Frankel, Carol Propper, Jenny Donovan, Alex Faulkner, and an anonymous referee for their comments and advice.

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(Accepted 12 May 1992)

Oestrogen replacement after oophorectomy: comparison of patches and implants

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Premenopausal women undergoing prophylactic oophorectomy are given oestrogen replacement to prevent menopausal symptoms. Oestrogen implants are effective in treating castrated women.¹ The aim of this study was to compare the implant with the newer, transcutaneous system (the patch) in terms of hormone

Appendix

TABLE AI—Transformation used for prostatectomy, based on Fowler et al¹⁶ and Rosser and Kind¹¹

Original study scores	General health index	Rosser score
Disability		
Activity index		
15		I
12-14-99		II
9-11-99		III
Distress		
Symptom score		
Mild	15-18	A
Mild	12-14-99	B
Moderate	15-18	B
Moderate	12-14-99	C
Severe	15-18	C
Severe	12-14-99	D

TABLE AII—Transformation used for total hip replacement, based on Eftekhar¹³ and Rosser and Kind¹¹

D'Aubigne and Postel number	Description	Rosser score
Disability		
6	Normal in activity for age	I
5	Walks without aid but has limp	II
4	Long distance walks possible but limited without aids	III
3	Walking limited, but can stand for long periods	IV
2	Duration and distance can walk limited with and without walking aid	V
1	Bedridden or can walk only a few yards	VI
Distress		
6	No pain	A
5	Slight or intermittent, decreasing with activity	B
4	Present only after activity, disappears quickly with rest	B
3	Tolerable, permits limited activity	C
2	Severe on attempts to walk, prevents all activity	D
1	Severe, spontaneous	D

TABLE AIII—Transformation used for total hip and total knee replacement, based on Liang et al²² and Rosser and Kind¹¹

Original study scores						Rosser score
<i>Mobility</i>	<i>Physical</i>	<i>Social</i>	<i>Disability Weight*</i>	<i>BUCPX</i>	<i>Average</i>	
5	4	5	0	1	0-970-1	I
5	4	4	-0-061	0-939	0-939-0-970	II
5	4	3	-0-061	0-939	0-909-0-939	III
5	3	2	-0-121	0-879	0-815-0-909	IV
4	3	1	-0-248	0-752	0-744-0-815	V
4	1	1	-0-265	0-735	0-731-0-744	VI
2	1	1	-0-273	0-727	0-727-0-731	VII
<i>Distress</i>						
<i>Symptom/problem complex score</i>						
0-0-2-0						A
2-0-2-5						B
2-5-3-0						C
3-0-4-07						D

*As weights for the points equating to Rosser disability II and III were identical, this number was taken to be the lower limit for II and the upper limit for III, rather than the midpoint (as for all other levels).

concentrations achieved and prevention of hot flushes.

Subjects, methods, and results

Premenopausal women undergoing bilateral oophorectomy were randomly allocated either oestradiol patches (0.05 mg oestradiol/24 hours; n=12) or oestradiol implants (50 mg crystalline oestradiol pellet; n=16) administered seven days after surgery. Blood samples for measurement of oestradiol, follicle stimulating hormone, and luteinising hormone concentrations were taken preoperatively, six days postoperatively, and after two and four months of treatment. Hormone concentrations were measured by routine radioimmunoassay. Oestradiol concentrations

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BMJ 1992;305:90-1

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Demographic data and serum hormone concentrations in patch and implant groups. Values are means (SE)

		Patch group (n=12)	Implant group (n=16)	95% Confidence interval of difference between means	p Value
Age (years)		45.8 (2.0)	44.0 (1.7)	2.7 to 6.4	>0.01
Weight (kg)		64.1 (2.3)	66.1 (1.88)	-8.1 to 4.0	>0.1
Height (cm)		162 (1)	164 (2)	-0.08 to 0.03	>0.1
Oestradiol (pmol/l)	{Preoperatively	241 (49)	379 (90)	-371 to 94	>0.1
	{Six days postoperatively	63 (3)	All <60		>0.1
Follicle stimulating hormone (IU/l)	{Preoperatively	8.1 (1.9)	9.6 (1.1)	-5.8 to 2.7	>0.1
	{Six days postoperatively	37.3 (4.1)	47.1 (5.6)	-25.1 to 5.4	>0.1
Luteinising hormone (IU/l)	{Preoperatively	6.4 (1.0)	12.0 (2.4)	-11.7 to 0.37	>0.1
	{Six days postoperatively	16.3 (2.5)	22.7 (2.6)	-14.0 to 1.1	>0.1
Oestradiol (pmol/l)	{After two months	178 (31)	226 (22)	-124 to 30	>0.1
	{After four months	191 (42)	213 (27)	-121 to 77	>0.1
Follicle stimulating hormone (IU/l)	{After two months	46.7 (4.9)	22.1 (3.6)	12.3 to 36.9	<0.001
	{After four months	53.4 (7.9)	31.6 (6.9)	0.3 to 43.4	0.047
Luteinising hormone (IU/l)	{After two months	29.6 (3.17)	16.9 (2.1)	5.2 to 20.8	<0.001
	{After four months	32.1 (4.9)	19.2 (3.4)	1.1 to 24.8	0.034

in the postmenopausal range were expressed as <60 pmol/l. Presence of hot flushes was recorded preoperatively and after four months of treatment. Compliance with treatment was confirmed at interview. Change from preoperative hormone concentration to that six days postoperatively was analysed by McNemar's test for oestradiol (expressed as <60 pmol/l or >60 pmol/l) and by paired Student's *t* tests for follicle stimulating hormone and luteinising hormone. Unpaired Student's *t* tests were performed for analyses between groups.

Mean age, weight, and height were not significantly different between the two groups (table). Preoperative hormone concentrations were within the premenopausal range and nei her preoperative nor postoperative concentration was significantly different between the groups. Six days after oophorectomy 89% of the subjects (25/28) had an oestradiol concentration <60 pmol/l ($p<0.001$). Follicle stimulating hormone and luteinising hormone concentrations increased significantly by six days postoperatively (follicle stimulating hormone: mean change 33.9 IU/l (95% confidence interval 26.3 to 41.6 IU/l), $p<0.001$, $df=27$, $t=9.0$; luteinising hormone: mean change 10.3 IU/l (6.1 to 14.6 IU/l), $p<0.001$, $df=27$, $t=5.0$).

Mean oestradiol concentrations after two and four months of treatment did not differ significantly between the two groups. Mean follicle stimulating hormone and luteinising hormone concentrations were significantly higher in the patch group at two months ($p<0.001$) and four months ($p<0.05$). Preoperatively none of the patients complained of hot flushes. After four months of treatment two of the 12 patients in the patch group and three of the 16 in the implant group complained of hot flushes.

Comment

Although recommended starting doses were selected in this study, the 0.05 mg patch and 50 mg implant were not equivalent in terms of hormone profiles; in terms of preventing hot flushes, however, they were equally effective. Hormone concentrations are not routinely measured in patients receiving oestrogen replacement, so this difference in hormone profiles would go undetected.

The two groups of women were equivalent in terms of hormone profile before starting oestrogen

replacement. Concentrations of oestradiol, follicle stimulating hormone, and luteinising hormone in the implant group after two and four months of treatment were similar to those reported in other studies employing the same dose.¹ Although the 0.05 mg patch can suppress gonadotrophin release in women after a natural menopause,² it was ineffective in these women with surgical menopause. Kamel *et al* showed that even a 0.2 mg patch was unable to sustain suppression of follicle stimulating hormone in oophorectomised women.³ The differences in gonadotrophin concentrations between the two groups may have resulted from the higher sustained oestradiol concentrations in the implant group, a finding also observed by Stanczyk *et al*.⁴ Oestrogen acts in a dose dependent manner to reduce gonadotrophins and prevent both the short term and long term sequelae of the menopause.⁵ Our results show that the intermediate doses of the patch and implant are not equivalent in terms of gonadotrophin suppression. This raises the question whether the oestradiol provided by the patch will be as effective as the implant in conferring the many long term benefits of oestrogen replacement to these oophorectomised women.

We thank the special trustees of St Thomas's Hospital and St Thomas's Baby Fund for financial help.

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(Accepted 22 May 1992)

Correction

Is duplicate publishing on the increase?

A typesetting error occurred in this short report by Tony Waldron (18 April, p 1029). The second paragraph of the methods and results section should begin: "In 1988, six of the 110 main articles ... had been published elsewhere."