ACKNOWLEDGEMENT

Supported in part by a grant from Pfizer.

Authors' affiliations

A El Maghraoui, A Bezza, F Tabache, A Abouzahir, D Ghafir, V Ohayon, M I Archane, Internal Medicine Department, Military Hospital Mohamed V, Rabat, Morocco
S Chaouir, Radiology Department, Military Hospital Mohamed V, Rabat, Morocco

Correspondence to: Professor A El Maghraoui; a_elmaghraoui@hotmail.com

Accepted 14 May 2002

REFERENCES

1 **Davies D**. Ankylosing spondylitis and lung fibrosis. Q J Med 1972;41:395–417.
2 **Appelrouth D**, Gottlieb NL. Pulmonary manifestations of ankylosing spondylitis. J Rheumatol 1975;2:446–53.
3 **Feltelius N**, Hedenstrom H, Hillerdal G, Hallgren R. Pulmonary involvement in ankylosing spondylitis. Ann Rheum Dis 1986;45:736–40.
4 **Bouchea DK**, Sundstrom WR. The pleuropulmonary manifestations of ankylosing spondylitis. Semin Arthritis Rheum 1989;18:277–81.
5 **Van der Linden S**, Valkenburg HA, Cats A, Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.
6 **Casserly IP**, Fenlon HM, Breanatch E, Sant FM. Lung findings on high-resolution computed tomography in idiopathic ankylosing spondylitis. Correlation with clinical findings, pulmonary function tresting and plain radiography. Br J Rheumatol 1997;36:677–82.
7 **Fenlon HM**, Casserly I, Sant SM, Breanatch E. Plain radiographs and thoracic high-resolution computed tomography in patients with ankylosing spondylitis. AJR Am J Roentgenol 1997;168:1067–72.
8 **Turetschek K**, Ebner W, Fleischmann D, Wunderbaldinger P, Erlacher L, Zontsich T, *et al*. Early pulmonary involvement in ankylosing spondylitis: assessment with thin-section CT. Clin Radiol 2000;55:632–6.

Effect of low dose weekly methotrexate on bone mineral density and bone turnover

S Patel, G Patel, D Johnson, L Ogunremi, J Barron

Ann Rheum Dis 2003;**62**:186–187

Wijnands and Burgers recently reported on a patient with psoriasis who developed stress fracture of the leg thought to be related to methotrexate treatment.[1] The role of methotrexate in the aetiology of fractures remains uncertain, because nearly all subjects reported had other risk factors for fracture, such as the underlying disease being treated. We recently examined a group of patients with psoriasis (without features of arthritis, to avoid the bias which may occur due to the arthritis and compensatory action of methotrexate on inflammatory disease activity)[2] to assess the effect of methotrexate on bone density and turnover.

After approval from the local ethics committee, patients with psoriasis, but without psoriatic arthritis or diseases or drug treatment known to adversely effect the skeleton, were recruited. We obtained information by interview and measured bone mineral density (BMD) by dual *x* ray absorptiometry (DXA) using a Lunar DPX device (Lunar Corp, Madison, WI). Daily calibration measurements using an external phantom were performed and monitored for machine drift. No significant drift was noted during the study period. Precision was calculated by the method of Gluer *et al*,[2] and at our centre is 1.3% for the lumbar spine and 1.8% for the femoral neck. Morning samples of blood and second void urine were taken for biochemical analysis. Data are presented as mean (SD) unless stated. The significance of differences between groups was tested using paired and unpaired Student's *t* tests where appropriate. One sample *t* test was used to determine if age adjusted BMD (Z scores) were significantly different from the densitometer control database. Correlations were examined using linear regression. A value of $p<0.05$ was considered significant.

Baseline assessments were performed on 30 patients, and 20 subsequently agreed to have repeat bone densitometry a mean of 21 months (range 17–24) later. The patients comprised 12 men and 18 women with a mean age of 56 years (range 32–85). Of the 18 women, 10 were postmenopausal (mean duration 21 years, range 3–39). All patients had been treated with methotrexate for a median duration of 2.0 years (interquartile range (IQR) 1.4–5.6). The cumulative median dose was 1387 mg (IQR 654–2250) and the weekly median dose was 9.8 mg (IQR 6.8–15.1).

Bone density was normal at the lumbar spine and femoral neck at baseline. Lumbar spine BMD was 1.205 (0.215) g/cm^2, the T score was –0.09 (1.98), and the Z score 0.833 (1.703). Respective values for the femoral neck were 0.938 (0.174) g/cm^2 , –0.654 (1.463), and 0.224 (1.109). BMD did not change significantly from baseline in the 20 patients who participated in the longitudinal phase of this study. There was no relationship between weekly or cumulative methotrexate dose and change in BMD over this period of time. Baseline biochemistry of the patients was normal including parathyroid hormone and markers of bone turnover. There was no significant correlation between the duration of methotrexate use or dose (weekly and cumulative), BMD or markers of bone turnover. There were no differences in BMD Z scores for either skeletal sites or bone markers when women were classified according to menopausal status. Similarly the sex of the subject did not affect BMD Z scores or bone markers.

We report the effects of methotrexate on BMD and bone turnover at baseline and over two years in patients treated with methotrexate for psoriasis. We found that the prevalence of osteoporosis was no greater than would be expected for the age of the patient (Z scores were normal) and that for most patients, markers of bone turnover at baseline were within the normal range. Also no change in BMD was found when a subgroup of 20 patients were followed up prospectively. Bone turnover was normal and there was no change in BMD with chronic treatment. The rationale for choosing the patients studied was to avoid any confounding effects of underlying disease such as rheumatoid arthritis, which can itself cause local and systemic osteoporosis and abnormal bone turnover.[2 4] None of our patients had systemic inflammatory disease and a recent study confirms that chronic psoriasis is not associated with osteoporosis.[5]

In our study BMD was measured at the standard skeletal sites for the diagnosis of osteoporosis. We did not measure BMD at sites of stress fracture reported with methotrexate,

which typically are the metatarsals or distal tibia as reported by Wijnands and Burgers.[1] These skeletal sites have a high cortical bone content and are under different and potentially greater mechanical strain than the spine or hip site. Thus whether methotrexate causes regional bone loss and whether mechanical strain is important in the pathogenesis of these stress fractures remains uncertain. Other limitations of our study include the relatively small sample size and short duration of follow up (21 months) which may result in type 2 errors. We also had to rely on the Lunar DPX manufacturer's control database to act as a control group as we did not have an aged match control group at baseline. Other confounding factors are that as the longitudinal phase was some time after initiation of methotrexate, early bone loss might have been missed, although this seems unlikely, as baseline Z scores were normal. We were only able to recruit 20 of the original 30 patients who participated in the cross sectional phase of this study, but this was owing to patient preference rather than side effects or lack of efficacy of the treatment. All the patients received methotrexate continuously during follow up. Although the dose of methotrexate in the patients studied was relatively low (median weekly dose 9.8 mg), we did not find a relationship between weekly or cumulative dose and bone turnover or BMD (both baseline and longitudinally).

In summary, our findings suggest that weekly methotrexate treatment in the doses used in this study, is unlikely to increase fracture risk at the common skeletal sites for osteoporotic fractures.

Authors' affiliations
S Patel, G Patel, D Johnson, Department of Rheumatology, St Helier Hospital, Epsom and St Helier NHS Trust, UK
J Barron, Department of Chemical Pathology, St Helier Hospital
S Patel, L Ogunremi, Osteoporosis Unit, Department of Rheumatology, St George's Hospital, UK

Correspondence to: Dr S Patel, Department of Rheumatology, St Helier Hospital, Carshalton, Surrey SM5 1AA, UK; spatel@sthelier.sghms.ac.uk

Accepted 10 June 2002

REFERENCES

1 **Wijnands M**, Burgers A. Stress fracture in long term methotrexate treatment for psoriaritic arthritis. Ann Rheum Dis 2001;60:736–8.
2 **Mazzantini M**, Di Munno O. Methotrexate and bone mass. Clin Exp Rheumatol 2000;18:S87–92.
3 **Gluer CC**, Blake G, Blunt BA, Jergas M, Genant K. Accurate assessment of precision errors: how to measure the reproducibility of bone densitometry techniques. Osteoporos Int 1995;5:262–70.
4 **Lems WF**, Dijkmans BAC. Should we look for osteoporosis in patients with rheumatoid arthritis?Ann Rheum Dis 1998;57:325–7.
5 **Millard TP**, Antoniades L, Evans AV, Smith HR, Spector TD, Barker JN. Bone mineral density of patients with chronic plaque psoriasis. Clin Exp Dermatol 2001;26:446–8.

Evaluation of a screening tool for inflammatory joint disease

J A Barbour, J Binding, M Bridges, C Kelly

Ann Rheum Dis 2003;**62**:187–188

The benefit of early treatment of inflammatory joint disease (IJD) with disease modifying drugs (DMARDs) to avoid progressive irreversible joint damage is well established. The time delay from onset of symptoms to starting a DMARD is determined by a number of factors, and early synovitis clinics have been developed to facilitate speedy referral and initiation of DMARD treatment. The efficiency of these clinics is dependent on appropriate referral.[1] Diagnosing early IJD is not easy; even specialists have been shown to disagree when tested.[2] Therefore an effective screening tool could be used to maximise identification of patients likely to have IJD and minimise unnecessary use of urgent appointments.

A simple eight point questionnaire (box 1) was devised to separate patients with and without IJD. It uses well recognised diagnostic criteria for rheumatoid arthritis (morning stiffness, rheumatoid factor, and erosions) but also includes more general markers of inflammation (erythrocyte sedimentation rate (ESR)), benefit from non-steroidal anti-inflammatory drugs (NSAIDs)/steroids, synovitis, and family history.

We prospectively studied 100 consecutive patients whom their general practitioner (GP) suspected might have IJD and had referred to one consultant for early assessment over a 10 month period. GP letters were initially screened by the consultant and then passed to the nurse practitioner who applied the questionnaire (box 1) to all patients before the consultant's assessment.

Characteristic distribution for IJD was positive if more than one joint was affected by pain or stiffness, but negative if the pattern affected predominately the distal interphalangeal joints of the hands or the base of the thumbs. Synovitis was defined as the affected joint being tender and swollen. The most recent ESR was used, radiographs of hands and feet were used for assessment of erosions, and benefit from NSAID/steroids was taken as a reported patient global assessment. The diagnosis was taken as that made by the consultant at the first assessment. In cases where there was some doubt, it was taken as the most likely diagnosis at the subsequent review appointment. Seventy six women and 24 men not known to have IJD were included with mean ages of 55 years (women) and 50 years (men). The consultant diagnosed 31 as having IJD, of whom 30 scored 3 or more on the questionnaire (27 rheumatoid arthritis, 2 psoriatic arthritis, 1 palindromic

Box 1 Questionnaire.

The presence or absence of the following items was recorded.
- Early morning stiffness >1 hour
- Characteristic distribution for IJD
- First degree relative with IJD
- Clinical evidence of synovitis
- ESR ≥20 mm/1st h (men), ≥30 mm/1st h (women)
- Positive rheumatoid factor (≥1/80)
- Erosions on hands or feet *x* ray
- Benefit from NSAID or steroids