of the three month follow up (that is, two months after discharge) in our study[1] in order to reflect the course of the effects and whether the different responsiveness of the SF-36 compared with the WOMAC remained consistent. In addition, we will publish further results of three monthly assessments up to the two year follow up of our patients during the next year.

The second issue deals with the fact that some items ask about activities of daily living and social participation which are not demanded or hardly possible to perform during a stay in the clinic. These are mainly the items contained in questions four (4a–4d) and five (5a–5c) comprising the role physical and role emotional scales. For this reason, we reported these two scales as part of the SF-36 for the sake of completeness, but we did not include them in the analysis of the comparison of WOMAC and the SF-36. Nevertheless, item 8, which is the bodily pain scale, is also affected by this problem. Müller *et al* dealt with this issue recently.[2] The authors created a modified SF-36m, which was adapted in items 4, 5, and 8 to the situation of a clinic stay. They concluded that bodily pain and role emotional did not show significantly different effects from those obtained by the original SF-36, but that the role physical scale was slightly more responsive in the SF-36m.

We used the SF-36 for three reasons. Firstly, the SF-36 assesses health status comprehensively—that is, not only pain and disease-specific scales as physical function, etc but also psychometric dimensions and dimensions of social participation. As a result, it gives an overall assessment of the patient's health status which is compatible with the WHO's new ICIDH or the future ICF concept defining health.[3 4] Secondly, the SF-36 can also be administered to "healthy" people and to patients with different diseases, which allows a comparison of the results with those for other patient groups and the general population. Thirdly, the SF-36 is one of the best tested, best known, and most widely used health measure all over the world.

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LETTERS

Is pamidronate effective for acute rheumatic pain?

Parenteral pamidronate is licensed in the United Kingdom for the management of Paget's disease, tumour related hypercalcaemia, and metastatic bone pain, where it can rapidly relieve symptoms.[1] It is also widely used for the prevention and treatment of osteoporosis, although this represents unlicensed use of the drug, and there is some evidence that it can be rapidly effective for pain relief in patients with osteoporotic vertebral fractures.[2 3] It has been used with some effect for the management of ankylosing spondylitis,[4] but the full extent of any analgesic properties of the drug has not been fully explored. These properties became apparent to us quite by chance in the three cases described here.

Case reports

Patient A

A 25 year old female nurse with known ankylosing spondylitis was admitted to hospital with worsening back and right buttock pain uncontrolled by regular opiate analgesia and a variety of potent non-steroidal anti-inflammatory drugs. Parenteral methylprednisolone was prescribed, followed by pamidronate 30 mg for "bone protection". In the event, pamidronate was given but not methylprednisolone, deferred owing to unexplained pyrexia. Shortly after receiving her pamidronate, her intractable pain was so greatly improved that methylprednisolone was declined and she was discharged three days later. The improvement seen has been sustained for over six months. The unexpected analgesic effect of pamidronate in this case led to its use in two subsequent cases.

Patient B

A 38 year old housewife with chronic low back pain was admitted with a short history of acute back pain and a modestly raised C reactive protein (14 mg/l). Isotope bone scan showed increased uptake in the fifth lumbar intervertebral disc. Magnetic resonance imaging identified abnormal signal from this disc suggestive of discitis. An infective cause was felt to be unlikely: antibiotics were not prescribed, but in view of her persistent symptoms, pamidronate 30 mg was given by intravenous infusion, with sufficient sustained improvement in her acute back pain to allow discharge two days later.

Patient C

A 33 year old male factory worker with a history of juvenile chronic arthritis since early childhood and spondyloarthropathy was admitted with generalised bone pain despite weekly oral methotrexate, phenylbutazone, and oral analgesia. Intercurrent diarrhoea was investigated but remained unexplained. Parenteral pamidronate 30 mg was given, leading to sustained improvement in his rheumatic pains.

Discussion

We believe these cases represent the first time that sustained analgesic efficacy has been attributed to a single dose of parenteral pamidronate in acute rheumatic pain not related to osteoporosis or neoplasia. The mechanism whereby pamidronate provides rapid onset sustained pain relief for metastatic bone disease or osteoporotic fractures is unknown. Many of the known effects of bisphosponates on bone structure and cell populations are unlikely to be rapidly analgesic.[5] However, it has been suggested that bones have complex sensory innervation, with nociception mediated by neuropeptides including substance P, prostaglandin E_2, and calcitonin gene related peptide which may be influenced by bisphosphonates.[6] There is no reason to believe that such an analgesic effect would be confined to bone affected by osteoporosis or neoplasm and might well extend to bone pain due to inflammation. In the three cases described many other factors might have led to the apparent response to parenteral pamidronate, including chance. However, the results suggest that the potential role of pamidronate in the control of acute rheumatic pain warrants further evaluation.

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Antibodies to β_2 glycoprotein I and cardiolipin in SSc

Systemic sclerosis (SSc) is a multisystem disease in which organ damage is characterised by fibrosis, microvascular occlusion, and proliferation of the vascular intima. The reported prevalence of anticardiolipin antibodies (aCL) in SSc varies from 0 to 25%,[1–7] and reports of clinical associations have been variable.[3 4 6 7] To our knowledge, only one study has examined antibodies to β_2 glycoprotein I ($a\beta_2$GPI) in SSc and shown a correlation with pulmonary hypertension and raised mean pulmonary artery pressure.[8] In our study we examined the frequency of $a\beta_2$GPI and aCL in SSc and Raynaud's phenomenon (RP).

Twenty six patients with SSc (16 diffuse, 10 limited), 23 with RP, and 21 healthy volunteers (employees at the research facility) were included in this retrospective study. Informed consent was obtained. All 16 patients with diffuse SSc and one patient with limited SSc patients met American Rheumatism Association (ARA) preliminary criteria for scleroderma.[9] The remaining nine with limited SSc had at least three of the following: sclerodactyly, calcinosis, Raynaud's phenomenon, oesophageal dysmotility, telangiectasia, or positive anticentromere antibodies. The patients with RP had no manifestations of connective tissue disease. Clinical and laboratory assessments were recorded at the initial visit.

$a\beta_2$GPI and aCL were measured by enzyme linked immunosorbent assay (ELISA; INOVA Diagnostics, Inc, San Diego, CA and Hemagen Diagnostics, Inc Waltham, MA, respectively). Commercially obtained HEp-2 slides (Immuno Concepts, Sacramento, CA) were used for indirect immunofluorescence (IIF). Samples were tested for antibodies to topoisomerase I (Scl-70), U1 ribonucleoprotein (U1-RNP), and Sjögren's syndrome antigens A and B (SS-A/SS-B) by double immunodiffusion.

Student's *t* test (two tailed) was used for comparison of means, and Fisher's exact test (two tailed) for analysis of frequencies. Age distributions were compared with the Mann-Whitney test because healthy controls described their age in decades, not years.

Table 1 summarises the demographics and laboratory data for the study group. The patients with SSc were significantly older than both the healthy controls ($p=0.005$) and the patients with RP ($p=0.02$). All mean laboratory values were within the normal range. Figure 1 compares the values for tests among the study groups except $a\beta_2$GPI IgG, where all tests were negative. IgM $a\beta_2$GPI were found in two patients with SSc (8%), one patient with RP (4%), and none of the healthy controls ($p>0.05$). Three (12%) patients with SSc, five (22%) with RP, and one (5%) of the healthy controls had positive tests for IgG or IgM anticardiolipin ($p>0.05$). The sera positive for aCL were not the same as those positive for $a\beta_2$GPI.

The two patients with SSc positive for $a\beta_2$GPI had mean disease duration of 19 months; both had cutaneous manifestations and one had hypoxia with decreased carbon monoxide transfer factor (TLCO). The three patients with SSc and aCL had mean disease duration of 112 months. One had hypoxia (with normal TLCO and non-restrictive pulmonary function tests), one had restrictive lung disease and digital ulcers, and one had oesophageal hypomotility. None of the study participants had thrombocytopenia or a history of deep venous thrombosis. Twenty two per cent of the group with Raynaud's disease had aCL, which is higher than the 8.7% reported by Vayssairat *et al*.[10] Patients with positive tests did not differ from those who had negative clinical manifestations or laboratory values.

All of the patients with SSc and RP and 13% of the healthy controls had positive IIF tests on HEp-2 substrates. None of the patients with SSc had antibodies to topoisomerase I (Scl-70) or SS-A/SS-B. No IIF pattern correlated with $a\beta_2$GPI or aCL.

In our study we found that the frequency of antibodies to β_2GPI and aCL was low in scleroderma, 8% and 12% respectively. There were no clear clinical or laboratory correlations with a positive test.

Table 1 Demographics and laboratory results in patients with SSc, RP, and normal controls

	Scleroderma (n=26)	Raynaud's phenomenon (n=23)	Normal controls (n=21)
Women	21	22	13
Men	5	1	8
Age groups		*(p=0.02)	*(p=0.005)
20–30	2	4	6
31–40	8	12	7
41–50	6	4	5
50+	10	3	3
Disease duration (months), mean (range)	69 (6–244)	89.7 (1–364)	N/A
Anticentromere antibodies	14 (54%)	5 (22%)	0 (0%)
Nucleolar antibodies	5 (19%)	4 (17%)	1 (5%)
Haemoglobin (g/l)	129 (SD 32)	134 (SD11)	N/A
Platelets (cells×10^9/l)	339 (SD 126)	293 (SD 61)	N/A
CK (μmol/l)	128 (SD 144)	79 (SD 38)	N/A
BUN (mg/l)	140 (SD 40)	130 (SD 30)	N/A
Creatinine (mg/l)	9.1 (SD 1.3)	9.2 (SD 1.0)	N/A

BUN, blood urea nitrogen; CK, creatine kinase.
*Comparison of age distribution versus SSc.

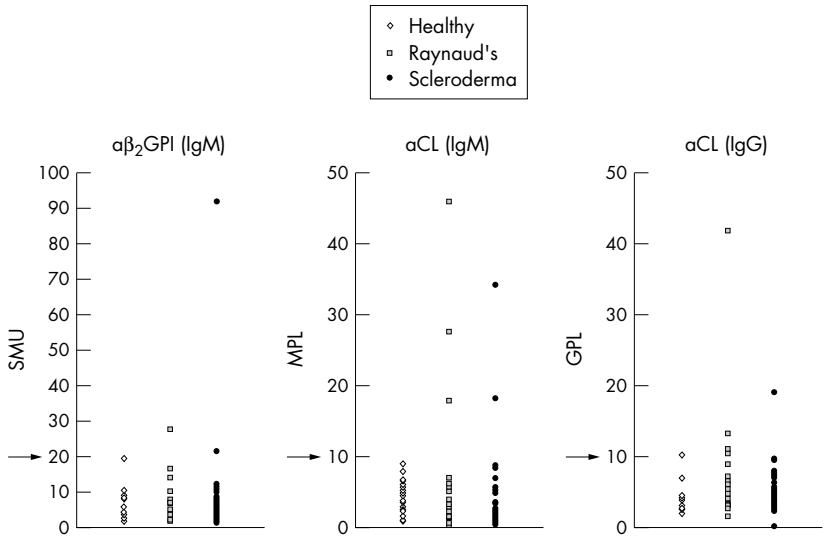

Figure 1 Comparison of $a\beta_2$GPI and aCL antibody levels in patients with SSc, RP, and normal controls. The numbers on the ordinate represent optical density values converted to SMU (standard IgM β_2GPI units), MPL (1 MPL unit = the binding of 1 μg/mL IgM aCL), or GPL (1 GPL unit=the binding of 1 μg/ml IgG aCL). The arrows indicate the cut off values for each dataset.

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