Further Studies on the Incidence of the Synalbumin Insulin Antagonist

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Summary. The incidence of excessive synalbumin antagonism has been studied in a small randomly selected population survey. One hundred and forty-two volunteers were tested, 70 men and 72 women, between the ages of 18 and 45 years, none of whom had overt diabetes. — Fifteen men (21%) and 26 women (36%) were synalbumin positive with an overall incidence of 28%, which is not dissimilar to the previously reported incidence of 25%.

Étude sur la fréquence de l'antagoniste de l'insuline, la synalbumine

Résumé. La fréquence de l'antagonisme synalbuminique excessif a été étudiée au cours d'une enquête portant sur une petite population choisie au hasard. Cent quarante-deux volontaires ont été testés, 70 hommes et 72 femmes, âgés de 18 à 45 ans; personne n'avait de diabète manifeste. — Quinze hommes (21%) et 26 femmes (36%) étaient synalbumine positifs, la fréquence totale étant de

28%, ce qui ne diffère pas de la fréquence de 25% rapportée antérieurement.

Weitere Untersuchungen zur Häufigkeit des Synalbumin-Insulin-Antagonisten.

Zusammenfassung. Die Häufigkeit eines excessiven Synalbumin-Antagonismus wurde bei einer kleinen, nach Zufalls Gesichtspunkten ausgewählten Bevölkerungsgruppe geprüft. Es wurden 142 Freiwillige (70 Männer und 72 Frauen) zwischen 18 und 45 Jahren untersucht, von denen keiner einen manifesten Diabetes aufwies. — 15 Männer (21%) und 26 Frauen (36%) erwiesen sich als synalbumin-positiv, entsprechend einer Gesamthäufigkeit von 28%; ein Wert, der nicht sehr von dem früher angegebenen Prozentsatz von 25 abweicht.

Key-words: Antagonism, insulin, random sample, rat diaphragm, synalbumin.

Introduction

Human plasma-albumin inhibits the effect of insulin *in vitro* [6, 13, 16, 19] and *in vivo* [7, 8, 10, 11]; also several workers have confirmed the original observation of Vallance-Owen *et al.* [19] that albumin prepared from the plasma of diabetic patients is more antagonistic to insulin than that obtained from the plasma of normal subjects [1, 3, 9, 12]. Previous studies have shown that this excessive synalbumin insulin antagonism can be regarded as a biochemical marker to ascertain whether or not a given individual is constituted as an essential diabetic without reference to carbohydrate intolerance [17]. Thus far however, a completely randomised sample of the general population has not been studied for the prevalence of excessive synalbumin antagonism.

Materials and Methods

A survey was carried out on the population of Belfast between the ages of 18 and 45, based on a series of numbers selected at random by the data processing unit of the University. One hundred and forty-two volunteers, 70 males and 72 females, were

studied; all were apparently healthy and none was pregnant.

Serum: Venous blood was withdrawn into a dry syringe from these volunteers, who had fasted for at least eight hours. After clotting had occurred, all samples were centrifuged for 15 min at $1400 \times g$ to separate the serum.

Preparation of albumin: Albumin was prepared from the serum with acid ethanol and alcoholic sodium acetate by the method of Fernandez *et al.* [4] as modified by Vallance-Owen and McMaster [22].

Detection of insulin antagonism: Insulin antagonism was determined by the rat diaphragm procedure previously described [20, 21].

The albumin fractions obtained were dissolved in buffer solution [5] containing glucose 0.3% W/V to make a final concentration of 1.25%, and any insoluble matter removed by centrifugation. Insulin was added to the buffer alone and to the dissolved albumin to make a final concentration of 1000 microunits/ml. In any one experiment the glucose uptake of the hemidiaphragm was determined in (a) buffer alone (basal uptake); (b) buffer plus added insulin (standard); (c) buffer with 1.25% albumin plus added insulin. The uptake was ordinarily measured twice in 2 ml aliquots of each solution, hemidiaphragms from different rats being used, and the results expressed in milligrams of glucose/100 ml solution/10 mg dry weight of diaphragm over the 90-min incubation period.

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Results

Each albumin sample tested at 1.25% was either significantly antagonistic to insulin to at least the 5% level (synalbumin positive) or was non-antagonistic to the hormone (synalbumin negative), and as the individual observations within each group — either antagonistic or non-antagonistic — were essentially similar, they have been recorded together in the table.

Table 1. *Albumin assay results for the total sample of 142 subjects*

Origin and status of albumin tested at 1.25% (No)	Mean glucose uptake above basal level ^a + SEM (mg glucose/100 ml/10 mg diaph.)	
	Buffer + 1000 mu/ml insulin	Albumin in Buffer + 100 mu/ml insulin
<i>Males</i>		
Antagonistic (15)		8.16 ± 0.72
Non-antagonistic (55)		13.76 ± 0.25
	13.40 ± 0.22	
<i>Females</i>		
Antagonistic (26)		6.28 ± 0.34
Non-antagonistic (46)		13.32 ± 0.26

^a Amount of glucose taken up by diaphragm when no insulin is present in incubation medium.

Fig. 1. Histogram showing glucose uptake values above the basal level for the 142 individual samples tested at 1.25% against 1000 mu/ml insulin. These results have been standardized against our overall mean insulin effect at 1000 mu/ml, which is 14.0 mg/100 ml/10 mg diaphragm

Overall 41 of the 142 randomly selected subjects were synalbumin positive (28%) and 101 synalbumin negative (72%); not dissimilar to the incidence previously reported [17, 18]. However, of the 70 males, 15 (21%) and of the 72 females, 26 (36%) were synalbumin positive. The higher incidence in females up to 45 years of age is of interest, having regard to the higher incidence of overt diabetes in women compared with men over the age of 45 years [14, 15].

Fig. 1 shows that the glucose uptake values above the basal level for these 142 individual samples when tested at 1.25% against 1000 microunits/ml — equated

against the mean value of 14.0 mg/100 ml/10 mg diaphragm for the standard insulin solution — have a bimodal distribution.

This is further confirmation, on a completely random sample, of the previously reported bimodal distribution of the synalbumin antagonists [17] and lends additional indirect support to the evidence already published that excessive synalbumin antagonism is inherited as an autosomal dominant character. The overall incidence of synalbumin positivity in this series, namely 28%, is not dissimilar from that previously reported from Northern England as 25% [17, 18], although somewhat higher than the figure of 18% so far reported from Northern India [2].

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