

SHORT REPORTS

Male sexual dysfunction during treatment with cimetidine

It has been suggested that the histamine H₂-receptor antagonist cimetidine, which is widely used in the management of duodenal ulcer, should be used mainly for long-term treatment of this disease.¹ Continuous treatment with cimetidine is thought to be safe, since the documented toxicity is low. Nevertheless, we describe here three patients who developed sexual dysfunction while being treated with cimetidine.

Case reports

Case 1—A 33-year-old father of two children was treated with cimetidine (1 g/day) for four weeks for duodenal ulceration. The ulcer healed but the patient complained spontaneously that during the first week of treatment he had suffered loss of libido and thereafter had been unable to achieve erection. Within four days of discontinuing treatment his sexual function had returned to normal. Levels of luteinising hormone (LH), follicle stimulating hormone (FSH), testosterone, oestradiol, and prolactin were normal during treatment (see table).

Case 2—A 50-year-old father of four children started on a nine-month course of cimetidine (1 g/day) for duodenal ulceration. Within three weeks he suffered severe loss of libido with progression to impotence. He eventually complained after seven months of treatment, and a seminal analysis showed oligospermia. His libido has not returned during the 11 months since stopping treatment (during which he has had surgery for the ulcer). Testicular biopsy at the time of surgery (eight months later) showed active spermatogenesis in all tubules and was considered normal. FSH and prolactin concentrations were abnormal during and after treatment, while testosterone levels were towards the upper limit of normal (see table).

Case 3—A 51-year-old man started a proposed one-year course of cimetidine (1 g/day) for duodenal ulceration. When specifically questioned after 11 months the patient complained that he had noted loss of libido soon after starting treatment and that this had subsequently progressed to impotence. The symptoms did not improve after treatment was stopped. LH and FSH concentrations were raised during and after treatment (see table), though testosterone values were normal.

Hormone concentrations during and after treatment

	LH (IU/l)	FSH (IU/l)	Testos- terone (µg/l)	Oestradiol (ng/l)	Prolactin (mIU/l)
<i>Case 1</i>					
On treatment	7.4	1.6	6.61	36	344
Off treatment: 1 month	12.3	5.9	5.76	20	863
<i>Case 2</i>					
On treatment	7.7	14.2	8.10		677
Off treatment: 3 months	9.3	11.0	7.60	7.6	520
7 months	5.5	13.6	8.90	14.7	439
<i>Case 3</i>					
On treatment	11.0	9.0			653
Off treatment: 4 months	11.3	9.0	8.20	33	488
8 months	15.4	13.0	8.29	44	375
<i>Upper limit of normal*</i>					
	7.7	7.2	9.20	40	400

*In our laboratory for patients aged over 40 years.

Comment

These three patients developed symptoms of sexual dysfunction during treatment with cimetidine, despite healing of their ulcers. Twenty-three cases of impotence (in patients aged 37 or older in whom the onset occurred from 0-7 months after treatment started) have been reported to the Committee on Safety of Medicines (personal communication) so that our patients are symptomatically not unique, although the abnormal endocrine profiles have not been previously reported. The mechanism of the loss of libido and impotence has not been defined but an endocrine basis must be suspected.²

The sexual dysfunction in our patients may be related to the abnormally high pituitary hormone concentrations. Hyperprolactinaemia in men (usually with pituitary tumours) may be associated

with sexual dysfunction,³ but the prolactin levels were not consistently raised in our patients. Cimetidine exerts an antiandrogenic effect in animals,⁴ and the abnormally high gonadotrophin concentrations, in the presence of high normal testosterone values, are compatible with an antiandrogenic effect.⁵ Preliminary studies (to be reported) indicate that gonadotrophin concentrations tend to be higher in cimetidine-treated than in untreated patients with duodenal ulcer, especially those aged over 40, so only older men may be liable to this type of reaction to cimetidine. We cannot yet explain the persistence of the abnormal gonadotrophin concentrations after discontinuing treatment in our patients, but in other (asymptomatic) individuals the high gonadotrophin values have returned to normal.

We have not proved a causal connection between cimetidine and the hormonal and sexual dysfunction of our patients. Nevertheless, because long-term administration of cimetidine seems to be useful for treating duodenal and gastric ulcers, sexual function should be monitored in these patients since our findings, together with the evidence from animal experiments, provide a prima facie case for such a relationship.

We thank Mr K Baxby for his helpful comments on two of these patients and Dr W H W Inman for permission to quote the reports of impotence to the Committee on Safety of Medicines.

¹ *Lancet*, 1978, 2, 1237.

² *British Medical Journal*, 1978, 4, 1516.

³ Franks, S, et al, *Clinical Endocrinology*, 1978, 8, 277.

⁴ Leslie, G B, and Walker, T F, in *Cimetidine*, ed W L Burland and M A Simkins, p 24. Amsterdam, Excerpta Medica, 1977.

⁵ Neumann, F, et al, in *Androgens and Antiandrogens*, ed L Martini and M Motta, p 163. New York, Raven Press, 1977.

(Accepted 22 February 1979)

Departments of Therapeutics and Biochemical Medicine, Ninewells Hospital and Medical School, Dundee

N R PEDEN, MA, MRCP, medical registrar
 JANICE M CARGILL, MB, MRCP, medical registrar
 MARGARET C K BROWNING, BSc, senior biochemist
 J H B SAUNDERS, MB, MRCP, senior medical registrar
 K G WORMSLEY, DSc, FRCP, consultant physician

Ectopic pregnancy by transmigration of sperm after sterilisation with Hulka-Clemens clips

Pregnancy after correct application of Hulka-Clemens clips is rare. We report on a case of tubal ectopic pregnancy after correctly performed sterilisation with these clips, in which fertilisation occurred after sperm transmigration.

Case Report

A 32-year-old multigravida was admitted to hospital with a four-day history of lower abdominal pain and 37 days' amenorrhoea. Eight months earlier she had been sterilised under laparoscopic vision, using Hulka-Clemens clips applied through a second incision. Ruptured ectopic pregnancy was diagnosed and laparotomy performed. A ruptured right tubal ectopic pregnancy was found lateral to the Hulka-Clemens clip on that side. Both clips seemed to be correctly placed across the isthmic portions of the tubes. A right partial salpingectomy was performed, with removal of the clip on that side.

The diagnosis of ectopic pregnancy was confirmed histologically and the clip was correctly placed across the tube. At one side of the clip the tube seemed completely obstructed, but at the other side the lumen of the tube was patent and opened into the space occupied by the clip. Although this is unusual, it is difficult to imagine how it allowed the tube to remain functionally patent. A hysterosalpingogram was performed, which showed tubal patency on the left side. A further laparotomy, and an Irving-type sterilisation were performed, and the clip was removed from the left side.