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Vitamin C depletion and pressure sores in elderly patients with femoral neck fracture

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Abstract

Objective—To evaluate the contribution of specific nutritional deficiencies (as indicated by zinc; vitamin A, C, and E; albumin; and haemoglobin concentrations) to the risk of pressure sores.

Design—Observational cohort study.

Setting—St James's University Hospital, Leeds.

Subjects—21 elderly patients presenting consecutively to the orthopaedic unit with femoral neck fracture.

Main outcome measure—Full thickness epidermal break over a pressure bearing surface.

Results—10 patients (48%) developed a pressure sore during their hospital stay. Indices of zinc status and concentrations of albumin, haemoglobin, and vitamins A and E were similar in patients who developed a pressure sore and those who did not. Mean leucocyte vitamin C concentration, however, was 6.3 (SD 2.2) µg/10⁸ cells in patients who developed a pressure sore as compared with 12.8 (4.6) µg/10⁸ cells in patients who did not.

Conclusions—Low concentrations of leucocyte vitamin C appear to be associated with subsequent development of pressure sores in elderly patients with femoral neck fractures.

Introduction

Up to 10% of all hospital patients and 30% of all elderly patients suffer from pressure sores.¹ Elderly patients with femoral neck fractures are particularly at risk, and as many as 60% may develop sores, most of which occur within the first five days of admission to hospital.² Many such patients spend unacceptably long periods on high pressure surfaces, particularly in casualty and in the operating theatre, and many go on to develop sores, though the relation may not be causal.³ It is possible that acute illness may be more important by exacerbating liability to pressure necrosis because of reduced feeling and mobility, pain, low

blood pressure, and nutritional deficiency. Other factors, such as confusion and incontinence, may also be important.^{4,5}

The benefits of supplementary nutritional support in patients with femoral neck fracture have been reported,^{6,7} and there is evidence that undernutrition may be a predisposing factor in pressure sore development.⁸ However, the contribution of pre-existing specific nutritional deficiencies to the risk of pressure sore development has not been studied.

Zinc is an essential element which has a crucial role in immunity and healing and for which interactions with other vitamins have been described.⁹ Both topical and oral zinc supplementation have a beneficial effect on wound healing in zinc depleted subjects.¹⁰ Vitamin C has also been shown to promote wound healing and may have a role in immunological regulation.⁹ Elderly people are particularly at risk from both nutritional deficiencies and depressed immunity, and studies in this hospital have shown a high prevalence of zinc¹¹ and vitamin¹² depletion in elderly inpatients.

This study was undertaken to assess the contribution of nutritional status to the development of pressure sores in elderly patients with femoral neck fractures.

Subjects and methods

Twenty one unselected patients aged 75 or more admitted to the orthopaedic unit with a diagnosis of femoral neck fracture were invited to participate in the study, which was approved by the local clinical research (ethics) committee. Written informed consent was obtained from all patients or their next of kin. Pressure sores were defined as a full thickness epidermal break over a pressure bearing surface.

A preoperative fasting blood sample was obtained at 8-9 am on the day after admission for assay of various biochemical nutritional indices, including plasma and polymorphonuclear leucocyte zinc; plasma albumin

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and vitamin A and E; leucocyte total vitamin C; and haemoglobin concentrations. All samples were processed within 30 minutes of venepuncture. Permission was also sought to take a muscle biopsy sample during pinning and plating of the fracture for zinc analysis.¹³ Plasma and polymorphonuclear leucocyte zinc concentrations were measured as described.¹⁴ Vitamin A and E concentrations were measured by high performance liquid chromatography,¹⁵ and leucocyte vitamin C was measured spectrophotometrically by means of a well established technique.¹⁶ Albumin and haemoglobin concentrations were measured by standard methods.

Patients were subsequently grouped into those who developed pressure sores and those who did not, and results were compared with findings in a group of 12 well elderly people who were free living in the community. The zinc status of these subjects has been described.¹³ Results are expressed as means and standard deviation (SD). Differences between groups were compared by using Student's *t* test and taken as significant when *p*<0.05.

Results

Ten of the 21 patients (48%) subsequently developed pressure sores (table). Indices of zinc status, plasma vitamin A and E concentrations, and albumin and haemoglobin concentrations did not differ appreciably between patients who developed pressure sores and those who did not (table).

Plasma zinc values were lowest in patients who did not develop sores, associated with reduced plasma albumin concentrations (table). The polymorphonuclear leucocyte zinc concentration was similar to that in the healthy elderly controls¹³ both in patients with and in those without sores. A significant correlation was found between polymorphonuclear leucocyte and muscle zinc values (*r*=0.78; *p*<0.01). Values were similar to those obtained from the rectus abdominis in a study of elderly surgical patients.¹³

Vitamin E concentrations in the patients studied were similar to those in well elderly subjects, but vitamin A concentrations were lower in both patient groups than in the healthy elderly group (table).

Leucocyte total vitamin C concentration was significantly lower in the patients who developed pressure sores than in those who did not (6.3 (SD 2.2) µg/10⁸ cells as compared with 12.8 (4.6) µg/10⁸ cells; *p*<0.001). All the patients who had sores and eight of those who did not had values below this laboratory's winter reference range (<15 µg/10⁸ leucocytes)¹⁷ (figure).

Discussion

Using polymorphonuclear leucocyte and muscle zinc values, which are thought to provide a good index of zinc status, we found no evidence of zinc depletion in our patients and conclude that this was not a contributory factor to pressure sore development.

However, vitamin C depletion was associated with pressure sores in this study. This finding agrees with a

report of a higher incidence of pressure lesions in elderly women with femoral neck fractures who had vitamin C intakes of less than the dietary reference value for this age group (40 mg/day).¹⁸

Leucocyte vitamin C concentrations show an apparent decrease when numbers of neutrophils increase after surgery or infection, since these cells contain only one third of the vitamin C of mononuclear leucocytes.¹⁹ However, in this study patients were investigated preoperatively, immediately after admission, and both total and differential leucocyte counts were normal in both groups. In this setting leucocyte vitamin C value is a good index of vitamin C reserves.^{9,19} It is therefore reasonable to assume that in some of our patients there was a pre-existing vitamin C deficit which apparently influenced the subsequent development of a pressure lesion.

Vitamin C has been implicated in collagen formation via hydroxylation of proline and thus influences wound healing. It is a powerful antioxidant with anti-inflammatory potential by neutralisation of phagocyte derived oxidants. Supplementation with vitamin C increases lymphocyte proliferative responses, neutrophil migration, and neutrophil-macrophage infiltration to sites of infection.⁹ Hence a vitamin C deficiency would probably have an adverse effect on tissue recovery after a period of ischaemia. Indeed, a single report in 1974 showed improved healing of existing pressure sores in patients given supplements of vitamin C.²⁰

Although development of pressure sores in patients with femoral neck fractures has been well studied there is still no clear cut risk factor which determines why one patient should develop a sore given the same conditions as another patient. In summary we have shown that vitamin C but not zinc, vitamin A, or vitamin E depletion was associated with subsequent development of pressure sores in elderly subjects with femoral neck fractures.

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Leucocyte vitamin C concentrations in elderly patients with femoral neck fractures. Vertical bar is adult reference range. Horizontal bars are means

Biochemical indices of nutritional status. Values are means (SD)

	No	Sex	Age range (years)	Plasma zinc (µmol/l)	Polymorphonuclear leucocyte zinc (nmol/mg protein)	Muscle zinc (nmol/mg protein)	Vitamin A (µg/dl)	Vitamin E (mg/dl)	Albumin (g/dl)	Haemoglobin (g/l)
Patients who developed pressure sore	10	{ 8F 2M	76-96	9.4 (2.6)	1.02 (0.13)	4.7 (0.6)	38.3 (9.5)*	10.4 (2.5)	33.1 (3.8)*	116 (18)
Patients who did not develop pressure sore	11	{ 8F 3M	76-88	8.1 (1.6)*	1.02 (0.28)	4.5 (0.6)	42.9 (17.2)†	9.6 (4.8)	35.5 (4.8)*	125 (19)
Well elderly	12	{ 6F 6M	75-86	10.8 (1.1)	1.11 (0.20)	—	62.5 (16.5)	10.4 (2.3)	43.9 (2.6)	—

*Significantly lower than well elderly group (*p*<0.001). †Significantly lower than well elderly group (*p*<0.02).

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Comparison of Yuzpe regimen, danazol, and mifepristone (RU486) in oral postcoital contraception

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Abstract

Objective—To compare the effectiveness and acceptability of three regimens of postcoital contraception.

Design—Randomised group comparison of ethinyloestradiol 100 μ g plus levonorgestrel 500 μ g repeated after 12 hours (Yuzpe method); danazol 600 mg repeated after 12 hours; and mifepristone 600 mg single dose.

Setting—Community family planning clinic.

Subjects—616 consecutive women with regular cycles aged 16 to 45 years.

Main outcome measures—Number of pregnancies, incidence of side effects, and timing of next period.

Results—The raw pregnancy rates (with 95% confidence intervals) for the Yuzpe, danazol, and mifepristone groups were 2.62% (0.86% to 6.00%), 4.66% (2.15% to 8.67%), and 0% (0% to 1.87%) respectively. Overall, these rates differed significantly ($\chi^2=8.988$, $df=2$; $p=0.011$). The differences between the mifepristone and Yuzpe groups and between the mifepristone and danazol groups were also significant. Side effects were more common and more severe in the Yuzpe group (133 women (70%)) than in either the danazol group (58 (30%)) or the mifepristone group (72 (37%)). The Yuzpe regimen tended to induce bleeding early but mifepristone prolonged the cycle. Three women bled more than seven days late in the Yuzpe group compared with 49 in the mifepristone group.

Conclusions—Mifepristone was effective in reducing expected pregnancy rates and the Yuzpe method also had a clinical effect. Danazol had little or no effect. A further multicentre trial is needed.

Introduction

Many methods of postcoital contraception have been used. Postcoital oestrogen given for five days was first introduced in the 1960s and was widely used.^{1,2} The failure rate was between 0.5% and 1.6% and side effects of nausea, vomiting, and breast tenderness were common. Yuzpe *et al* later combined oestrogen and progestogen given over 12 hours. This achieved a 125-fold reduction in the dose of oestrogen, and the intensity and duration of side effects were reduced.³ Failure rates between 1.7% and 2.3% have been found.^{3,4}

A comparative study showed similar effectiveness to oestrogen treatment and suggested the Yuzpe regimen was preferable because of the shorter duration of treatment.⁵ Estimating the numbers of expected pregnancies is difficult but a reduced incidence has been shown when compared with numbers predicted

by various methods.^{2,6-9} The Yuzpe regimen has become an accepted and recommended method of postcoital contraception.¹⁰

Danazol has been suggested to be as effective as the Yuzpe method with fewer side effects.^{11,12} The anti-progesterone drug mifepristone has been shown to be an effective abortifacient and has been used as an interceptive and menstrual regulator,¹³⁻¹⁵ although it causes considerable cycle upset.^{16,17} We conducted a study to compare the effectiveness and side effects of these three methods (Yuzpe, danazol, mifepristone).

Subjects and methods

Women requesting emergency contraception after only one act of unprotected intercourse during their current cycle were considered for study if they presented within 72 hours of the act. Only women with regular cycles were included. The length of the cycle could vary from 21 to 35 days, but for one individual the variation over the previous three months could not exceed four days. Women who had been pregnant in the previous three months were excluded. The study was restricted to women who were aged 16-45 years, willing to sign consent, and available for follow up. Women with contraindications to oestrogen or progestogen (thromboembolic disease, liver disease, breast cancer, diabetes, jaundice, or pruritus of pregnancy), with known or suspected adrenal disease, or who were taking interacting drugs (liver enzyme inducers, broad spectrum antibiotics) were excluded. No woman had taken any sex steroids since her last menstruation. All women were interviewed by the same person (AMCW).

The date of the last menstruation, cycle length, and exact time of unprotected intercourse were noted. Any use of contraception (coitus interruptus, failed barrier), height, weight, and previous pregnancies and their outcome were recorded. Serum progesterone concentration was measured by quantitative radioimmunoassay.

Subjects were randomly allocated to receive the Yuzpe regimen (ethinyloestradiol 100 μ g and levonorgestrel 500 μ g repeated after 12 hours), danazol 600 mg repeated after 12 hours, or mifepristone 600 mg one dose only. The allocation schedule was constructed by using a computer based pseudorandom number generator with a uniform distribution. The schedule was prepared before the start of the study by JR, who did not participate in either the selection or assessment of women. The mifepristone was always taken in the clinic. The other two drug regimens were also always started within 72 hours of unprotected intercourse but the first dose was often taken after the visit to the clinic to obviate taking the tablets on an empty stomach or

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