels in elderly, even after correction for visceral fat accumulation, suggesting that other factors contribute to the impaired glucose homeostasis in ageing.

Although in line with the present WHO criteria for normal glucose tolerance, the measured higher glucose levels could also indicate an imbalance in hormones regulating glucose metabolism. In physiological conditions ingestion of carbohydrates causes a rise in glucose and insulin secretion that in turn suppresses glucagon secretion. The two hormones act in concert to minimise the postprandial rise in glucose. A disturbance in glucose tolerance may be a consequence of the decrease and delay in insulin rise, or an increase in glucagon secretion and action.

The effect of age on insulin secretion has not been well defined. Basal insulin secretion, measured by the c-peptide level, and insulin secretory response to any increment in plasma glucose are decreased with age [10]. This is in line with insulin and c-peptide responses in the 1st hour of OGTT in our study. Higher insulin levels in the 2nd hour of OGTT in the elderly could indicate a defect in the insulin action or insulin clearance. The study of Basu *et al.* [11] elegantly showed that the age-associated deterioration in glucose tolerance is a consequence of insulin secretion, action and clearance.

Irregularities in glucagon response to postprandial hyperglycaemia may exist many years before glucose intolerance gets manifest [12]. Our elderly subjects had higher fasting and stimulated glucagon levels. Lack of suppression of glucagon could cause higher glucose levels by impairing glucose and insulin-induced inhibition of endogenous glucose production [13]. However, the role of glucagon in the development of glucose intolerance is dependent on insulin secretion. When insulin secretion is adequate, glucagon increase does not cause hyperglycaemia [14]. If relative insulin deficiency is present, such as in the elderly, lack of glucagon suppression can impair glucose tolerance [15].

Key points

- Maintenance of glucose tolerance in non-obese healthy elderly subjects differs from that in non-obese younger subjects.
- Higher fasting and stimulated glucose levels during OGTT in the elderly may be the consequence of abdominal obesity, in spite of normal body mass index.
- Ageing is associated with a decrease in insulin secretion, action and clearance.
- Glucose intolerance in the elderly may be a consequence of lack of glucagon suppression in presence of relative insulin insufficiency.

Conflicts of interest

None

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End-of-life care for older patients dying in an acute general hospital—can we do better?

SIR—The successful provision of a high standard of care to the dying in our population represents a significant healthcare challenge, a challenge influenced by patient age, disease process, place of care, and by the expertise of the professionals caring for patients at the end of life.

Recent estimates predict that by the year 2020, 26% of the UK population will be aged 65 years and older [1, 2]. It is also known that the majority of patients who die in acute hospital care are over 65 years of age [3]. Though it is recognised that excellent end-of-life care is provided in the hospice setting [4], there is less evidence relating to the provision of this care in hospitals.

In anticipation of these predicted demographic changes, statutory and specialist bodies [1, 2, 5–9] have produced guidelines and recommendations suggesting how better end-of-life care should be provided to older people in all care settings. These documents highlight the current inequity of access to good end-of-life care, the societal, professional, organisational and statutory obstacles to improvement in this area, and to outline how these inequities should be remedied. One such document, the Liverpool Care Pathway for the Dying Patient (LCP) [4, 10] provides an evidence-based framework for the delivery of care to dying patients, promotes excellent documentation of all aspects of the care provided and lends itself easily to the audit process. Originally designed to enable transfer of the hospice model of care to other care settings, the LCP is used increasingly in the hospital sector.

The purpose of this study is 3-fold. We wish to review the extent to which evidence of the care being provided to older patients dying in an acute hospital was documented, to ascertain whether or not the future implementation of the LCP on the wards of the Department of Medicine for the Elderly (DME) would benefit patients and staff, and to ascertain whether any of the admissions to hospital of patients who subsequently died there might have been avoided and these patients more appropriately managed within the community.

Method

This study is a retrospective case-note review of the medical and nursing notes and drug charts of those patients who died under the care of the DME at University Hospital

Aintree in a selected month. The cohort of patients was identified and their case-notes retrieved by the hospital medical records department. The chief investigator (FT) used a proforma developed by the authors to retrieve the required data from the case-notes relating to each patient’s final admission only. Data retrieved included basic demographic information, evidence of family and professional support in the community prior to admission, the reason for admission, diagnosis(es), and detailed information relating to the care provided to patients as they approached death, as documented in the case-notes.

Results

Twenty-five patients died during the study period and were included in the study. Their demographic data are presented in Table 1. Evidence of domestic and community support was poorly documented. Patients had a range of primary diagnoses while several had multiple active disease processes. Only one patient had a malignant diagnosis.

The details of care provided at the end of life are presented in Table 2. Recognition that a patient’s death was imminent, occurred most frequently between 24 and 48 h prior to death, and the likelihood that the death of their relative was approaching was discussed with family members in the majority of cases. Of note, there was no documentation

Table 1. Demographic data (*n* = 25)

Gender			
Female	18 (72%)		
Mean age	82.4 years (S.D. 10.3)		
Admitted from			
Home	16 (64%)		
Nursing home	5 (20%)		
Family home	2 (8%)		
Sheltered accommodation	2 (8%)		
Marital status			
Single	3 (12%)		
Married	7 (28%)		
Widowed/separated	15 (60%)		
Community support	Yes	No	Do not know
Living alone	10 (36%)	12 (48%)	3 (11%)
District nurses involved	5 (20%)	11 (44%)	9 (36%)
Social services involved	5 (20%)	13 (52%)	7 (28%)
Primary diagnosis			
Lower respiratory tract infection	8 (32%)		
Acute cardiac event	6 (24%)		
Stroke	6 (24%)		
Sepsis	2 (8%)		
Other ^a	3 (12%)		
Admission necessary			
Yes	19 (76%)		
Possibly not	6 (24%)		

^aAdenocarcinoma of sigmoid colon (1), old age (1), general deterioration (1).