- 16 Fleming R, Coutts JRT. Induction of multiple follicular growth in normally menstruating women with endogenous gonadotrophin suppression. *Fertil Steril* 1986;45:226-30.
- 17 Neveu S, Hedon B, Bringer J, *et al*. Ovarian stimulation by a combination of a gonadotrophin releasing hormone agonist and gonadotrophins for in vitro fertilisation. *Fertil Steril* 1987;47:639-43.
- 18 Zorn JR, Barata M, Brami C, *et al*. Ovarian stimulation for in vitro fertilisation combining administration of gonadotrophins and blockade of the pituitary with D-Trp-LHRH microcapsules: pilot studies with two protocols. *Hum Reprod* 1988;3:235-9.
- 19 Serafini P, Stone B, Kerin J, Batzofin J, Quinn P, Marrs RP. An alternate approach to controlled ovarian hyperstimulation in "poor responders": pretreatment with a gonadotrophin-releasing hormone analog. *Fertil Steril* 1988;49:90-5.
- 20 Zarutskie PW, Kuzan FB, Dixon L, Soules MR. Endocrine changes in the late follicular and post-ovulatory intervals as determinants of the in-vitro fertilisation pregnancy rate. *Fertil Steril* 1986;47:137-43.
- 21 Trounson A, Howlett D, Rogers P, Hoppen H-O. The effect of progesterone supplementation around the time of oocyte recovery in patients super-ovulated for in-vitro fertilisation. *Fertil Steril* 1986;45:532-5.
- 22 Smits J, Devraey P, Camus M, *et al*. The luteal phase and early pregnancy after combined GnRH-agonist/human menopausal gonadotrophin treatment for superovulation in in-vitro fertilisation or gamete intrafallopian transfer. *Hum Reprod* 1988;3:585-90.
- 23 O'Neill C, Pike IL, Porter RN, Gidley-Baird A, Sinosich MJ, Saunders DM. Maternal recognition of pregnancy prior to implantation: methods for monitoring embryonic viability in vitro and in vivo. *Ann NY Acad Sci* 1985;442:429-39.
- 24 Gidley-Baird AA, O'Neill C, Sinosich MJ, Porter RN, Pike IL, Saunders DM. Failure of implantation in human in vitro fertilisation and embryo transfer patients: the effects of altered progesterone/oestrogen ratios in humans and mice. *Fertil Steril* 1986;45:69-74.
- 25 Sandow J, Englebart K, von Reckenberg W. The different mechanisms for suppression of pituitary and testicular function. *Med Biol* 1985;63:192-200.

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Perimenopausal risk of falling and incidence of distal forearm fracture

S J Winner, C A Morgan, J Grimley Evans

Abstract

A postal survey of 2000 women and 2000 men sampled from the electoral roll in Oxford was undertaken to ascertain whether changes with age in the risk of falling might explain the stepwise increases in age specific incidence rates of distal forearm fracture which occur in women at around the age of 50. Corrected response rates were 83% for women and 72% for men. In women, but not in men, there was a rise in the risk of falling from 45 years, peaking in the 55-59 year age group, and sinking to a nadir at ages 70-74. In both sexes rates rose in extreme old age. These variations were not attributable to preferential response from people who had suffered a fracture.

It is concluded that changes in the risk of falling interact with osteoporosis to produce a perimenopausal rise in the incidence of forearm fractures and contribute to the fluctuations in incidence of these fractures in old age.

Introduction

In women the age specific incidence of fractures of the distal forearm rises steeply between the age groups 40-44 and 55-59 but thereafter shows no consistent further increase (see figure).^{1,2} The incidence in men is constant with age. This pattern is conventionally attributed entirely to perimenopausal osteoporosis in women increasing the likelihood that a fracture will result if a fall occurs, but the frequency of falls among women during their middle years has not been examined. We carried out a postal survey to examine the possibility that an increase in the frequency of falls in middle age might contribute to the steep rise in incidence of distal forearm fracture in women at this time of life.

Subjects and methods

The age and sex of all residents of Oxford city who suffered a fracture of the distal forearm during 1986 were identified from the fracture clinic records at the John Radcliffe hospital to confirm that the local epidemiological pattern was broadly similar to that found elsewhere.

A postal questionnaire designed for self completion was sent to 2000 women residents of Oxford city, selected at random from the 1986 electoral register in postcode districts OX1-4. Subjects were asked for age

at last birthday and for "yes" or "no" answers to questions used in a previous survey: "Have you had any falls in the last year?" and "If so, did you break any bones in your falls?" Local press and radio coverage was organised without disclosing the hypothesis being tested. To assess response bias 500 initial non-responders were sent a second copy of the questionnaire after four weeks. A similar study was undertaken of men identified from the 1988 electoral register.

Results

A total of 124 fractures of the distal forearm were identified in Oxford city residents age 20-74. Estimated age specific yearly incidence rates (table 1) showed the expected stepwise increase in middle aged women and not in men.

FALLS AND FRACTURES

Women—Replies were received from 1335 women. After allowing for an estimated 19.2% obsolescence in the 1986 electoral register at the time of the survey⁴ the crude response rate of 67% corrected to roughly 83%. Ten respondents gave insufficient information and 16 were under 20, leaving 1309 women; of these 286 (22%) reported falling, of whom 30 suffered a fracture. The 1141 initial responders and 168 who responded to the second mailing did not differ significantly in the

TABLE 1—Numbers and yearly incidence rates of distal forearm fracture in Oxford, 1986

Age group (years)	Women		Men	
	No of fractures	Yearly incidence (per 10 000)	No of fractures	Yearly incidence (per 10 000)
20-24	6	12.8	12	25.6
25-29	3	11.4	2	4.1
30-34	5		1	
35-39	2	9.8	4	10.0
40-44	3		1	
45-49	3	21.1	4	10.3
50-54	7		1	
55-59	15	60.2	3	6.5
60-64	16		0	
65-69	17	62.0	1	7.3
70-74	16		2	

University Division of Geriatric Medicine, The Radcliffe Infirmary, Oxford OX2 6HE

S J Winner, MRCP, clinical lecturer
C A Morgan, FRACP, visiting fellow
J Grimley Evans, FRCP, professor

Correspondence to: Dr Winner.

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proportions who reported falls (22.4% (n=256) and 17.9% (n=30) respectively; SE of difference 3.42).

Men—Replies were received from 1332 men, giving a crude response rate of 67%. After allowing for 7.2% obsolescence in the 1988 register¹ the corrected response rate was 72%. Eight men gave insufficient information and 28 were under 20, leaving 1296; of these 227 (18%) reported falling, 17 suffering a fracture. Initial responders and the 163 responders to the second mailing included similar proportions who reported falls (17.9% (n=203) and 14.7% (n=24) respectively; SE of difference 3.18).

Table II shows the proportions of men and women reporting falls stratified by five year age groups (figure). Variations in prevalence with age were unaltered when respondents reporting fractures were excluded (table II).

Discussion

The John Radcliffe Hospital fracture clinic serves a population geographically wider than Oxford city, and few Oxford residents would have been treated elsewhere for fracture of the forearm. The fracture data were not rigorously validated as estimates of incidence were sought only to confirm that the phenomenon that we were investigating actually occurred in Oxford.

A few prospective community studies of falling have been reported,⁵⁻⁶ but the main surveys providing data on age specific rates have been retrospective, based on recall of falls by members of geographically defined populations in response to questionnaires administered by trained interviewers.^{3,7,8} These studies have shown a steep rise in the prevalence of falling with age at ages over 64, but our survey includes comparable data on younger adults.

Our main finding was an increase in the risk of falling among women, but not men, from ages 45-49 up to 55-59, followed by a decrease till age 70. At higher ages our data show the well documented increase in prevalence of falling in both sexes. Might the increase in risk of falling in middle aged women be an artefact? Publicity for the survey and the wording of the questionnaire were designed to conceal our interest in falls in middle life. A postal survey using a self administered questionnaire is subject to selection bias in favour of those who may have special reason to comply because they have a fall to report. There was no reason to suspect that this bias would affect middle aged women more than older and younger women. The high rates in middle age remained even after exclusion of those respondents who suffered fractures, who were

more likely to report the responsible fall. In both sexes initial responders and the samples of non-responders included similar proportions who had fallen, which was conventional epidemiological evidence against serious response bias.⁹

The increase in the prevalence of falling in women occurred in the same age groups as the increase in the age specific incidence of distal forearm fracture but was of a lower order of magnitude (figure). This suggests

Age and sex specific incidences of distal fracture of forearm in women and men in Malmö (1958-60)¹ and Newcastle (1982)² and proportion of women and men in Oxford reporting falls in the previous year (1988) Bars are SE

TABLE II—Proportion of women and men reporting falls by age

Age group (years)	All respondents				Respondents excluding those reporting fractures			
	Women		Men		Women		Men	
	No in age group	No (%) reporting falls	No in age group	No (%) reporting falls	No in age group	No (%) reporting falls	No in age group	No (%) reporting falls
20-24	65	12 (19)	67	10 (15)	65	12 (19)	67	10 (15)
25-29	95	11 (12)	85	16 (19)	95	11 (12)	82	13 (16)
30-34	86	14 (16)	104	21 (20)	86	14 (16)	103	20 (19)
35-39	108	17 (16)	129	25 (19)	108	17 (16)	128	24 (19)
40-44	130	17 (13)	122	24 (20)	130	17 (13)	121	23 (19)
45-49	78	15 (19)	111	16 (14)	76	13 (17)	110	15 (14)
50-54	92	22 (24)	114	18 (16)	88	18 (21)	111	15 (14)
55-59	107	34 (32)	100	12 (12)	104	31 (30)	99	11 (11)
60-64	92	22 (24)	123	23 (19)	90	20 (22)	122	22 (18)
65-69	121	25 (21)	114	14 (12)	119	23 (19)	113	13 (12)
70-74	111	22 (20)	83	16 (19)	109	20 (18)	80	13 (16)
75-79	120	34 (28)	82	17 (21)	113	27 (24)	81	16 (20)
80-84	60	20 (33)	42	8 (19)	56	16 (29)	42	8 (19)
≥85	44	21 (48)	20	7 (35)	40	17 (43)	20	7 (35)
Total	1309	286 (22)	1296	227 (18)	1279	256 (20)	1279	210 (16)

that the rise in the incidence of fractures was due to an interaction between the increase in falling and some other factor which increases the risk of fracture given that a fall has occurred, such as perimenopausal osteoporosis. The incidence of forearm fracture remains high in women above 59 but shows fluctuations which are similar in different surveys (figure)^{1,2,10} but are unexplained. Our survey showed a decline in reported falls between the age groups 55-59 and 70-74, which may contribute to the first of these fluctuations.

The mechanisms underlying the perimenopausal increase and later decrease in risk of falling are unclear. Women having menopausal symptoms sometimes report a sense of unsteadiness. Dizziness may be a menopausal symptom,¹¹ but this has not been suggested of falls. Though several factors have been shown to be associated with falls in elderly people,^{3,5,8} there is little

comparable information for younger age groups. Our findings suggest that falling in women at perimenopausal ages deserves particular attention.

- 1 Alffram P, Bauer GCH. Epidemiology of fractures of the forearm. *J Bone Joint Surg* 1962;44A:105-14.
- 2 Miller SWM, Grimley Evans J. Fractures of the distal forearm in Newcastle: an epidemiological survey. *Age Ageing* 1985;14:155-8.
- 3 Prudham D, Grimley Evans J. Factors associated with falls in the elderly: a community study. *Age Ageing* 1981;10:141-6.
- 4 Todd J, Butcher B. *Electoral registration in 1981*. London: Office of Population Censuses and Surveys, 1982.
- 5 Campbell AJ, Spears GFS, Borrie MJ, Fitzgerald JL. Falls, elderly women, and the cold. *Gerontology* 1988;34:205-8.

- 6 Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988;319:1701-7.
- 7 Campbell AJ, Reinken J, Allan BC, Martinez GS. Falls in old age: a study of frequency and related clinical factors. *Age Ageing* 1981;10:264-70.
- 8 Blake AJ, Morgan K, Bendall MJ, *et al*. Falls by elderly people at home: prevalence and associated factors. *Age Ageing* 1988;17:365-72.
- 9 Zarkovich SS. *Quality of statistical data*. Rome: Food and Agriculture Organisation of the United Nations, 1966.
- 10 Melton LJ, Riggs BL. Risk factors for injury after a fall. *Clin Geriatr Med* 1985;1:525-36.
- 11 Bungay GT, Vessey MP, McPherson CK. Study of symptoms in middle life with special reference to the menopause. *Br Med J* 1980;281:181-3.

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Peripheral blood flow in menopausal women who have hot flushes and in those who do not

Jean Ginsburg, Paul Hardiman, Barbara O'Reilly

Abstract

Objective—To compare blood pressure, heart rate, and peripheral vascular responsiveness in menopausal women who have hot flushes and in those who do not, and to assess the effect on these variables of treating women who have hot flushes with oestriol, a natural oestrogen, given vaginally.

Design—An open, non-randomised cohort study of flushing and non-flushing menopausal women. A before and after investigation of the effects of vaginal oestriol treatment on the circulation.

Setting—Referral based endocrinology clinic.

Patients—88 Consecutive menopausal women, 63 complaining of frequent hot flushes and 25 who had not flushed for at least a year.

Intervention—Treatment with vaginal oestriol 0.5 mg at night for six weeks in 18 of the women who had hot flushes.

Measurements and main results—Peripheral blood flow was measured by venous occlusion plethysmography at rest and in response to stressful mental arithmetic and anoxic forearm exercises. Blood flow in the forearm and its variability were significantly higher in flushing than in non-flushing women (4.1 (SD 1.7) and 3.1 (0.9) ml/100 ml tissue/min and 17% and 13% respectively). Blood pressure, heart rate, and blood flow in the hand were, however, similar in the two groups. No difference was found in the peripheral incremental response to either stress or anoxic exercise. Vaginal oestriol significantly lowered forearm blood flow from 4.4 (1.5) to 3.3 (1.1) ml/100 ml tissue/min but dilator responsiveness was unaffected.

Conclusions—The peripheral circulation is different in menopausal women who have hot flushes compared with those who do not, with selective vasodilatation in the forearm. The lowered blood flow in the forearm after vaginal oestriol in flushing women may be relevant to the alleviation of vasomotor symptoms induced by oestrogen treatment.

Introduction

Although menopausal hot flushes are the commonest symptoms of the climacteric, occurring in around 70% of women,¹ why some women flush frequently for years while others never flush or do so only for a short time is not understood. Women with severe symptoms at the climacteric are said to be more likely to be hypertensive or to have episodes of high blood pressure than those who do not flush frequently.² There are, however, no critical studies to substantiate such beliefs.

We previously showed that the symptoms of menopausal flushes are accompanied by objective changes: a rapid but transient increase in blood flow through the arm and in pulse rate,³ the pattern of change resembling that seen in response to indirect heating of the body.^{4,5} This suggests that the flush may reflect inappropriate activation of the mechanisms for heat loss and may explain why menopausal women often complain of feeling hot and why hot flushes may be precipitated or aggravated by vasodilator stimuli such as drinking a hot drink, stress, and a rise in ambient temperature.

Because of this and the fact that clonidine, an α agonist prescribed for relief of menopausal flushing, reduces dilator responses to exogenous vasoactive amines,⁶ partly through influencing peripheral vasodilator responsiveness,⁷ we compared vascular responsiveness in menopausal women who had frequent hot flushes with that in women of the same age who either had never flushed or had not experienced flushes for at least a year.

Patients and methods

Circulatory studies were performed in 88 menopausal women who had had their last menstrual period at least six months earlier and whose follicle stimulating hormone concentration was raised into the menopausal range (>20 IU/l). Of these, 63 complained of hot flushes, whose frequency ranged from three to 40 a day (mean 10.2 a day). The remaining 25 either had never flushed or had not done so for at least a year. The mean age of the flushing and non-flushing women was similar: 50.1 (SD 8.6) and 51.9 (8.5) years respectively ($p>0.05$). There was no difference in the time since menopause between the two groups.

The women were all clinically and biochemically euthyroid. None had taken oestrogens in the preceding 12 months, and none was taking any drug affecting cardiovascular activity at the time of the investigation. Informed consent was obtained from each subject.

Blood flow in the forearm and in the hand was measured by venous occlusion plethysmography under standardised laboratory conditions, as in previous studies.^{3,6-10} Blood pressure and heart rate were recorded with an automatic recorder (Electro Medical Equipment, Brighton). Pulse rate was also calculated directly from the plethysmographic tracing as required. The precise position of the plethysmograph in relation to the styloid process of the radius was noted at the first laboratory visit and used in subsequent tests. Subjects were tested at least two hours after a light meal.

Department of
Endocrinology, Royal Free
Hospital Medical School,
London NW3 2QG
Jean Ginsburg, DM, senior
lecturer in endocrinology
Paul Hardiman, MRCOG,
clinical research fellow
Barbara O'Reilly, PhD,
technical research assistant

Correspondence to: Dr
Ginsburg.

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