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SHORT COMMUNICATIONS

Effect of Repetitive Health Examinations on Blood Sugar Levels: The Zagreb Preliminary Study

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Summary. In this study recruitment rates of subjects with borderline glucose tolerance were investigated (using the specific procedure described below) and were shown to be 1.8% of the population approached and 2.5% of the population screened. 75 g glucose load yielded higher numbers of subjects with borderline glucose tolerance levels at screening than a 50 g glucose load. However, the numbers of the people finally recruited into the cohort by confirmatory screening were the same when only the 50 g load was used at confirmatory screenings. Subjects recruited in this way remained in the study for 24 months. Repeated health checks had an effect of lowering concentrations of blood glucose after an oral load in treated and control groups, and in those with borderline and those with normal blood glucose values at the initial screening. It is concluded that the process of screening and observation itself has an effect upon glucose tolerance, independent of formal 'treatment'.

Key words: Glucose tolerance test, screening, hyperglycemia, randomized drug trial, repetitive health examination.

We would like to discuss here: (a) recruitment of a cohort for an intervention trial from an open population by repetitive screenings, including the differential effect of 50 g and 75 g glucose loads upon recruitment; (b) the effect of repeated follow-up examinations during twenty-four months on the glucose tolerance levels of this cohort.

Material and Method

In an attempt to recruit a cohort of "borderline" subjects from a general population for subsequent intervention by drug treatment, all the males aged 50, 51, and 52 (601 persons) and residing in the central Zagreb area were invited for screening. The aim of the screening was to select "borderline" subjects for long-term prophylactic drug treatment. The subjects could be "borderline" in any of three risk factors for ischaemic heart disease: blood pressure, serum cholesterol, or blood glucose after glucose load. An attempt was made to recruit the maximum possible number of subjects in the defined population, representing all men of the above-mentioned age residing in a specified area of central Zagreb. The study was considered as a feasibility one for a multifactor prophylactic trial of myocardial infarction in a general population.

The intention was to include in the feasibility trial only subjects who were repeatedly "borderline" in risk factor levels. The rule was that to be eligible for inclusion into the trial cohort a subject had to have "borderline" levels on at least two of the three occasions on which they were measured. Here, we only present data specifically concerning glucose tolerance in the population under study.

Glucose loads of 50 g and 75 g were alternately given to everyone who appeared for screening and was eligible for the load (223 persons received 50 g and 218 were given 75 g). On the basis of the screening and using two hour blood glucose values all the subjects were classified into: "normals" – below 110 mg/100 ml; "borderline" B – 110–120 mg/100 ml; "borderline" A – 121–160 mg/100 ml; and "pathologicals" – above 160 mg/100 ml. A subject was eligible for inclusion into the trial cohort if he had blood sugar levels in range A on any two out of three possible occasions. Those subjects who were in range B at initial screening received the second measurement and only if that measurement was in range A were they measured a third time. The subjects with levels of blood glucose in range A at initial screening received a second measurement and if that measurement was in range B they were rescreened a third time. Thus the final cohort selected on "borderline" glucose intolerance included the following set of subjects, chosen because their levels during all screening examinations were in range A or B on three possible occasions: A-A; A-B-A; B-A-A.

Glucose was determined by the glucose oxidase method [1].

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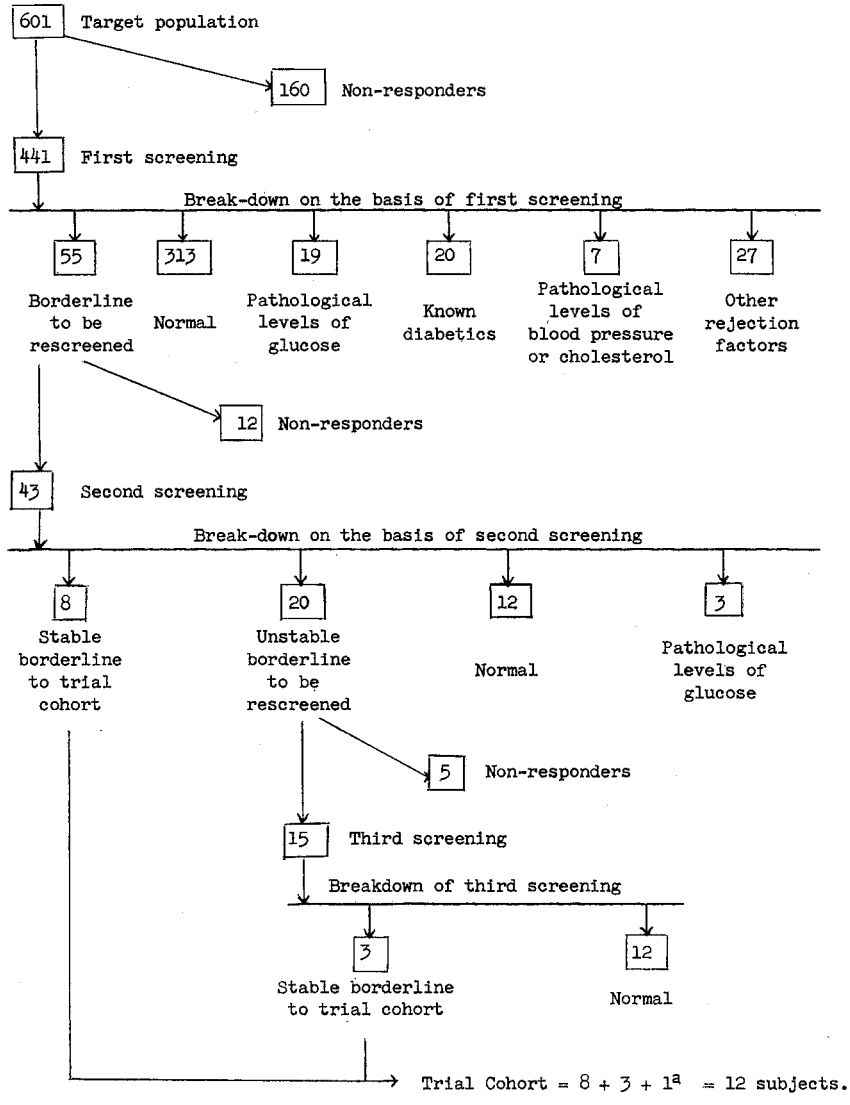
After the subjects were qualified as eligible they were invited to participate in a trial which commenced six months after the finish of screening. The recruited group was randomized into those who were treated by chlorpropamide 0.125−0.25 g a day and those who were observed only. The latter group received no drug but was examined at the same time intervals as the treated group. The treated group received the drug from 1.5 months till the 18 months point in the trial (i.e. the last 16.5 months of the twenty-four months observation period).

Results

Fig. 1 presents results of the first screening and two confirmatory screenings for the recruitment of the borderline cohort. For the first screening, one can notice a rather large number of "known diabetics" (twenty subjects). This might be explained by the fact that active detection and population studies for diabetes were going on in the area. It can be seen that the approach employed using the above specified criteria allowed the recruitment of eight persons into



[a] one subject with high normal glucose level (120 mg/100 ml) added by error to trial cohort.

Fig. 1. Flow chart of screening activities for glucose tolerance — Zagreb

the "borderline" cohort after two screenings and three persons after three screenings, i.e. eleven persons or 2.5% of the screened population, or 1.8% of the approached population.

The yield of "borderlines" was greater after 75 g load than it was after 50 g at screening (Table 1), but when at confirmation rescreenings only a 50 g load was given the final number of subjects appearing in

Table 1. *Glucose tolerance values for 50 and 75 gram loads*

SCREENING	50	75		Total
Normal	173	140	=	313
Borderline (eligible for rescreening)	18	37	=	55
Pathological - glucose	7	12	=	19
Pathological - other	3	4	=	7
Diabetics	11	9	=	20
Rejection factors	11	16	=	27
	223	218	=	441

RESCREENING	50 only			
Normal	2	10	=	12
Borderline (eligible for re-rescreening)	6	14	=	20
Pathological-glucose	3	0	=	3
Pathological - other	0	0	=	0
Non-responders	4	8	=	12
For trial	3	5	=	8
	18	37	=	55

RE-RESCREENING	50 only			
Normal	1	11	=	12
Pathological-glucose	0	0	=	0
Non-responders	2	3	=	5
For trial	3	0	=	3
	6	14	=	20

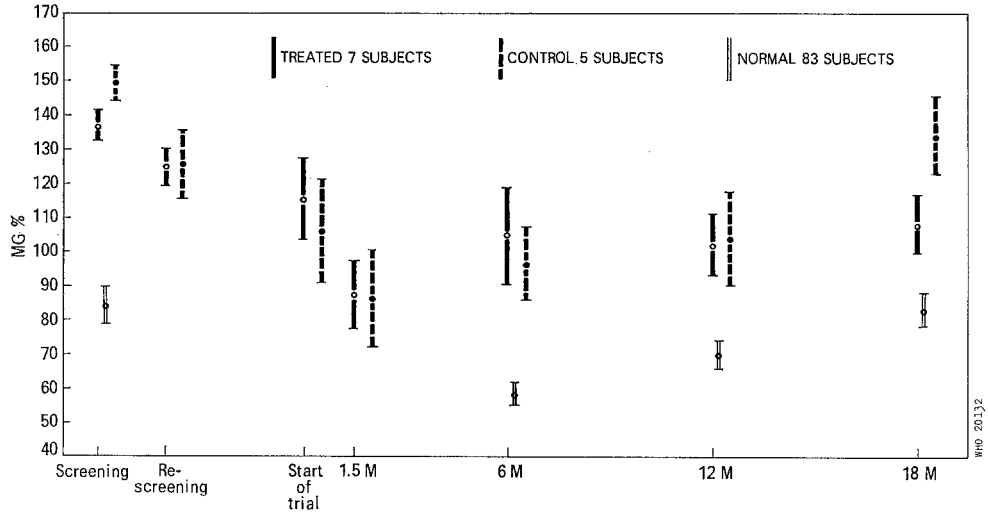


Fig. 2. Levels of glucose tolerance (120 min after load) at various periods in the study for the cohort undergoing examination at 18 months after start of trial (mean ± 2 standard errors)

the cohort was the same from the two groups which initially differed by glucose load.

During the period of recruitment and trial the mean two hour post glucose blood sugar level in both treated and non-treated groups fell significantly from the screening level, tending to level off within the second year of observation (Fig. 2). (There were no statistically significant differences in glucose levels between treated and control groups.) The same trend was also observed in the group of treated or control subjects with elevated blood pressure or cholesterol, but whose levels of glucose tolerance were normal at the start (see Fig. 2).

By way of possible explanation of the phenomenon observed, the behaviour of the observed cohort changed in several aspects. Records of dietary changes showed that a substantial percentage of subjects treated or observed for glucose tolerance reported changes: 58 and 60% in the treated and control groups respectively after six months of observation; 29 and 40% respectively after 24 months of observation. Physical activity changes were reported only by subjects in the treated group. Mean skinfold thickness value decreased over the 24 month period by 4 mm and 7 mm respectively in the treated and control groups. The "borderline" glucose tolerance group at the beginning of the study appeared to be heavier than blood pressure or cholesterol groups. During the 24 months of observation there was a weight decrease in treated and control groups (Table 2). In the cohort which was non-borderline for glucose no difference was found between the mean levels of glucose of those whose weight had decreased by 1 kg or more and those whose weight had not decreased. A more detailed discussion of the observed phenomenon is presented elsewhere [2].

Table 2. *Mean weights (in kilos) of the "borderline" glucose tolerance cohort, by period and treatment group*

		Treated	Control
Screening	$\bar{X}$	89.1	88.0
	SD	6.6	11.1
	N	7	5
Start of trial	$\bar{X}$	86.9	85.2
	SD	5.8	11.8
	N	7	5
6 months	$\bar{X}$	86.5	84.9
	SD	6.2	12.4
	N	7	5
12 months	$\bar{X}$	85.5	87.0
	SD	5.0	12.3
	N	7	5
18 months	$\bar{X}$	85.9	86.0
	SD	6.6	10.4
	N	7	5

The speculative explanation of the decrease in blood glucose concentrations is that repetitive health examinations per se have an effect which changes the behaviour of the observed population and influences the variable under study.

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