Smoking reduces insulin absorption from subcutaneous tissue

The degree of glycaemic control in insulin-dependent diabetic patients is highly influenced by the rate of insulin absorption from subcutaneous tissue to blood. We have recently shown a correlation between subcutaneous blood flow and insulin absorption.¹

Smoking increases the concentration of catecholamines in the blood.² In normal subjects inhaling cigarettes produces a transient rise in blood pressure and pulse rate and a fall in skin temperature. The peripheral vasoconstriction lasts from several minutes to more than one hour, and habitual smokers do not show tolerance to smoking by a decrease in these effects.^{3,4}

The duration of peripheral vasoconstriction caused by smoking might, therefore, have an effect on insulin absorption. We tested this hypothesis.

Patients, methods, and results

Nine ketosis-prone insulin-dependent diabetic patients (six women and three men), aged 22 to 62 years (mean $35 \pm \text{SD } 13$ years), were selected for the study after informed consent was obtained. All were known to have had diabetes for 3 to 17 years (mean $8 \pm \text{SD } 6$ years). Their daily insulin dose varied from 32 to 46 U (mean $38 \pm \text{SD } 6$ U). All were within standard weight $\pm 10\%$, and none had signs or symptoms of neuropathy or nephropathy. The patients were all habitual smokers smoking 5-40 cigarettes daily (mean $13 \pm \text{SD } 11$).

The study began in the morning after the subjects had abstained from smoking overnight. The patients had their normal breakfast and their normal morning dose of intermediate-acting insulin. After 30 minutes' rest in the supine position, 8 U (0.2 ml) of rapid-acting ^{125}I -labelled insulin ($1.2 \mu\text{Ci}/40$ U Actrapid) was injected subcutaneously. The disappearance rate of the

time was $158 \pm \text{SEM } 22$ minutes in the first 30-minute period before smoking, $336 \pm \text{SEM } 97$ minutes during smoking ($p < 0.05$, $n = 8$), and $207 \pm \text{SEM } 29$ minutes in the first 30-minute period after smoking ($p < 0.05$). In the last 30 minutes the mean half time was $155 \pm \text{SEM } 16$ minutes. These half lives correspond to an average decrease of 113% in insulin absorption during smoking and a 31% decrease in insulin absorption in the first 30 minutes after smoking.

Comment

The disappearance rate of ^{125}I -insulin from injection sites is known to correlate well with the amount of extractable insulin.⁵ Our results show that smoking has an influence on insulin absorption. The duration of impaired absorption is in accordance with the average duration of peripheral vasoconstriction after smoking.⁴

This effect of smoking, together with a direct metabolic effect of an increased concentration of catecholamines during smoking, might contribute to metabolic instability in insulin-treated patients. We have previously shown that diabetic smokers need on average 15-20% more insulin than non-smokers, and this percentage increases to 30% in heavy smokers.²

We thank Novo Industry, Copenhagen for supplies of ^{125}I -insulin.

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⁴ Maddock WG, Collier FA. Peripheral vasoconstriction by tobacco and its relation to thrombo-angitis obliterans. *Ann Surg* 1933;**98**:70-81.

⁵ Binder C. Absorption of injected insulin: a clinical-pharmacological study. *Acta Pharmacol Toxicol (Kbh)* 1969;**27**,suppl 2:1-84.

(Accepted 5 October 1981)

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Half time (mean $\pm$ SEM) of ^{125}I -insulin from injection sites before, during, and after smoking. Measurements started 60 minutes after the insulin injection. * $n = 8$, ** $n = 9$.

tracer was measured as described elsewhere,⁵ starting 60 minutes after the ^{125}I -insulin injection. Ninety minutes after the ^{125}I -insulin injection the patients were asked to smoke a cigarette (Prince, filter tipped, 815 mg tobacco, 2.0 mg nicotine) and inhale with their habitual depth and frequency, usually about once a minute. The smoking was finished after eight minutes, and the disappearance rate of the tracer was followed for an additional 60 minutes. Room temperature was kept constant ($22^\circ \pm \text{SD } 0.5^\circ\text{C}$) during the experiments. To prevent ^{125}I accumulating in the thyroid, the patients were given 100 mg potassium iodide for five days after the insulin injection. Student's t test for paired samples and linear regression analysis were used to analyse the data.

The figure shows the effect of smoking on the mean half time of ^{125}I -insulin from the injection site.

In one of the nine patients the external registration of counts failed during the smoking period for technical reasons. For all nine subjects mean half

Unusual cause of atrial fibrillation

Atrial fibrillation is one of the most common arrhythmias and is caused most often by mitral stenosis, ischaemic heart disease, or thyrotoxicosis. It may also occur as a transient manifestation in the Wolff-Parkinson-White syndrome. More rarely there may be no detectable underlying lesion. We describe a patient who developed atrial fibrillation during the course of a chlamydia B infection, possibly due to complicating myocarditis.

Case report

A 43-year-old man developed an influenza-like illness in November 1980 accompanied by a productive cough and wheeze but no chest pain. His wife and two children had similar illnesses at the time but of much shorter duration. Apart from a chronic duodenal ulcer, there was nothing relevant in his history, and in particular there was no previous cardiac trouble. Several weeks later he was noted to have developed atrial fibrillation, which led to his referral to hospital.

On examination he was overweight (108.5 kg), but there were no signs of

cardiac failure. Atrial fibrillation was present, but there was no cardiac enlargement and no murmurs. Chest radiography confirmed that the cardiac contour and size and lung fields were normal. Echocardiography showed no abnormality of either the mitral or aortic valve. Cardiac enzyme activities, electrolyte concentrations, and full blood count were all normal, and glandular fever screening test was negative. Complement fixation tests were negative for *Coxiella burnetii*, *Mycoplasma pneumoniae*, influenza A and B, adenovirus, parainfluenza, herpes simplex, respiratory syncytial virus, and cytomegalovirus. Titres for psittacosis, however, were as follows: 8 on 22 December 80, 512 on 14 January 81, 512 on 18 February 81, 64 on 16 April 81, and 32 on 17 June 81.

Treatment with tetracycline was started and continued for two months. By late January 1981 his symptoms had disappeared and when the titre to chlamydia B had fallen in May 1981 he was admitted to hospital for cardioversion because of persistence of atrial fibrillation. After successful cardioversion electrocardiography showed no evidence of pulmonary mitrale, ventricular hypertrophy, or myocardial ischaemia. Ten days later, after a mild flu-like illness, the heart lapsed into atrial fibrillation again despite maintenance quinidine treatment. Repeat cardioversion was not required as sinus rhythm occurred spontaneously after several days.

Closer questioning failed to elicit any exposure to or contact with birds by the patient or any member of the family.

Comment

Chlamydia B infection (psittacosis) is probably more common in this country than the reported cases indicate. In 1972 the total number of cases reported was 156¹ and in 1975 it was 177.² The benign course of the illness in most patients is undoubtedly responsible for many cases going undetected. There may not necessarily be a history of contact with infected birds, this being established in only 40 (26%) of the 156 cases reported in 1972.

Complications are rare, but may include meningitis,¹ encephalitis,² and occasionally cardiac disease. Endocarditis necessitating valve replacement has been reported,³ and myocarditis may rarely occur.⁴

We think that in the absence of any history of rheumatic fever and previous cardiac disorder, and with a normal echocardiogram, the atrial fibrillation in our patient occurring at the height of his psittacosis infection was directly related to it, possibly owing to mild accompanying myocarditis.

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(Accepted 5 October 1981)

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Extensor digitorum brevis—a predictor of neuropathy in the leg?

The measurement of conduction velocity in the deep peroneal nerve is a common investigation in patients with suspected peripheral neuropathy. An impression was formed that the extensor digitorum brevis muscle was difficult to palpate in patients who had slowed conduction in the peroneal nerve. Muscle wasting is common in peripheral nerve lesions,¹ so a formal study was performed to see whether wasting of this particular muscle was a reliable clinical predictor of electrophysiologically demonstrable nerve disease.

Patients, methods, and results

One hundred consecutive unselected patients, referred for routine measurement of nerve conduction velocity in the leg, were included in the study. No

investigation was performed which was not a part of routine nerve testing. The results were collected from March 1979 to May 1981. Most patients were referred with suspected peripheral neuropathy, injury, or compression neuropathy.

An attempt was made to palpate the extensor digitorum brevis and a decision on its palpability or otherwise was made and recorded before any measurements of conduction velocity were made. Motor conduction velocity in the deep peroneal nerve was measured using a pair of Ag/AgCl surface electrodes to record the compound action potential of the extensor digitorum brevis. Supramaximal rectangular isolated electrical stimuli (duration 0.1 ms) were applied to the deep peroneal nerve just proximal to the ankle, and to the common peroneal nerve at the neck of the fibula. The latency between the stimulus and the onset of the muscle action potential was measured with a Medelec MS6 oscilloscope; the conduction velocity was calculated by dividing the distance between stimulus sites by the difference in the two latencies. Where conduction velocity was measured in both legs, data from one or other side were rejected according to the toss of a coin. All observations and measurements were made by the author, and therefore the study incorporated no element of "blindness."

Of the 100 patients, 67 had a palpable extensor digitorum brevis, and in 33 the muscle was impalpable. There were 10 patients in whom myoelectrical activity could not be recorded with surface electrodes during nerve stimulation, and none of these had palpable muscles. In three of these patients, the dorsum of the foot was subsequently explored with a concentric needle electrode, but still no myoelectric activity could be recorded during nerve stimulation. Even if these 10 patients were excluded from the calculations, there was a highly significant reduction in the mean conduction velocity for the "non-palpable" group (table), with a significant increase in the distal latency from ankle to muscle. The values for the "palpable" group were close to those reported for normal subjects.²

Conduction velocity of deep peroneal nerve and conduction latency from ankle to muscle related to palpability or otherwise extensor digitorum brevis muscle

	Palpable muscle	Non-palpable muscle
Latency (ms)	5.0	6.6
SEM	0.19	0.57
No of patients	67	23
	p < 0.001*	
Conduction velocity (m/s)	45.7	34.5
SEM	0.75	1.5
No of patients	67	23
	p < 0.001*	
Age (range 9-87 years)	48.0	56.6
SEM	1.8	2.9
No of patients	67	33
	p < 0.05*	
Sex (No of cases):		
Male	44	20
Female	23	13
	p > 0.5†	

*Significance assessed by *t* test. †Significance assessed by χ^2 test.

The values for conduction velocity were separated into a high group (>40.0 m/s) and a low group (<39.9 m/s); the values for latency were divided into a long-latency group (>6.0 ms) and a short-latency group (<5.9 ms). The patients for whom myoelectric data could not be obtained were placed in the low-velocity and long-latency groups. Of the non-palpable group, 27 had low conduction velocity while 57 of the palpable group had high conduction velocity ($\chi^2=39.6$; $p<0.001$). Of the non-palpable group, 19 had long latency while 60 of the palpable group had short latency ($\chi^2=23.1$; $p<0.001$).

Comment

The attempt to palpate the extensor digitorum brevis is a very simple clinical test to apply, and these results suggest that failure to palpate it is an excellent predictor of disease in the peroneal nerve.

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(Accepted 7 October 1981)

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