An impaired insulin release associated with glucose intolerance in markedly aged subjects

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The presence of glucose intolerance in aged subjects is a well known physio-pathological condition[1-3]. However, the mechanisms by which it takes place are still unclear. Insulin release in aged subjects has been reported normal[4], elevated[3,5], or decreased[6,7]. These conflicting results may partly be due to the design of study, because in many studies, insulin response in aged subjects has been compared with that in young subjects in spite of glucose tolerance. Thus, the role for insulin in glucose intolerance in aged subjects remains to be fully elucidated. In the present study, insulin release after oral glucose was studied in thirty nine non-obese markedly aged subjects (above 80 yr of age) to elucidate the possible role of insulin release in age-related glucose intolerance.

Subjects and methods

Subjects

Thirty nine (14 males and 25 females) non-obese aged subjects (80-95 yr of age) were recruited in the present study. All were inpatients and followed an almost isocaloric diet (1800-2000 kcal/day). Subjects with diabetes mellitus, endocrinological diseases, impaired renal function (creatinine clearance <50ml/min), hepatic diseases, or those using drugs affecting glucose metabolism or those with a family history of diabetes were excluded from the study. Eleven hypertensive subjects were treated with ACE-inhibitor and/or Ca antagonist.

Glucose tolerance test

After an overnight fast, 75g oral glucose tolerance test was performed. The blood was drawn from antecubital vein at 0, 30, 60, 90, and 120min. During the test, the subjects were in bed rest. According to the World Health Organization (WHO) criteria, subjects were divided into two groups; normal glucose tolerance and impaired glucose tolerance (IGT). Subjects with diabetic pattern were excluded from this study.

Measurements

The blood glucose was measured by glucose oxidase method[8]. Plasma insulin (IRI) was assayed by radioimmunoassay[9]. Insulinogenic index was calculated by the formula : increment in IRI (ΔIRI) divided by increment in blood glucose (ΔBG) at 30min.

Statistical analyses

The values are expressed as the mean ± SD. An analysis of variance and two-tailed non-paired Student's t test were used for the statistical analyses.

Results

Blood glucose response

Twenty subjects (5 males and 15 females) showed normal glucose tolerance. The age was 85.9 ± 4.8yr (80-93), and body mass index (BMI) was 19.6 ± 2.3 (16.9-23.8). Nineteen subjects (9 males and 10 females) showed IGT. The age was 84.2 ± 4.7yr (80-95), and BMI was 20.6 ± 3.5 (16.6-24.5).

Plasma insulin response

Insulin response after glucose ingestion was shown in Fig. 1. IRI reached to the peak value of 73 ± 37 μU/ml at 30min in subjects with normal glucose tolerance. The IRI response to glucose was delayed in subjects with IGT, and the IRI level (33 ± 26 μU/ml) at 30min was significantly lower than that in subjects with normal glucose tolerance.

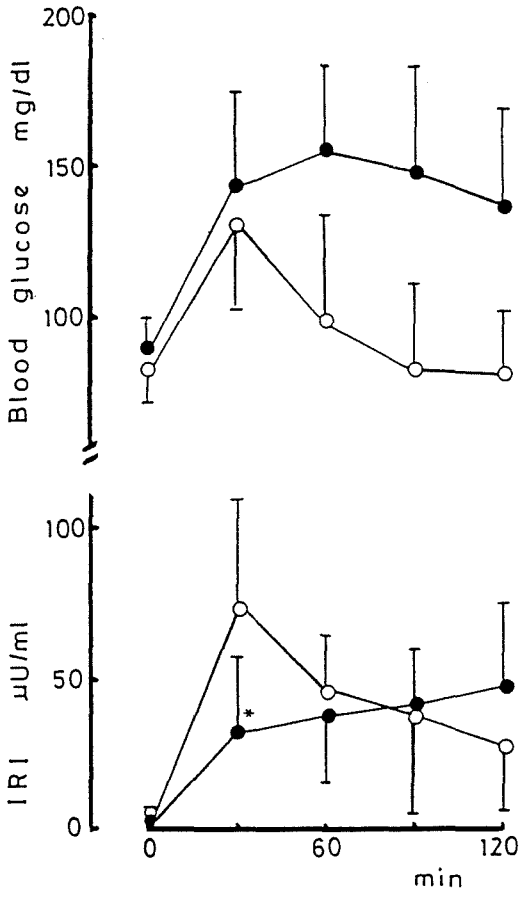

Fig. 1 Blood glucose and plasma insulin levels during 75g OGTT in markedly aged subjects.
The bars represent SD.

○ subjects with normal glucose tolerance (n = 20)

● subjects with IGT (n = 19)

* $p < 0.002$, significantly different from subjects with normal glucose tolerance.

Insulinogenic index

Insulinogenic index in subjects with IGT (0.62 ± 0.48) was significantly ($p<0.001$) lower than that in those with normal glucose tolerance (1.47 ± 0.71).

Discussion

In the present study, the only subject above 80 yr of age was recruited, because the markedly aged subject may be more available for evaluating an age-related glucose intolerance. After OGTT, twenty subjects exhibited normal glucose tolerance and almost normal insulin release when compared with plasma insulin response in healthy young subjects in our clinic. Thus, it is possible that aging is not necessarily associated with glucose intolerance when insulin secretions are still normal. The present results supported the report of Pacini et al.[10] that showed no significant changes in insulin release in aged subjects with normal OGTT.

The subject with IGT was associated with the loss of early insulin release as shown in Fig 1 Insulinogenic index was also lower in subjects with IGT than that in subjects with normal glucose tolerance. Diet restriction or decreased physical activity has been known to result in IGT[11,12]. However, the present subject had a good appetite and followed isocaloric diet. The physical activity was reduced similarly in all subjects. Obesity has been known to result in IGT[13], yet body mass index was not significantly different from each other between subjects with normal glucose tolerance and those with IGT. Hypertension may reduce glucose tolerance[14], yet the number of subjects with hypertension was not significantly different from each other between two groups (6 in subjects with normal glucose tolerance and 5 in subjects with IGT).

Although the reasons why insulin release after glucose ingestion decreased in some of markedly aged subjects are unclear in the present study, we conclude that aging is not necessarily associated with glucose intolerance when insulin secretions are still normal and that age-related glucose intolerance is associated with the impairment of insulin release.

Summary

To elucidate the possible role of the insulin release in age-related glucose intolerance, 75g oral-GTT was performed in thirty-nine non-obese markedly aged subjects (above 80 yr of age). Twenty subjects showed normal glucose tolerance, and nineteen subjects showed impaired glucose tolerance (IGT). Insulin release in subjects with IGT was significantly lower than that with normal glucose tolerance. Insulinogenic index at 30min (ΔIRI/ΔBG) was significantly ($p<0.001$) lower in subjects with IGT (0.62 ± 0.48, mean ± SD) than in subjects with normal glucose tolerance (1.47 ± 0.71). These results suggest that aging is not necessarily associated with glucose intolerance when insulin secretion is not impaired and that age-related glucose intolerance is associated with an impaired insulin release.

References

1. Davidson MB, Metabolism, **28**, 688-705, 1979.
2. DeFronzo RA, Diabetes Care, **4**, 493-501, 1981.
3. Jackson RA, Blix PM, Matthews JA, Hamling JB, Din BM, Brown DC, Beilin J, Rubenstein AG and Nabarro JDN, J Clin Endocrinol Metab, **55**, 840-848, 1982.
4. DeFronzo RA, Diabetes, **28**, 1095-1101, 1979.
5. Jackson RA, Hawa MI, Roshania RD, Sim BM, DiSilvio L and Jaspan JB, Diabetes, **37**, 119-129, 1988.
6. Barbagallo-Sangiorgi G, Laudicina E, Bompiani GB and Durante F, J Geriatr Soc, **18**, 529-533, 1970.
7. Chen M, Bergman RN, Pacini G and Porte D Jr, J Clin Endocrinol Metab, **60**, 13-20, 1985.
8. Hugget A and Nixon DA, Lancet, **2**, 368-370, 1957.
9. Yalow RS and Berson SA, J Clin Invest, **39**, 1157-1175, 1960.
10. Pacini G, Valerio A, Beccaro F, Nosadini R, Cobelli C and Crepaldi G, J Am Geriatr Soc, **36**, 317-323, 1988.
11. Chen M, Halter JB and Porte D, J Am Geriatr Soc, **35**, 417-421, 1987.
12. Lipman RL, Raskin P, Love T, Triebwasser J, Lecocq FR and Schnure JJ, Diabetes, **21**, 101-107, 1972.
13. Wang JT, Ho LT, Tang KT, Wang LM, Chen YD and Reaven GM, J Am Geriatr Soc, **37**, 203-209, 1989.
14. Ferranini E, Buzzigoli G, Bonadonna R, Giorico MA, Oleggini M, Graziadei L, Pedrinelli R, Brandi L and Bevilacqua S, New Engl J Med, **317**, 350-357, 1987.

(Received January 31, 1992)