The legs became swollen with patchy anaesthesia and reduced movement, but the dorsalis pedis pulses remained easily palpable. Qualitative urine analysis confirmed the presence of myoglobinuria. Over the following 48 hours the urine output fell and serum urea concentration rose and he developed progressive respiratory and renal failure. He was treated by intermittent positive pressure ventilation with positive end expiratory pressure for four days and haemodialysis for four weeks. He made a good recovery, and on review at five months his residual deficit was bilateral foot drop and a left radial nerve palsy.

Comment

The pathophysiology and management of the crush syndrome have been extensively reviewed,^{3,4} with most case reports emphasising the shock and renal failure. Brown and Nicholls reported serum potassium concentrations of 6.3 and 8.8 mmol/l soon after admission in two patients with severe crush injury. Early rises in serum potassium concentration and early acidosis are probably due to the release of the cation and fixed acids from damaged muscle rather than to any impairment of renal function. Our patient developed classic symptoms of the crush syndrome, but early metabolic changes were more immediately life threatening. These metabolic changes may be the cause of the sudden death that occurs soon after rescue in crushed patients. Lightweight portable electrocardiographic monitors may permit recognition of hyperkalaemia at an early stage in victims of crushing. If no such diagnostic facilities are available it should be remembered that cardiac arrhythmias occurring at an early stage after release from prolonged crushing may be due to hyperkalaemia and acidosis.

¹ Bywaters EGL, Beall D. Crush injuries with impairment of renal function. *Br Med J* 1941;i:427-32.

² Santangelo ML, Usberti M, Di Salvo E, et al. A study of the pathology of the crush syndrome. *Surg Gynecol Obstet* 1982;154:372-4.

³ Brown AA, Nicholls RJ. Crush syndrome: a report of two cases and a review of the literature. *Br J Surg* 1977;64:397-402.

⁴ Weeks RS. The crush syndrome. *Surg Gynecol Obstet* 1968;127:369-75.

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Side effects of thyrotrophin releasing hormone

Bolus injections of thyrotrophin releasing hormone are widely used for studying endocrine disorders. The test has been considered to be relatively free of side effects, but we report four cases in which serious symptoms developed.

Case reports

The thyrotrophin releasing hormone test has been performed on 1500 patients in our departments over the past 10 years. The test is carried out with 400 µg thyrotrophin releasing hormone (Roche, Basle, Switzerland) either alone or in combination with 100 µg gonadotrophin releasing hormone (Hoechst AG, Frankfurt, West Germany) injected over two minutes. Serious side effects developed in four patients (table).

Symptoms observed after thyrotrophin releasing hormone test

Case No	Hormone injected	Symptoms		
		Unconsciousness	Convulsions	Fall in blood pressure
1	TRH and GnRH	+	+	+
2	TRH	+	-	+
3	TRH	-	+	-
4	TRH and GnRH	+	+	not measured

TRH = thyrotrophin releasing hormone.
GnRH = gonadotrophin releasing hormone.

Case 1—A 53 year old man with suspected secondary hypothyroidism after a head injury was given an injection of thyrotrophin releasing hormone and gonadotrophin releasing hormone, and about five minutes later he lost consciousness. His blood pressure fell and for a few minutes was unmeasurable. His pulse rate was 80 beats/minute, and he had general tonic convulsions. He regained consciousness after about five minutes and had completely recovered by the next day. Subsequent electroencephalographic and neurological examinations yielded normal results.

Case 2—A 63 year old man with persistent atrial fibrillation and a history of head injury was given an injection of thyrotrophin releasing hormone to investigate a suspected relapse of primary hyperthyroidism. Between five and 10 minutes after the injection he lost consciousness for about five minutes and his blood pressure fell slightly (100/65 mm Hg). His pulse was normal. Convulsions did not occur, and an electrocardiogram taken 10 minutes later was unchanged. He recovered completely after three hours.

Case 3—A 67 year old woman, admitted with suspected primary hypothyroidism, was given an injection of thyrotrophin releasing hormone, and about 10 minutes later general tonic convulsions occurred, although she did not become unconscious. Her blood pressure was 150/90 mm Hg, and the electrocardiogram showed sinus tachycardia with a heart rate of 120 beats/minute. Diazepam (Vival) 15 mg was given intravenously, which had an immediate effect on the convulsions. By the next day she had recovered completely.

Case 4—A 32 year old man with hypogonadism (Klinefelter's syndrome) lost consciousness two minutes after an injection of thyrotrophin releasing hormone and gonadotrophin releasing hormone, and clonic convulsions occurred for two to three minutes. His blood pressure was not measured, but his pulse was normal (76 beats/minute).

Comment

Vasovagal syncope cannot be excluded in any of these cases, but it usually occurs within one to two minutes, whereas the reactions in our patients occurred two to 10 minutes after injection. As such serious side effects have not been reported with gonadotrophin releasing hormone and as thyrotrophin releasing hormone was the only drug given in two cases we believe that thyrotrophin releasing hormone might be responsible for these side effects.

Convulsions occurred in three out of four patients. Tonic clonic convulsions have been observed in an epileptic patient after intravenous injection of thyrotrophin releasing hormone 500 µg,¹ and Grussendorf *et al*² reported side effects similar to those seen in our patients in four patients after injection of thyrotrophin releasing hormone and gonadotrophin releasing hormone (200 µg and 100 µg respectively). Thyrotrophin releasing hormone has several effects on the central nervous system.^{3,4} Three of our patients and all of those previously described had either suffered prior cerebral trauma or had cerebral or pituitary damage or dysfunction. About 7% of our patients who did not suffer the same reaction, however, had had previous head injuries of some kind.

It is not known whether the dose of thyrotrophin releasing hormone is important in the aetiology of these side effects, but this is likely. We therefore recommend a standard dose in the thyrotrophin releasing hormone test of 200 µg, which gives sufficient release of thyroid stimulating hormone and prolactin. Moreover, in view of the serious complications that may arise after injection of thyrotrophin releasing hormone greater consideration should be given to whether there is a need for such a test.

¹ Maeda K, Ranimoto K. Epileptic seizures induced by thyrotrophin releasing hormone. *Lancet* 1981;i:1058-9.

² Grussendorf M, Blittersdorf RV, Raue F, Hufner M. Severe complications after injections of TRH [Abstract]. *Acta Endocrinol (Copenh)* 1982; suppl 246:82.

³ Jackson IMD. Thyrotrophin-releasing hormone. *N Engl J Med* 1982; 306:145-55.

⁴ Kruse H. Thyrotrophin-releasing hormone: interaction with chlorpromazine in mice, rats and rabbits. *J Pharmacol* 1975;6:249-68.

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