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Sauna-induced acceleration in insulin absorption from subcutaneous injection site

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Summary and conclusions

The effect of the Finnish sauna on insulin absorption from a subcutaneous injection site was examined in eight insulin-dependent diabetic patients by measuring externally the disappearance rate of ¹²⁵I-labelled rapid-acting insulin. The sauna (twice for 25 minutes at 85°C) accelerated insulin absorption by 110% as compared with room temperature ($p < 0.01$). After the sauna blood glucose concentrations were 3.0-3.3 mmol/l (54.1-59.5 mg/100 ml) lower than on the control day ($p < 0.05$). The fall in blood glucose values was proportional to the increased rate of insulin absorption ($r = 0.80$; $p < 0.01$).

The hypoglycaemic effect of a sauna in insulin-treated diabetics is clearly at least partly due to enhanced insulin absorption from the injection site. Such an effect might be prevented by taking a snack or reducing the insulin dose.

Introduction

Most Finns take a sauna bath once or twice a week. Anecdotal evidence, however, suggests that insulin-treated diabetics have hypoglycaemic symptoms after a sauna. Apart from factors such as diet and exercise, a major determinant for a fall in the blood glucose concentration in diabetes is insulin availability.¹ Besides the dose and type of insulin used, the rate of insulin delivery from the injection site affects the blood glucose concentration. Thus exercise accelerates insulin absorption from the injection site, resulting in a decline in the blood glucose concentration.²⁻⁴ At rest there are differences in the rate of insulin absorption from various injection sites.^{5,6} Furthermore, changes in blood glucose concentration are proportional to the rate of insulin absorption.^{5,6} Both at rest⁷ and during exercise⁸ variations in blood flow at the injection site may at least partly contribute to the alterations in rate of insulin absorption. Skin blood flow is greatly dependent on environmental temperature.⁹ I therefore decided to see whether a hot Finnish sauna can influence insulin

absorption from injection sites. I also examined the relation between the rate of insulin absorption and changes in the blood glucose concentration.

Patients and methods

I studied eight insulin-dependent diabetic men aged 21-54 years (mean age 34 ± 4 years) who were known to have had diabetes for 1-13 years (mean 6 ± 2 years). They were taking a total of 26-27 U (mean 39 ± 6 U) of intermediate or intermediate plus rapid-acting insulin in one (four patients) or two (four patients) injections daily. Seven had taken insulin from the onset of their disease. One patient, who had been diabetic for 13 years, had been taking insulin for two years, his current dose being 46 U/day. Injection sites were regularly rotated between the leg, arm, abdomen, and buttock. No patient had evidence of lipodystrophy at any injection site, none was obese, and all used a weight-maintaining diet containing about 45% carbohydrate, 35% fat, and 20% protein. Each patient took a sauna once or twice a week. There was no clinical evidence of diabetic neuropathy, nephropathy, or retinopathy and no history of other endocrine disease in any patient. All patients volunteered for the study after its nature and purpose and the possible risks had been explained.

The studies began in the morning after an overnight (12-14 hour) fast, 16-24 hours after the last insulin injection. An indwelling catheter was inserted into an antecubital vein for obtaining samples for blood glucose determinations.¹⁰ Two baseline samples were drawn 15 minutes apart and the mean blood glucose concentration taken as the fasting value. The patients were then given subcutaneous injections in the thigh of 10 U ¹²⁵I-labelled rapid-acting insulin (Actrapid MC) and 6-40 U intermediate-acting insulin (Monotard MC). The radioactive and unlabelled insulins were injected 5-10 cm apart. The total amount of insulin given was 80-90% of the patients' usual morning dose. To prevent ¹²⁵I accumulating in the thyroid the patients were given 0.5 g potassium iodide the night before and for four days after the insulin injection. Immediately after the injections the subjects were given breakfast providing 430 kcal and containing 50% carbohydrate, 30% fat, and 20% protein. A snack of 130 kcal was given 120 minutes after insulin injection. (1000 kcal $\approx$ 4.2 MJ.)

Each subject was studied on two separate days. Throughout the control day the subjects sat in a room at 22°C. On the day of the experiment they entered the sauna 60 minutes after the insulin injections. After 25 minutes at 85°C they left the sauna for five minutes for external counting of radioactivity at the injection site and then returned to the sauna for a further 25 minutes. The order of the control and sauna days was randomised. The total dose of insulin,

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meals, and amount of physical activity were identical on the control and sauna days.

The disappearance of ^{125}I -insulin was measured externally, as described.⁴⁻⁶ Counts were measured at 30-minute intervals for 240 minutes after the injections. Student's *t* test (paired when applicable) and linear regression analysis were used to analyse the data.¹¹ The correlation between sauna-induced changes in insulin disappearance and blood glucose concentrations was calculated by comparing the areas between insulin disappearance curves and blood glucose curves between the sauna and control days during the period from 60 to 240 minutes. Results are presented as means $\pm$ SEM.

Results

Figure 1 shows the effect of the sauna on the disappearance rate of ^{125}I -insulin from the injection site. Before entering the sauna the disappearance rate was identical on the control and sauna days. Sauna increased the rate of insulin disappearance in each of the eight patients studied. As shown in figure 2, the absorption rate

FIG 1—Influence of sauna on disappearance of ^{125}I -insulin from subcutaneous injection site in leg. Values are means $\pm$ SEM. Sauna day *v* control day (paired *t* test): **p* < 0.05; ***p* < 0.02.

FIG 2—Disappearance rate of ^{125}I -insulin from injection site during 60-minute periods before, during, and after sauna (means $\pm$ SEM). □ Control day. ▨ Sauna day. Sauna day *v* control day: **p* < 0.01.

of ^{125}I -insulin was 110% greater during the sauna than during the same period on the control day (*p* < 0.01). During the cooling-off period after the sauna the disappearance rate of insulin was virtually identical with that on the control day (figs 1 and 2).

Fasting blood glucose concentrations were comparable on both days of the study (7.2 ± 1.9 mmol/l (130.0 ± 34.2 mg/100 ml) on the control day; 9.1 ± 1.6 mmol/l (164.0 ± 28.8 mg/100 ml) on the sauna day)

(*p* > 0.1). Figure 3 shows the changes in blood glucose concentrations after insulin injection and breakfast. The mean rise in blood glucose was comparable on the control day and sauna day before entering the sauna. The postprandial rise in blood glucose values during the sauna was slightly smaller and the decline after the sauna faster than on the control day. Two hours after the sauna blood glucose concentrations were $3.0\text{--}3.3$ mmol/l ($54.1\text{--}59.5$ mg/100 ml) lower than on the control day (*p* < 0.05) (fig 3).

FIG 3—Postprandial changes in blood glucose concentration on control and sauna days (means $\pm$ SEM). At zero time subjects injected with insulin and given breakfast. Snack given 120 minutes after insulin. Sauna day *v* control day: **p* < 0.05. (Blood glucose: 1 mmol/l $\approx$ 18 mg/100 ml.)

To examine the relation between the changes in the insulin disappearance rate and the blood glucose concentration on the sauna day I calculated the correlation between the sauna-induced changes in insulin disappearance and blood glucose values over the observation period from 60 to 240 minutes. As shown in figure 4, a positive correlation was observed between the increase in the insulin disappearance rate and the fall in plasma glucose values.

FIG 4—Correlation between sauna-induced increase in insulin disappearance rate and fall in blood glucose concentrations. (Blood glucose: 1 mmol/l $\approx$ 18 mg/100 ml.)

Discussion

In this study the rate of ^{125}I -insulin absorption was measured externally by determining the rate of disappearance of radioactivity from the injection site. Studies on animals show that after ^{125}I -insulin injection virtually all the radioactivity is bound to insulin at the injection site and that counts measured externally correlate well with the amount of extractable insulin.⁹

Furthermore, in man a correlation was observed between the disappearance rate of ^{125}I -insulin and changes in blood glucose values both at rest^{5, 6} and during exercise.⁴ Thus these data show that measuring the fall in radioactivity at the site of insulin injection by external counting reflects the insulin disappearance rate and suggest that the absorbed insulin is biologically active.

In my study sauna accelerated the absorption of insulin from the subcutaneous injection site in the leg. While in the sauna the disappearance rate of insulin from subcutaneous tissue was two-fold greater than during the same period on the control day (fig 2). As to the mechanism of the sauna-induced rise in insulin absorption, studies show that local heating increases subcutaneous blood flow and accelerates insulin absorption from the injection site, whereas local cooling decreases the insulin disappearance rate.¹² Although I did not measure skin temperature or blood flow, the augmented insulin delivery during the sauna may be explained at least partly by enhanced blood flow at the subcutaneous injection site. Interestingly local degradation of insulin may occur at the subcutaneous injection site.^{5, 13} Thus sauna by augmenting insulin absorption may decrease the local degradation of injected insulin, thus further increasing biological activity of insulin.

Of particular interest was the effect of the sauna on blood glucose concentrations. After the sauna the postprandial rise in glucose values was less and the values fell to lower levels than on the control day (fig 3). My observations may have clinical implications for the management of insulin-treated diabetics, particularly those who take a sauna soon after insulin injection. Since a large depot of injected insulin may remain at the injection site the stimulatory effect of the sauna on insulin absorption may result in a rapid fall in blood glucose. Thus in such patients a snack or small reduction in insulin dose (or both) may prevent hypoglycaemia after a sauna.

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SHORT REPORTS

Pulmonary fat embolism treated by intermittent continuous positive airway pressure given by face mask

Fat embolism is a serious complication in patients with severe injury and a fractured bone.¹ The main symptoms are fever, dyspnoea and tachypnoea, restlessness, and confusion. Clinical signs are a petechial rash, radiographic evidence of diffuse alveolar infiltrates in both lungs, hypoxaemia, and lipuria. Treatment consists in giving oxygen, mechanical ventilation, and corticosteroids.² We report on a patient treated by intermittent continuous positive airway pressure given via a face mask by the patient himself.^{3, 4}

Case report

A 25-year-old healthy man was admitted to hospital with a fracture of the shaft of his left femur caused by falling from a horse. The fracture was treated by continuous traction. After 39 hours he developed headache, his temperature rose to 38°C and pulse rate to 104/min, and he complained of chest pain and nausea. He was slightly dyspnoeic and had a petechial rash on his chest and abdomen. Chest radiographs were normal, his arterial oxygen pressure (PaO_2) was 6.3 kPa (47.3 mm Hg; normal range 10-14 kPa (75-105 mm Hg)), and his arterial carbon dioxide pressure (PaCO_2) was normal. Treatment was started with oxygen 5 l/min via a nasal catheter. Fractional inspired oxygen (FIO_2) cannot be calculated in this method but was probably in the range of 0.4-0.5. Heparin 10 000 units intravenously and dexamethasone 4 mg were given every six hours and dextran 500 ml infused every 12 hours. Twenty-four hours later his condition was unchanged. Radiographs now showed diffuse infiltrates of both lung fields, PaO_2 was 6.0 kPa (45 mm Hg), PaCO_2 4.8 kPa (36 mm Hg), and FIO_2 0.4-0.5.

At this stage we considered intubation and continuous mechanical ventilation plus positive end expiratory pressure, but we favoured intermittent continuous positive airway pressure since the patient had no cerebral symptoms, could co-operate, and could operate the apparatus himself. Continuous positive airway pressure was given for five minutes every half hour during the daytime and for five minutes every hour during the night. At a pressure of 100 mm H_2O (0.1 kPa) oxygen 7 l plus atmospheric air 7 l was given via a nebuliser (FIO_2 0.6). The earlier treatment was continued unchanged, including oxygen by nasal catheter, except that the oxygen flow was increased from 5 l/min to 7 l/min and the nasal catheter was taken out when continuous positive airway pressure was given. After five hours PaO_2 rose to 11.4 kPa (85.5 mm Hg), but PaCO_2 was unchanged, as were the x-ray pictures. After two days the chest radiographs were normal. After four days oxygen treatment could be stopped and continuous positive airway pressure was given without extra oxygen (FIO_2 0.21). After seven days all treatment was stopped, and 12 days after the injury (10 days after starting continuous positive airway pressure) fixation of the fracture was carried out without complications.

Comment

Continuous mechanical ventilation with positive end expiratory pressure is well known and widely accepted, having been used since 1969 in treating acute respiratory insufficiency. Its efficacy in reducing pulmonary venous admixture and improving arterial oxygenation seems to be related to increasing functional capacity when terminal closure and atelectasis are present.⁵ The same effect can be achieved by continuous positive airway pressure, which is useful in patients who can maintain spontaneous breathing. Positive end expiratory pressure and continuous positive airway pressure are similar in effect, but the former is used in connection with mechanical ventilation and the latter with spontaneous respiration. Continuous positive airway