SHORT REPORTS

Transvaginal compared with transvesical ultrasonography for recovery of oocytes for in vitro fertilisation

Oocyte recovery guided by transvaginal ultrasonography has been introduced into in vitro fertilisation units and compares favourably with laparoscopic oocyte recovery.^{1,2} The transition from laparoscopy to ultrasonography may, however, account for part of this difference—for example, anaesthetic requirements and risks of pneumoperitoneum are reduced. In Oxford the in vitro fertilisation unit is an outpatient service and used transvesical ultrasonography³ until transvaginal scanning was introduced. Thus we were able to make a direct assessment of the value of oocyte recovery by transvaginal scanning.

Patients, methods, and results

We report the results of 100 consecutive cycles of in vitro fertilisation. There was a definite transition between the final 50 women, undergoing transvesical ultrasonography and the first 50 women undergoing transvaginal ultrasonography (February-March 1987 and April-June 1987, respectively). The date when oocyte recovery by vaginal scanning was to be introduced was not known when the cycles of treatment were booked, so clinical factors did not affect the composition of the groups. Clinical and laboratory methods were unchanged over both periods. This unit uses norethisterone to schedule cycles and a fixed stimulation regimen to predetermine the day of oocyte recovery.⁴ Thus any differences in outcome cannot be attributed to subjective decision making about the timing of oocyte recovery, except in a few cycles in each group in which buserelin was used to desensitise the pituitary (transvesical scanning, seven; vaginal scanning, four). An ATL 100 scanner with 3.5 MHz sector probe and needle guide was used in transvesical scanning; a Phillips R1550 XP S scanner with a 5 MHz vaginal probe fitted with the Phillips smooth contour needle guide was used in transvaginal scanning. All recoveries of oocytes were performed with 17 gauge needles, the women being sedated only with intravenous pethidine and diazepam. The policy of the unit is to aim to transfer a maximum of three embryos, with exceptionally four embryos transferred when four poor quality embryos have resulted. In this series six women received four embryos (transvesical scanning, two; vaginal scanning, four).

The groups were similar clinically and in their responses to stimulation (table). The numbers of oocytes recovered and fertilised per recovery were significantly higher with transvaginal than transvesical ultrasonography ($p < 0.0001$ for both cases Spearman's rank coefficient). The number of embryos transferred was significantly different between the two groups ($p < 0.0001$, Spearman's rank coefficient), so, although the rate of clinical pregnancy in women receiving more than two embryos was not different between the two groups (transvesical scanning, 36%; transvaginal scanning, 39%), the proportion of the group undergoing transvaginal scanning who received more than two embryos was

significantly higher ($p < 0.01$, Fisher's exact test; transvesical scanning, 22%, transvaginal scanning, 46%). The rate of clinical pregnancy per cycle was doubled, in keeping with the higher yield of oocytes and embryos, in the group undergoing transvaginal scanning ($p < 0.01$, Fisher's exact test).

Comment

The attraction of transvaginal scanning is that it provides more detailed imaging and removes the undoubted distress and unpredictable delays to patients associated with techniques that require a full bladder. Our results confirmed expectations, and we immediately transferred to oocyte recovery by transvaginal scanning. Our initial experience produced results superior to our accumulated experience over about 300 cycles with transvesical scanning. The transvaginal method improved yields at each step of in vitro fertilisation, with a higher proportion of women receiving the optimal number of embryos and a higher proportion of cycles resulting in pregnancy. Since the introduction of transvaginal methods the low cost in vitro fertilisation unit in Oxford⁵ has achieved results comparable with those of leading centres, indicating that small units setting up in vitro fertilisation programmes should consider adopting transvaginal methods from the outset.

- 1 Torode HW, Picker RH, Porter RN, *et al.* Oocyte pickup by laparoscopy replaced by transvaginal aspiration in an in vitro fertilisation program. *Journal of In Vitro Fertilisation and Embryo Transfer* 1987;4:148-52.
- 2 Maleika F, Maleika MC, Hartter P, Engers G, Weiske WH. Comparison between trans-vaginal ultrasound and pelviscopic oocyte retrieval for IVF. *Human Reproduction* 1987;2 (suppl 1):54.
- 3 Little DJ, Bromwich PD, Walker AP, Macken AM, Newton JR. A simplified approach to oocyte recovery for in-vitro fertilization. *Br J Obstet Gynaecol* 1985;92:180-1.
- 4 Walker A, Bromwich P, Barlow DH, *et al.* A comparative study of fixed-schedule and individualised stimulation for in-vitro fertilisation. *Human Reproduction* 1987;2 (suppl 1):34.
- 5 Bromwich P, Walker A, Kennedy S, *et al.* In vitro fertilisation in a small unit in the NHS. *Br Med J* 1988;296:759.

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Clinical details of and results in women undergoing oocyte recovery by transvesical or transvaginal ultrasonography

	Vesical scanning	Vaginal scanning
<i>Clinical details</i>		
Mean age (range) (years)	32.7 (25-40)	31.6 (22-42)
Mean duration of infertility (range) (years)	5.0 (2-12)	5.9 (1-14)
No (%) with infertility factor:		
Tubal	41 (82)	42 (84)
Male	9 (18)	5 (10)
Endometriosis	4 (8)	3 (6)
Unexplained	9 (18)	8 (16)
On day of stimulation with HCG*:		
Median plasma oestradiol (range) (pmol/l)	3290 (833-14 430)	3090 (648-15 170)
Median plasma progesterone (range) (nmol/l):	0.6 (0.3-13.4)	1.3 (0.3-7.3)
No (%) >6 nmol/l	4 (8)	3 (6)
Median diameter of leading follicle (range) (mm)	18 (14-28)	17 (11-25)
<i>Results</i>		
No (%) of cycles started	50 (100)	50 (100)
No (%) of oocyte recoveries performed	48 (96)	48 (96)
No (%) with at least one oocyte	45 (90)	47 (94)
Median no of oocytes/recovery (range)	3 (0-12)	4 (0-10)†
Median no of oocytes fertilised/recovery (range)	1 (0-5)	2 (0-7)†
Median no of embryos transferred (range)	1 (0-4)	2 (0-4)†
No (%) with 1 or 2 embryos transferred	20 (40)	16 (32)
No (%) with >2 embryos transferred	11 (22)	23 (46)†
No (%) of embryo transfers	31 (62)	39 (78)
Clinical pregnancies:		
No	6	12
Rate per cycle (%)	12	24†
Rate per embryo transfer (%)	19	31†

*HCG = Human chorionic gonadotrophin.

†Significant differences (see text).

Effect of high dose somatostatin analogue on growth hormone concentrations in acromegaly

Octreotide, a somatostatin analogue, given subcutaneously successfully reduces growth hormone concentrations in acromegaly, but not to within the normal range (< 5 mIU/l).¹⁻⁵ Unfortunately, somatostatin also suppresses plasma insulin concentrations and can impair glucose tolerance.^{2,3} In view of this we compared the biochemical effects of increasing doses of octreotide in patients with acromegaly.

Patients, methods, and results

After their informed consent had been obtained six patients with active acromegaly were given octreotide 0.3, 1.5, or 3 mg daily in divided doses by subcutaneous injection at 0800, 1600, and 2200. A control profile was taken, and then the patients were given each dose for three days, during which blood was taken for measurement of growth hormone, insulin, and glucose concentrations at fixed times ($n = 15$) over 24 hours. Standard meals were provided on each test day. In a long term study four of the patients continued to take octreotide 1000 µg thrice daily for a mean of four months (range three to six).

The table shows the fall in 24 hour growth hormone and insulin concentrations with the three doses of octreotide compared with the pretreatment concentrations. Compared with the lowest dose regimen, the highest dose caused a significant reduction in both variables; there was no other significant difference among the three doses. In addition, there was no significant change in mean glucose

Mean (SEM) concentrations of growth hormone, insulin, and glucose over 24 hours with each dose regimen. For statistical analysis (Student's paired *t* test) growth hormone and insulin concentrations were log transformed

	Dose of octreotide (μ g thrice daily)			
	Control	100	500	1000
Growth hormone (mIU/l):				
24 h Profile	40 (18)*	8.5 (3.2)†	3.8 (0.5)	3.1 (0.4)
10 h After dose	45 (16)*	17.7 (4.0)‡	5.2 (0.6)§	2.8 (0.2)
Insulin (mU/l):				
24 h Profile	33 (7.1)*	17 (3.7)†	12.7 (3.0)	10.6 (1.5)
Glucose (mmol/l):				
24 h Profile	5.2 (0.3)	5.3 (0.2)	5.5 (0.2)	5.4 (0.2)

*Control v 100, 500, and 1000 μ g $p < 0.001$.

†100 v 1000 μ g $p < 0.05$.

‡100 v 500 μ g $p < 0.05$.

§500 v 1000 μ g $p < 0.02$.

concentration with any of the doses. Growth hormone concentration was within normal limits 10 hours after 1000 μ g octreotide but not after 100 or 500 μ g. Daily measurements of growth hormone concentration showed no change on each of the three days of each dose regimen.

Twenty four hour profiles obtained in the four patients on the last day of the long term study did not differ from those obtained in the acute study at this dose.

No patient experienced subjective or objective side effects while taking octreotide. There was no change in blood count, biochemical profile, or thyroxine, cortisol, prolactin, luteinising hormone, follicle stimulating hormone, and sex hormone concentrations at the highest dose.

Comment

Several studies have indicated that octreotide is an effective treatment for acromegaly, although in the recommended dose (50-100 μ g thrice daily) it is unsuccessful in suppressing growth hormone concentrations throughout the interval between two injections.^{2,5} Our data² and those of others⁴ have shown that after 100 μ g subcutaneously suppression of growth hormone is maximal at two to four hours. Timsit *et al* reported that 500 μ g thrice daily given subcutaneously did not normalise growth hormone in one of two subjects studied.⁵ They indicated that continuous subcutaneous infusion of octreotide (100 μ g/24 h) normalised growth hormone throughout the day in six of seven patients studied. Our study confirms that subcutaneous octreotide in doses of 1000 μ g thrice daily can normalise growth hormone concentration in acromegaly. Indeed, in all six patients in our study the mean 24 hour growth hormone concentration was normal with the highest dose used and there was no evidence that growth hormone concentration increased between doses, as it did with the 100 and 500 μ g doses.

It has been reported that octreotide may worsen glucose tolerance in acromegaly by suppressing plasma insulin concentrations.^{2,3} Our study confirmed that the reduction in insulin concentration was greater with 1000 μ g than 100 μ g thrice daily. Nevertheless, in both the short and long term studies there was no evidence of an appreciable deterioration in 24 hour plasma glucose concentration with any of the dose regimens, which might be due to a simultaneous greater reduction in counterregulatory factors enhancing insulin sensitivity. Previous studies of low dose subcutaneous octreotide have indicated that the drug is well tolerated. Although further long term data are necessary, our study suggests that higher doses are also without important side effects.

- Ch'ng JLC, Sandler LM, Kraenzlin ME, Burrin JM, Joplin GF, Bloom SR. Long term treatment of acromegaly with a long acting analogue of somatostatin. *Br Med J* 1985;290:284-5.
- Sandler LM, Burrin JM, Williams G, Joplin GF, Carr DH, Bloom SR. Effective long-term treatment of acromegaly with a long-acting somatostatin analogue (SMS 201-995). *Clin Endocrinol (Oxf)* 1987;26:85-95.
- Lamberts SW, Uitterlinden P, Verschoor L, van Dongen KJ, del Pozo E. Long-term treatment of acromegaly with the somatostatin analogue SMS 201-995. *N Engl J Med* 1985;313:1576-80.
- Comi RJ, Gordon P. The response of serum growth hormone levels to the long-acting somatostatin analog SMS 201-995 in acromegaly. *J Clin Endocrinol Metab* 1987;64:37-42.
- Timsit J, Chanson P, Langer E, *et al*. The effect of subcutaneous infusion versus subcutaneous injections of a somatostatin analogue (SMS 201-995) on the diurnal GH profile in acromegaly. *Acta Endocrinol (Copenh)* 1987;116:108-12.

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Dialysis myelopathy: quadriparesis due to extradural amyloid of β_2 microglobulin origin

We report a case of cervical myelopathy due to extradural deposition of amyloid derived from β_2 microglobulin. Posterior cervical laminectomy resulted in considerable improvement.

Case report

A 47 year old West Indian man was admitted for investigation of a four month history of progressive stiffness and weakness of his arms and legs and numbness of the lower half of his body. He had started receiving haemodialysis in 1970. In 1978 he developed hyperparathyroidism necessitating parathyroidectomy. Subsequent dialysis arthropathy was confirmed by the presence of synovial amyloid derived from β_2 microglobulin in the right knee. In 1985 he received a cadaver renal transplant but developed chronic rejection, and he resumed haemodialysis nine months after transplantation. In 1986 biopsy of a cyst in the clavicle showed deposition of amyloid derived from β_2 microglobulin.

When admitted to hospital he was unable to walk, move from a chair to bed, or hold a pen to write. Examination showed a spastic quadriparesis with pronounced rigidity, hyperreflexia, and extensor plantar reflexes. Joint position sense was reduced, and the response to pin prick was reduced below the upper thorax. Myelography showed posterior displacement of the thecae at the sacrum, L3-5, and T7. There was almost complete obstruction to flow of contrast medium from T1 to C2. Computed tomography of the cervical region showed widespread extradural soft tissue densities with almost total obliteration of the subarachnoid space at C5-6. The cord was noticeably compressed (figure).

Posterior cervical laminectomy was performed. The spinal cord was completely surrounded by concentric rings of yellow fibrous tissue, which was removed. Histological examination showed extensive extracellular deposits of amyloid within fibroelastic ligament. Immunoperoxidase stains were positive for β_2 microglobulin but negative for serum amyloid A proteins and κ and λ light chains. Postoperative recovery was good. He could walk and climb stairs, and sensation returned to normal.

Computed tomogram of cervical cord at C2-3.

Comment

Compression of the spinal cord due to extradural amyloid is rare.^{1,2} In previous cases no primary cause for the formation of amyloid was found, although monoclonal gammopathy was implicated in one report.² This is the first reported case of compression of the cord due to extradural deposition of amyloid derived from β_2 microglobulin.

Dialysis arthropathy, bone cysts, and recurrent carpal tunnel syndrome due to deposition of amyloid are recognised complications of long term haemodialysis.³ Biochemical and immunohistochemical studies have identified the precursor molecule of the amyloid as β_2 microglobulin. β_2 Microglobulin concentrations are raised in patients undergoing dialysis