acid or H-7 dihydrochloride reduced the IL16 RT-PCR signals. As okadaic acid and H-7 reduced the cell viability prominently, the decreased IL16 signals probably result from the induction of cell death. In contrast, incubation of the cells with PMA, ionomycin, cAMP, MAS-7, or staurosporine did not reduce the viability.

Protein kinase inhibitor staurosporine has been reported to induce apoptosis in some cells.[5] Enumeration of dead cells and observation of morphological changes by microscopy upon staurosporine treatment did not give any indication of reduced cell viability at concentrations 10- to 100-fold above the concentrations used in our experiments. RA SF are resistant to induction apoptosis by overexpression of sentrin, Bcl-2, and mutant forms of p53.[6–9] Therefore the RA SF, especially, may be able to respond to a staurosporine induced pathway with enhanced IL16 transcript amounts. Because protein kinase C activator PMA reduced IL16 transcripts in SF, the data suggest that in SF the transcription of IL16 might be regulated through protein kinase C dependent pathways.

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Obstructive sleep apnoea as a cause of fatigue in ankylosing spondylitis

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Fatigue is a common symptom in ankylosing spondylitis (AS) occurring in 65% of patients[1 2] and forms part of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).[3 4] Fatigue has been attributed to sleep disturbance from back pain and stiffness and usually increases with increased disease activity, but can occur independently of AS activity, suggesting the possibility of other causes.[1 2] One such cause in the middle aged population is sleep apnoea syndrome (SAS). SAS is defined as 10 or more episodes an hour of airflow interruption for ⩾10 seconds during sleep. It occurs in up to 4% of middle aged people,[5] and is associated with increased morbidity and mortality due to higher rates of cardiovascular disease and increased accidents.[6 7]

We suggest that AS predispose subjects to SAS through several mechanisms, including: restriction of the oropharyngeal airway from temporomandibular joint involvement or cervical spine disease causing pharyngeal and tracheal compression (as has been described in rheumatoid arthritis[8]); cervical spine disease causing compression of the respiratory centres in the medulla resulting in central depression of respiration; or restrictive pulmonary disease. We carried out an observational study to assess the prevalence of SAS, and to investigate whether it contributes to fatigue in AS.

PATIENTS AND METHODS

Consenting volunteers with classical AS (modified New York Criteria 1984) were recruited prospectively from a hospital rheumatology clinic and assessed using: (*a*) the BASDAI[3 4]; (*b*) the Epworth Sleepiness Scale (ESS),[9] a validated self administered eight item questionnaire that assesses daytime sleepiness in adults (a score of ⩽10 is normal); (*c*) the Hospital Anxiety and Depression Scale (HAD)[10] (a score of ⩽7 indicates normal mood); (*d*) height, weight, neck circumference; (*e*) spinal mobility by occiput-wall distance, chest expansion, and Schöber's test; (*f*) respiratory measurements consisting of full spirometry and carbon monoxide diffusion studies, arterial blood gases, and night oximetry on two consecutive nights (using a five channel EdenTec Recorder and EdenTrace Software Version 1.3, Nellcor, Puritan and Bennett, Ltd) to assess heart rate, chest impedance, nasal airflow, oxygen saturation, and snoring level.

RESULTS

Of 22 recruited patients, 17 (77%) completed the assessments, 14 male and three female. Pulmonary function testing was normal in nine (53%) patients, classically restrictive in six (35%), borderline restrictive in two (12%), and obstructive in none. Two (12%) patients fulfilled criteria for SAS when

Table 1 Results

Variable	Total group n=17 (SD)	No SAS n=15 (SD)	*t* Test (p)	SAS n=2 (SD)	Patient 1	Patient 2
Age (years)	47.1 (12.8)	46.9 (13.5)	0.76	49.0 (7.1)	54	44
Disease duration (years)	26.2 (13.3)	26.1 (14.2)	0.86	27.0 (4.2)	30	24
BASDAI	4.9 (1.8)	4.8 (1.9)	0.59	5.5 (1.3)	4.6	6.4
Fatigue component of BASDAI	6.0 (2.5)	5.8 (2.5)	**0.04**	8.0 (0.7)	8.5	7.5
HAD	5.3 (3.0)	4.9 (2.9)	0.35	8.0 (2.8)	6	10
ESS	9.7 (5.5)	8.6 (5.1)	**<0.01**	16.5 (0.7)	17	22
Alcohol (units/week)	6.7 (8.9)	7.5 (9.1)	**0.01**	0.0 (0.0)	0	0
Smoking (cigarettes/day)	6.7 (8.7)	6.2 (8.4)	0.77	10.0 (14.1)	0	20
Body mass index	26.4 (5.0)	25.6 (4.6)	0.13	32.7 (3.1)	30.5	34.9
Neck circumference (cm)	39.4 (8.7)	39.2 (9.2)	**0.02**	41.0 (4.2)	38	44
Occiput wall (cm)	5.9 (5.0)	5.5 (4.4)	0.71	9.0 (9.9)	2	16
Schobers (cm)	4.8 (4.0)	5.1 (4.2)	0.23	3.0 (1.4)	4	2
Chest expansion (cm)	2.9 (1.8)	3.1 (1.8)	0.09	1.5 (0.7)	2	1

SAS, sleep apnoea syndrome; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HAD, Hospital Anxiety and Depression Scale; ESS, Epworth Sleepiness Scale.

assessed by night oximetry. Both these patients had an obstructive type of SAS (table 1). [3]

Compared with those without SAS, the two patients with SAS had significantly higher mean ESS scores (SAS 16.5 (0.7) *v* no SAS 8.6 (5.1), p<0.01), fatigue component of the BASDAI (SAS 8.0 (0.7) *v* no SAS 5.8 (2.5), p=0.04), and neck circumference (SAS 41.0 (4.2) *v* no SAS 39.2 (9.2), p=0.02). The overall BASDAI scores (SAS 5.5 (1.3) *v* no SAS 4.83 (1.9), p=0.59) and body mass index (SAS 32.7 (3.1) *v* no SAS 25.6 (4.6), p=0.13) were not significantly different between the two groups. Neither of the two patients with SAS drank alcohol, but no other significant differences were found between the two groups (table 1).

DISCUSSION

SAS and AS can coexist. We found a higher prevalence of SAS in patients with AS (12%) than has been reported in the general population (1–4%).[11] However the sample size was small and a larger study would be required to determine the true prevalence. As might be expected, the patients with SAS had high subjective scores of daytime sleepiness, which was mirrored by the high scores on the fatigue component of the BASDAI. The overall BASDAI scores of the patients with SAS were not significantly different from the remainder of the cohort, suggesting that disease activity in these two patients did not differ from that of the cohort, and the high fatigue component scores were rogue results reflecting the underlying SAS and not AS activity. None of the specific measurements of spinal involvement in the affected patients were significantly different from those of the cohort, suggesting that the degree of spinal involvement in AS was not a contributing factor in the development of SAS in these two subjects. The two affected patients were both obese middle aged men and had a classical restrictive pattern on pulmonary function testing, all of which are known to be risk factors for the development of SAS. Both patients were treated with continuous positive airway pressure ventilation at night, and their levels of fatigue improved subjectively, which was reflected in a fall of their ESS scores (patient 1: 17 to 9, patient 2: 22 to 12).

SAS can be a contributing factor to fatigue in AS. Patients with excessive fatigue or scoring high on the fatigue component of the BASDAI without other evidence for continuing disease activity should be assessed for other causes of fatigue. Detection and treatment of SAS can lead to improvement in fatigue symptoms in these patients and reduce the associated morbidity and mortality of SAS.

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