Oestrogen replacement therapy after hysterectomy

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Abstract

Objective—To identify those women who might benefit from oestrogen replacement after hysterectomy.

Design—Targeted health screening.

Setting—Large group practice.

Subjects—All women aged under 50 who had had a hysterectomy.

Main outcome measures—Concentration of follicle stimulating hormone, symptom profile, uptake of oestrogen replacement therapy.

Results—145 of 1953 women aged 32–49 had had a hysterectomy. 35 of the 41 with bilateral oophorectomy and 27 of 104 with one or more ovaries conserved were taking oestrogen replacement. 62 of the 68 who had ovaries conserved and were not taking oestrogen replacement attended for review, of whom 14 had a follicle stimulating hormone concentration ≥ 20 IU/l. 16 of the 19 women identified as potentially able to benefit from oestrogen replacement started treatment and were still on treatment at six months of follow up.

Conclusion—Systematic review of women who had had a hysterectomy identified an important group who would potentially benefit from oestrogen replacement therapy.

Introduction

Oestrogen replacement can benefit menopausal women by reducing the incidence of ischaemic heart disease, stroke, and osteoporosis.¹ This treatment can confer benefits after hysterectomy. Although the ovaries are usually conserved when a hysterectomy is performed in women under the age of 45, the operation may advance ovarian failure by about four years.² In older women the ovaries are usually removed and oestrogen replacement given.

It was suspected that a significant proportion of younger women who had had a hysterectomy and might benefit from oestrogen replacement therapy were not receiving it. I conducted a study to identify these women and offer them treatment.

Subjects and methods

Bridgnorth medical practice serves 15 000 patients in a small country town. The ovarian status and use of oestrogen replacement by women aged under 50 who had had a hysterectomy were obtained from patients' records.

Women who had had their ovaries removed were invited to discuss oestrogen replacement with their doctor unless there were absolute contraindications (breast or endometrial carcinoma, severe active liver disease, undiagnosed vaginal bleeding).¹

Women who had had a hysterectomy with ovarian conservation and were not taking oestrogen replacement were invited for an assessment of menopausal

symptoms by a practice nurse an arbitrary minimum of one year after their operation. Menopausal symptoms were rated as present or absent on a precoded sheet. Concentration of follicle stimulating hormone was measured as an index of ovarian failure (polyclonal radioimmune assay, postmenopausal reference range ≥ 30 IU/l). Patients were asked to consult their doctor if symptoms were troublesome or their follicle stimulating hormone concentration was 20 IU/l or above.³

Results

Of 1953 women aged 32 to 49, 145 had had a hysterectomy. Forty one had also had bilateral oophorectomy. The mean age of these 41 women was 44 (range 33–49) years, and the mean age at operation was 41 (28–48) years. Thirty five of the 41 women were taking oestrogen replacement, with a median duration of treatment of three years (range <1–13). Of the six women not taking oestrogen replacement, two had no evidence of malignancy, two ovarian carcinoma, one endometrial sarcoma, and one had no evidence of malignancy but subsequently developed chronic active hepatitis. All but the last woman were judged to be suitable for oestrogen replacement.¹ Three women started treatment. One woman with ovarian carcinoma declined treatment after other medical advice and the fifth woman did not accept an invitation to attend.

In all, 104 women had had a hysterectomy with conservation of ovaries; 27 were already taking oestrogen replacement therapy. Of the 77 who were not taking oestrogen, nine had had a hysterectomy in the past year. The remaining 68 were invited for an assessment and 62 (91%) attended (table). Fourteen women had a raised follicle stimulating hormone concentration, 13 of whom started oestrogen replacement. One woman declined treatment. Menopausal type symptoms were common but only hot flushes were reported significantly more often by the women with a raised follicle stimulating hormone concentration (57% v 25%, $\chi^2=3.7$, df=1; $p=0.05$). Of the 19 women who were identified as potentially able to benefit from oestrogen replacement, 16 started treatment and all were still taking it six months later.

Discussion

Oestrogen deficiency has particularly severe consequences in younger women and this study concentrated on women under 50.¹ The quoted follicle stimulating hormone postmenopausal reference range of ≥ 30 IU is comfortably over any spontaneous midcycle ovulatory peak and a concentration of 20 IU/l was selected to indicate ovarian failure.³

Oestrogen replacement therapy was already being taken by 85% of women who had had oophorectomy, a much higher rate than reported in previous studies.^{4,5}

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	Follicle stimulating hormone		p Value
	< 20 IU/l	≥ 20 IU/l	
No of women	48	14	
Mean (range) age (years)	44 (34-49)	46 (41-49)	NS
Mean (range) age at operation (years)	39 (30-47)	41 (38-45)	NS
Mean (range) follicle stimulating hormone (IU/l)	6 (1-19)	38 (20->50)*	
No (%) with hot flushes	12 (25)	8 (57)	0.05
No (%) with vaginal dryness	19 (40)	4 (29)	NS
No (%) with psychological symptoms	34 (71)	12 (86)	NS
No (%) with reduced libido	18 (38)	6 (43)	NS

*Maximum concentration reported by laboratory as >50 in three women.

This may reflect the enthusiasm of the practice staff but could indicate changing prescribing patterns within general practice.

Women who have had a hysterectomy are ideal patients for oestrogen replacement therapy. Un-

opposed oestrogen is the treatment of choice and the *British National Formulary* recommends 10 years' use. These women do not have periods or premenstrual-type symptoms and receive the full benefit of the oestrogen mediated lipid improvements.¹

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- 1 Whitehead M, Godfree V. *Hormone replacement therapy. Your questions answered*. Edinburgh: Churchill Livingstone, 1992.
- 2 Siddle N, Sarrel P, Whitehead M. The effect of hysterectomy on the age at ovarian failure. *Fertil Steril* 1987;47:94-100.
- 3 Tindall VR. *Jeffcoate's principles of gynaecology*. London: Butterworths, 1987.
- 4 Spector TD. Use of oestrogen replacement therapy in high risk groups in the United Kingdom. *BMJ* 1989;299:1434-5.
- 5 Barlow DH, Grosset KA, Hart H, Hart DM. A study of the experience of Glasgow women in the climacteric years. *Br J Obstet Gynaecol* 1989;96:1192-7.

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ANY QUESTIONS

What is the cause of the headache that occasionally occurs as a side effect of treatment with ranitidine?

Ranitidine is an H₂ receptor blocker used in peptic ulcer, and, although headache is recorded as an adverse reaction, it seems to be uncommon. Histamine has been implicated in cluster headache, but this is not documented as a side effect of H₂ blockers. The mechanism of headache is obscure since only H₂ receptors are present on intracranial vessels, but both H₁ (vasoconstrictor) and H₂ (vasodilator) receptors are found on extracranial arteries. The usual effect of physiological doses of histamine is pronounced vasodilatation mediated by H₁ and H₂ receptors, which is accompanied by a throbbing diffuse headache and flushing, quite distinct from migraine.¹ This might be inhibited by an H₂ blocker. Experimentally intracarotid histamine does not alter cerebral blood flow when the blood-brain barrier is intact. Whether ranitidine causes a relative excess of H₁ activity followed by a rebound of H₂ activity is a guess that might explain the occasional headaches after its use. A non-specific headache of tension type might be another explanation in sufferers from peptic ulcer.—JMS PEARCE, consultant neurologist, Hull

- 1 Gross PM, Harper AM, Teasdale GM. Cerebral circulation and histamine. 1. Participation of H₁- and H₂-receptors in vasodilatory responses to intracarotid infusion. *J Cereb Blood Flow Metab* 1981;1:97-108.

Can non-steroidal anti-inflammatory drugs given before operations affect wound healing? If so, is their effect important enough for doctors to recommend prohibition of their use during this period?

The implications of an affirmative reply are obvious, aside from the known side effects of non-steroidal anti-inflammatory drugs, which could be a particular problem during and after surgery—increased bleeding of the wound bed, confusion, and postoperative gastric haemorrhage.¹ The specific question is whether non-steroidal anti-inflammatory drugs adversely affect wound healing. I infer that the questioner is concerned with surgery other than that directly on the intestinal tract and, in particular, whether non-steroidal anti-inflammatory drugs adversely impair healing after orthopaedic surgery. There is anecdotal evidence for impairment² and experimental evidence³ against impairment, but controlled comparisons directly addressing this issue are lacking. To withdraw symptomatic relief in the form of non-steroidal anti-inflammatory drugs from patients with, for example, actively painful osteoarthritis during the postoperative phase may greatly impair the patients' postoperative rehabilitation and therefore their recovery from surgery. That could be a more decisive disadvantage than a minor delay in healing, should this in fact occur.

In the absence of strong evidence for or against the

use of anti-inflammatory drugs before operation I recommend, firstly, that adequate pain relief with analgesics should be assured without the use of non-steroidal anti-inflammatory drugs except when these are definitely indicated, such as in postoperative gout. Secondly, when there seems to be a good clinical indication for non-steroidal anti-inflammatory drugs before an operation a drug with a short half life should be used.—MICHAEL L SNAITH, senior lecturer in rheumatology, Sheffield

- 1 Connelly CS, Panush RS. Should nonsteroidal anti-inflammatory drugs be stopped before elective surgery? *Arch Intern Med* 1991;151:1963-6.
- 2 Proper SA, Fenske NA, Burnett SM, Luria LW. Compromised wound repair caused by perioperative use of ibuprofen. *J Am Acad Dermatol* 1988;18:1173-9.
- 3 Mbugua SW, Skoglund LA, Likken P. Effects of phenylbutazone and indomethacin on the post operative course following experimental orthopaedic surgery in dogs. *Acta Vet Scand* 1989;30:27-35.

Are there appreciable amounts of nitrosamines in smoked fish such as kippers (which are cold smoked), smoked mackerel, and salmon (hot smoked), and if so what amount can be safely consumed each week without long term risk.

Nitrosamines, notably N-nitrosodimethylamine, have been found in measurable amounts in several samples of both raw and processed fish.¹ The levels observed have been up to 10 mg/kg, average being about 0.3 mg/kg. Smoking using gas heating produced a substantial increase in the levels in kippers but electric heating did not.²

Artificial smokes applied as a solution do not contain nitrosamines. The effects of traditional wood smoking vary depending on temperature and the type of wood used, which affects the formation of nitrous oxide. In view of the highly variable concentrations it is impossible to state the upper level of fish consumption that would carry no long term risk, but at the levels reported fish would make a minor contribution to total intakes which are well below the provisional acceptable daily intakes. Epidemiological studies show that the consumption of smoked fish is not significantly associated with the incidence of gastric cancer.³—D A T SOUTHGATE, head of nutrition, diet, and health department, Institute of Food Research, Norwich

- 1 Ministry of Agriculture, Fisheries and Food. *Nitrate, nitrite and N-nitroso compounds in food. Second report of the steering group on food surveillance*. London: HMSO, 1987. (Food surveillance report No 20.)
- 2 Ministry of Agriculture, Fisheries and Food. *Nitrate, nitrite and N-nitroso compounds in food. Second report of the steering group on chemical aspects of food surveillance*. London: HMSO, 1992. (Food surveillance report No 32.)
- 3 Choi NW, Miller AB, Fodor JG, et al. Consumption of precursors of N-nitroso compounds and human gastric cancer. In: Bartsch H, O'Neill IK, Schutte-Herm R, eds. *Relevance of N-nitroso compounds to human cancer: exposure and mechanisms*. Lyon: International Agency for Research in Cancer Scientific Publication, 1987:492-6.