Subcutaneous or intramuscular insulin injections

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Abstract

To find out whether diabetic children may inject their insulin intramuscularly rather than subcutaneously, a random sample of 32 patients aged 4.3-17.9 (median 11.3) years was studied. Distance from skin to muscle fascia was measured by ultrasonography at standard injection sites on the outer arm, anterior and lateral thigh, abdomen, buttock, and calf. Distances were greater in girls ($n=15$) than in boys ($n=17$). Whereas in most boys the distances were less than the length of the needle (12.5 mm) at all sites except the buttock, in most girls, the distances were greater than 12.5 mm except over the calf. Over the fascial plane just lateral to the rectus muscle the distance from skin to peritoneum was less than 12.5 mm in 14 of the 17 boys and one of the 15 girls. Twenty five of the 32 children injected at an angle of 90° , and 24 children raised a skinfold before injecting. By raising a skinfold over the anterior thigh, the distance from skin to muscle fascia was increased by 19% (range 0-38%).

We conclude that most boys and some girls who use the perpendicular injection technique may often inject insulin into muscle, and perhaps on occasions into the peritoneal cavity.

For many years diabetic patients were advised to inject insulin into a skinfold, inserting the needle at an angle of 45° . Since the introduction of disposable plastic insulin syringes, which have much shorter (12.5 mm) needles, the recommended injection technique was altered. Most patients were advised to insert the needle at an angle of about 90° to nearly its whole length. To obtain a painless injection they were advised to stretch the skin before injecting, although thin patients were sometimes advised to raise a skinfold.¹ In this way it was felt that insulin would consistently be deposited into subcutaneous adipose tissue and the risk of penetrating muscle was considered to be negligible.

Frid and Linden were the first to cast doubt on the latter assumption when they showed by computed tomography that the depth of subcutaneous fat over many sites in the thigh and abdomen was often less than 10 mm in lean adult patients.² Their results were confirmed in a more recent report which showed by ultrasonography that the depth of subcutaneous fat over the deltoid muscle and the abdomen was less than 10 mm in 11 of 13 adult male volunteers.³ These results suggest that adults

who use the perpendicular injection technique may sometimes deposit insulin into muscle rather than fat.

Intermittent intramuscular administration of insulin could lead to variations in glycaemic control if the rate of absorption from muscle differed from that of the subcutaneous tissue. Recent studies in which modern imaging techniques were used to ensure accurate placement of insulin, have shown that insulin tends to be absorbed much faster from muscle than from subcutaneous adipose tissue.^{3 4}

To assess the risk of inadvertent intramuscular injection of insulin in children of different ages and stages of development, we measured the distance from skin to muscle fascia at recommended injection sites by high resolution real time ultrasonography.

Patients and methods

A random sample of 32 diabetic children was recruited from the paediatric diabetic clinic at this hospital. All the subjects were white, except one who was Afro-Caribbean. Details of the insulin injection technique, sites used, and whether parent or child gave the insulin were recorded for each child. Injection sites were examined for areas of lipohypertrophy or lipodystrophy. All subjects were weighed, and height was measured with a Harpenden stadiometer. Percentage body mass index was used as a measure of the relative body weight of subjects,⁵ and was calculated as: $A/B \times 100\%$ where A = actual weight/(actual height)² and B = 50th centile weight for age/(50th centile height for age)². Weight and height were measured in kilograms and metres respectively. Subjects were examined to assess the stage of pubertal development using Tanner's criteria and were divided into prepubertal (stage 1) and pubertal (stages 2-5) groups.⁶

The glycated haemoglobin (HbA_{1c}) (HbA_{1c}) measurement from the most recent clinic attendance (within three months) was recorded as an index of glycaemic control. Clinical details of subjects are shown in table 1. One prepubertal girl was included who was a newly diagnosed diabetic patient. She had a short history, was well, and had not lost weight. Her body mass index (108%) did not differ from the group as a whole.

Distances from skin to muscle fascia were measured with high resolution real time ultrasonography with an electronically focused 5MHz linear array transducer (Ultramark 9), and the accuracy of linear depth measurement was within 0.5 mm. The same investigator (MAS) made all measurements, and patients lay supine

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Table 1 Clinical characteristics of study subjects. Results are expressed as median (range)

	Boys		Girls	
	Tanner stage 1 (n=9)	Tanner stage 2-5 (n=8)	Tanner stage 1 (n=7)	Tanner stage 2-5 (n=8)
Age (years)	9.2 (4.3-11.6)	15.3 (12.1-17.9)	9.1 (4.9-11.5)	14.5 (9.7-15.6)
Duration of diabetes (years)	4.8 (1-7.3)	5.7 (2.1-9)	2.6 (0-7.9)	4.2 (1.2-10.9)
% Body mass index	108* (103-120)	98* (93-125)	107 (79-121)	108 (96-132)
Glycated haemoglobin (%)	9.8 (8.4-11.3)	10.3 (7.8-14.1)	8.8 (8.6-11.9)	9.8 (7.5-14.3)

*p=0.02.

and prone during the study. Measurements at all sites were made in the transverse plane. Compression of the skin and underlying tissues was avoided during measurement by applying a layer of aqueous ultrasonic contact gel as a short transducer standoff device. By viewing the real time image it was possible to obtain measurements when there was no compression of skin or underlying tissues.

The within investigator variability was calculated from 10 measurements of uncompressed distance from skin to muscle fascia at the same site (anterior thigh) in the same subject. The results were concealed from the investigator by covering the figures at the bottom of the screen. The coefficient of variation for these measurements was 3.3%.

The distances from skin to muscle fascia were measured at the following sites, on the left hand side of the body:

(i) Outer arm—the lateral aspect of the arm one third of the way between the acromion of the scapula and the head of the radius.

(ii) Anterior thigh—the anterior aspect of the thigh in the midline halfway between the anterior superior iliac spine and the superior aspect of the patella. Measurements were repeated at this site with the skin squeezed in the way that some patients prepared for injection. Further measurements were then taken at the same site while pressing with the ultrasound transducer with sufficient pressure to cause maximum compression or displacement of underlying tissues.

(iii) Lateral thigh—the lateral aspect of the thigh halfway between the anterior superior iliac spine and the superior aspect of the patella.

(iv) Anterior abdomen—anterior to the thickest part of rectus muscle halfway between the anterior superior iliac spine and the umbilicus.

(v) Lateral abdomen (to peritoneum)—the distance from skin to peritoneum was measured lateral to the rectus muscle over the aponeuroses of the other abdominal muscles halfway between the anterior superior iliac spine and the umbilicus.

(vi) Buttock—the point in the centre of the upper outer quadrant of the buttock.

(vii) Calf—the posterior aspect of the calf in the midline halfway between the medial malleolus and the medial condyle of the tibia.

All subjects or their parents, or both, gave written informed consent, and the study was approved by the local ethics committee.

STATISTICAL ANALYSIS

Median values and ranges are given because data were not normally distributed. The Mann-

Whitney U test was used to analyse the significance of differences. A probability of <0.05 was accepted as significant.

Results

PATIENTS

The median ages (range) of boys and girls did not differ: boys 11.6 years (4.3-17.9), girls 11.2 years (4.9-15.6). Median percentage body mass index was also similar (boys—105% (93-125), girls—107% (79-132)), but pubertal boys were leaner than prepubertal boys (p=0.02) (table 1).

INSULIN INJECTIONS

Insulin injections were administered by parent (10/32), child (14/32), or both parties (8/32). Numbers of sites used were: one, 6/32; two, 16/32; more than two, 10/32 children. Sites used were thigh (29/32), arm (22/32), abdomen (4/32), buttock (13/32), and calf (2/32). Inquiry about injection technique revealed that 24/32 children raised a skinfold before inserting the needle, 3/32 did not, and 5/32 did so on occasions. The needle was inserted at 90° by 25/32 children. The remainder injected at various angles between 45 and 90°. Twenty nine of 32 children reported that the needle was inserted as far as the hub.

INJECTION SITES

Six children had lipohypertrophy, but in no case was it evident at the site of measurement.

Distances from skin to muscle fascia (uncompressed)

Figures 1 and 2 show distances from skin to

Figure 1 Distance from skin to muscle fascia at injection sites in prepubertal (○) and pubertal (●) boys. Horizontal line at 12.5 mm indicates length of needle. Distances were significantly greater in prepubertal boys over the arm (p=0.02) and anterior thigh (p=0.05).

Figure 2 Distance from skin to muscle fascia at injection sites in prepubertal (○) and pubertal (●) girls. Horizontal line at 12.5 mm indicates length of needle. Distances were significantly less in prepubertal girls over the abdomen ($p=0.003$) and calf ($p=0.02$). Two girls were not included in the arm measurements as the results were technically unsatisfactory.

muscle fascia at the sites mentioned in boys and girls, respectively.

The most striking observation was that distances from skin to muscle fascia were much greater in girls than in boys; $p=0.03$ for the calf, $p<0.001$ for all other sites. In most boys the distance from skin to muscle fascia was less than 12.5 mm at all sites except the buttock. In contrast, most girls had subcutaneous fat layers of greater than 12.5 mm except over the calf, where prepubertal girls had little subcutaneous fat. The sex differences were most pronounced in pubertal children, girls having more subcutaneous fat than boys at all sites ($p<0.02$). Prepubertal girls, however, also tended to have more subcutaneous fat than their male counterparts, but the differences were significant only over the anterior thigh and the buttock ($p<0.01$).

When prepubertal and pubertal groups were compared, distances from skin to muscle fascia tended to be greater in girls during puberty rather than before, but were significant only over the abdomen ($p=0.003$) and the calf ($p=0.02$). In contrast, pubertal boys tended to have less subcutaneous fat over injection sites than prepubertal boys, and the differences were significant over the arm ($p=0.02$) and the anterior thigh ($p=0.05$).

Distances from skin to muscle fascia over raised skinfold

After the standard measurement over the anterior thigh had been made, a skinfold was raised and the measurement was repeated at the same site. Median values (range) for distances from skin to muscle fascia over the anterior thigh were 13 (6–28) mm and 15 (6–32) mm before and while squeezing the skin, respectively. The distance from skin to muscle fascia was increased by 3 mm (0–5 mm) when a skinfold was raised, a change of 19% (0–38%).

Distance from skin to peritoneum over lateral abdomen

Just lateral to the rectus muscle is an area about

Table 2 Distance (mm) from skin to peritoneum just lateral to left rectus muscle, half way between the anterior superior iliac spine and the umbilicus

	Median (range)	No in whom distance <12.5 mm
Prepubertal boys (n=9)	11 (8–13)	7
Pubertal boys (n=8)	10 (8–38)	7
Prepubertal girls (n=7)	14 (7–20)	1
Pubertal girls (n=8)	31 (20–49)	0

2 mm wide that consists of skin, subcutaneous fat, and the aponeuroses of the abdominal muscles that converge to form the rectus sheath. Being devoid of muscle, the distance from skin to peritoneum is remarkably short, and is less than the length of the needle in most prepubertal and pubertal boys (table 2).

Distances from skin to muscle fascia (compressed)

Additional measurements were taken over the anterior thigh while pressing with the ultrasound transducer with sufficient force to cause maximum compression or displacement of underlying tissues, as seen on the real time image. A comparison of these with measurements of uncompressed tissue at the same site showed that distances from skin to muscle fascia were reduced by 33% (17–45%) as a result of pressure. This reduction emphasises the importance of avoiding contact between transducer and skin during measurements.

Discussion

The present study shows that girls have a deeper subcutaneous fat layer than age matched boys over all standard sites for insulin injection. In girls the subcutaneous fat layer tends to be deeper during puberty rather than before, whereas in boys the reverse is true. These observations are consistent with the findings of Tanner and Whitehouse.⁷ They reported a steady increase in skinfold measurements from the age of about 6 years to maturity in girls, whereas the increase was much less pronounced in boys, with a slight reduction in skinfold measurements during the period corresponding to the pubertal growth spurt. The difference in the subcutaneous fat layer between prepubertal and pubertal boys may have been exaggerated in the present study because the relative percentage body mass index was greater in prepubertal than in pubertal boys.

We found that in most boys the distance from skin to muscle fascia was less than the length of the needle (12.5 mm) at all sites except the buttock. In contrast, most girls had subcutaneous fat layers of more than 12.5 mm at all sites except the calf. Our findings in girls are perhaps surprising in view of the results from studies in adults. Frid and Linden showed that subcutaneous fat in the thigh and abdomen was often less than 10 mm thick in 14 non-obese adults, three of whom were female.² In contrast, another study showed that the majority of 10 non-obese patients (six female) had subcutaneous fat layers more than 12 mm thick over the

upper medial thigh and the abdomen.⁴ Both these studies measured the depth of subcutaneous fat with computed tomography whereas other investigators have used ultrasonography.^{3,8} Vaag *et al* found that the overall mean thickness of the subcutaneous fat layer in the anterolateral aspect of the thigh was 4 (range 2–10) mm in lean men, and 7 (range 2–13) in lean women.⁸ All these studies were of relatively small numbers of adult subjects who had all been selected because they were not obese. It is therefore impossible to estimate the risk of accidental intramuscular injections of insulin within a clinic population of diabetic adults from these data. Our results suggest that in children, most boys and some girls who do not raise a skinfold and who use the perpendicular injection technique deposit insulin in muscle rather than fat. Furthermore, it suggests that both sexes are at risk of accidental intramuscular injections of insulin when using the calves as the site of injection.

In the present study we investigated a random sample of children who attended a paediatric diabetic clinic. Twenty five of the 32 children used the perpendicular injection technique and in 24 the insulin was injected into a skinfold. Our results showed that by raising a skinfold the distance from skin to muscle fascia at the apex of the skinfold was increased by 3 (range 0–5) mm over the anterior thigh. It therefore seemed that most children, perhaps unwittingly, had adopted a sensible practice that increased the chance of insulin being deposited in fat rather than muscle. Our measurements, at the apex of the skinfold, took no account of the fact that some children inject into the down slope of a raised skinfold. This could further increase the chance of insulin being deposited in fat rather than in muscle.

Considering the abdomen as a site for injection, we were surprised to find that in the fascial plane lateral to the rectus muscle the distance from skin to peritoneum was less than the length of the needle in most boys and in a few girls. Although this fascial plane is only 2 mm wide it runs along the whole length of the rectus muscle, and its position makes it a relatively popular area for injection. It is therefore possible that insulin is occasionally given into the peritoneal cavity instead of the subcutaneous fat. We presume that absorption from the peritoneal cavity is faster than from subcutaneous tissues, and intraperitoneal insulin would have the theoretical advantage of presumably being absorbed into the portal circulation.

To compare absorption rates of subcutaneous and intramuscular insulin we have confined our review of publications to those studies that were controlled for depth of injection by direct measurement of subcutaneous tissue. One study showed a 50% higher rate of absorption of soluble insulin from an injection into a superficial thigh muscle compared with injection into a subcutaneous site, but no such difference was found with injections into these two types of tissue in the abdominal wall.⁴ Another study compared rates of absorption of soluble insulin from subcutaneous, superficial, and deep intramuscular sites, and even superficial intramuscular

injections resulted in more rapid absorption of insulin than subcutaneous injections.³ In contrast, rates of absorption of soluble insulin from superficial and deep subcutaneous fat were similar.⁹

Vaag *et al* examined the metabolic consequences of intramuscular compared with subcutaneously administered insulin.⁸ They found that insulin given intramuscularly before meals resulted in a more physiological profile of plasma-free insulin and a more stable blood glucose profile than subcutaneous administration. They also found pronounced differences in intramuscular absorption rates during rest and light physical activity, however, which were not evident after subcutaneous administration. This seems to be a serious disadvantage which should deter us, perhaps, from recommending the intramuscular route.

As a result of the present study and the review of publications, we plan to alter our recommendations for insulin injection in children. We suggest that insulin should be injected either at an angle of 45° into the apex of a skinfold,¹⁰ or alternatively that it should be injected perpendicularly into the down slope of the skinfold. Furthermore, to try to ensure an adequate basal insulin supply overnight, we advise using the buttocks or thighs for the evening injection because absorption of insulin from these sites is slower than from the abdomen or arm.^{11,12} At other times we suggest using a single anatomical region for injections to reduce day to day variation in absorption of insulin.¹³ Lastly, we suggest that the calf is not a good site for injection in children because there is insufficient subcutaneous fat, and because we often had difficulty in raising a suitable skinfold over the calf when examining the children.

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