Conclusion Long-term TDF treatment produced stable analgesia in patients with CNCP and was preferred by the majority of patients to their previous medication. TDF was generally well tolerated in comparison with similar agents.

REFERENCES

- 1 Cleeland CS. *JAMA* 1998;279:1914–15
- 2 Arkinstall W, Sandler A, Goughnour B, et al. *Pain* 1995;62:169–78
- 3 Jadad A, Carroll D, Glynn C, Moore R, McQuay H. *Lancet* 1992;339:1367–71
- 4 Moulin D, Iezz A, Amireh R, et al. *Lancet* 1996;347:143–7
- 5 Allan L, Hays H, Jensen N-H, et al. *BMJ* 2001, in press

SAT0126 EXPRESSION OF OPIOID RECEPTORS IN CHRONIC PAIN PATIENTS WITH FIBROMYALGIA, OSTEOARTHRITIS, PSYCHOSIS, RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

¹S Salemi, ²A Aeschlimann, ¹B Michel, ¹R Gay, ¹S Gay, ¹H Sprott. ¹Ctr Experimental Rheumatology, Department Rheumatology and Institute Physical Medicine, University Hospital, Zürich, Switzerland; ²Rheuma, Rehabilitationsklinik, Zurzach, Switzerland

10.1136/annrheumdis-2001.559

Background Chronic pain, usually considered to be continuous or episodic pain of at least six months duration, is a common cause of major disability. Chronic pain involves affective, behavioural and social dimensions. The opioid system plays a major role in the pain controlling systems.

Objectives Therefore, our main focus was to investigate the patients health status and differences in the expression of opioid receptors in skin and muscle tissues of chronic pain patients with fibromyalgia (FM), osteoarthritis (OA), psychosis (PS), rheumatoid arthritis (RA) and healthy controls (C).

Methods The Visual Analogue Scale (VAS) and the Short Form 36-item (SF-36) Health Survey questionnaire were given to the patients. Snap frozen sections from skin and muscle tissues (taken from the left deltoid region) were obtained from 8 FM (all female, 30–65 years of age), 4 OA (2 females and 2 males aged 48–72 years), 5 female PS patients (aged 40–79 years), 3 RA (1 female and 2 males aged 48–72 years), and 9 age-matched healthy females (C). Total RNA was extracted, reverse transcribed, amplified and quantified by real time PCR (TaqMan, Perkin Elmer) using fluorogenic probes and specific primers for Delta (DOR), Kappa (KOR) and Mu opioid receptors (MOR). Intensity of expression in each tissue was determined. The expression of 18S mRNA was used as an internal control.

Results We observed a significantly reduced score in all patient groups compared to the control group regarding physical function in the SF-36 as well as in the VAS. An increase of DOR mRNA expression was found in PS and RA muscle, a decrease of KOR mRNA expression could be detected in OA skin compared to C. An increased expression of DOR (81.0 fold $p = 0.001$) and of KOR (13.6 fold $p = 0.009$) mRNA was detected in FM skin compared to skin of healthy controls. This expression was more increased in FM than any other investigated chronic pain condition. MOR was detected only in one skin and one muscle sample of two different PS patients.

Conclusion Patients expressing high levels of DOR and KOR including patients with FM, PS, and RA might be treated with novel therapeutic approaches modulating opioid receptors expression by selective opioids.

Dr. Salemi was supported by the Zurzach foundation and Dr. Sprott by the AFSA and the Olga Mayenfisch foundation.

Abstract SAT0126 Table 1

	FM skin	FM Muscle	OA skin	OA Muscle	PS Skin	PS Muscle	RA Skin	RA Muscle
DOR	+	=	-	+	-	+	-	+
KOR	+	=	-	+	-	+	-	-

The statistical calculation of the diseases compared to healthy control was performed by the Mann-Whitney test. *: $p < 0.05$, +: increase, -: decrease, =: no change.

SAT0127 RANDOMISED, CROSSOVER AND OPEN-LABEL TRIALS DEMONSTRATE THE EFFICACY OF TRANSDERMAL FENTANYL (DUROGESIC®) FOR THE TREATMENT OF CHRONIC NON-CANCER PAIN

¹L Allan, ²K Milligan. ¹The Pain Clinic, Northwick Park and St Mark's NHS Trust, Harrow, UK; ²Department of Anaesthesia, South Cleveland Hospital, Middlesbrough, UK

10.1136/annrheumdis-2001.560

Background The value of opioids is recognised internationally in the management of chronic non-cancer pain (CNCP), and patient preference in relation to pain relief has become increasingly important in analgesic selection. When comparing opioids that have been titrated to effect we cannot logically expect to see much difference in efficacy.¹ Thus, patient preference, while important for all clinical decisions, deserves a special emphasis when treatment efficacies are comparable, or when therapies can markedly affect patients' quality of life.² The patient is, therefore, likely to be the best judge of the delicate balance between analgesic efficacy, side-effects and the overall pain experience. This reflects our choice of pragmatic outcome measures, such as quality of life and patient preference, in addition to pain measurements, for the clinical trials of opioids in CNCP.

Objectives

Methods We report here the results of a large, multicentre, 8-week, randomised, two-way crossover trial (study A) of transdermal fentanyl (TDF; Durogesic®) versus sustained-release morphine (SRM; MS Contin®), in which patient preference, pain control, quality of life and adverse events were assessed in patients with CNCP ($n = 256$).³ Subsequently, an open-label, non-randomised, 12-month study (study B) of TDF evaluated the long-term use of TDF in CNCP patients ($n = 532$),⁴ of whom 103 had participated in study A.

Results In study A, 65.1% of patients preferred treatment with TDF to SRM (27.8%), with 7.1% expressing no preference. The main reason for preference was better pain relief, as more patients considered that pain control was 'good' or 'very good' with TDF than with SRM therapy (35% vs 23%, respectively, $p = 0.002$). Furthermore, patients using TDF generally had higher overall quality-of-life scores than those receiving SRM in each of the SF-36 categories with significant differences for bodily pain, vitality, social functioning and mental health categories ($p < 0.005$). The TDF group were less likely to experience constipation (48% vs 29%, respectively, $p < 0.001$) than those receiving SRM. In study B, treatment with TDF provided stable, sustained, long-term pain control in large numbers of patients. After initial dose titration, the mean TDF dose stabilised without the loss of analgesic efficacy (only 7% of patients withdrew because of insufficient pain relief). Thus, the development of tolerance to TDF was not a clinical problem. TDF treatment was preferred over previous opioid treatment by 69% of patients, primarily because of superior pain relief, followed by greater convenience and fewer adverse effects.

Conclusion Superior pain relief, less constipation and better quality of life were associated with TDF compared with SRM therapy. TDF was generally well tolerated and effective.

REFERENCES

- 1 McQuay H. *Lancet* 1999;353:2229–32
- 2 Goodare H, Lockwood S. *BMJ* 1999;319:724–5
- 3 Allan L, et al. *BMJ* 2001, In press
- 4 Milligan K, et al. *J Pain* 2001, In press

SAT0128 PATTERNS OF COGNITIVE IMPAIRMENT IN BEHÇET'S DISEASE

¹G Triolo, ²R Monastero, ²G Lopez, ²M Mannino, ¹A Ferrante, ¹F Ciccio, ¹E Giardina, ²R Camarda. ¹Department of Internal Medicine, Section of Rheumatology; ²Division of Neurology, University, Palermo, Italy

10.1136/annrheumdis-2001.561

Background Cognitive dysfunction is a common finding in patients with Behçet's disease.

Objectives The pattern of neuropsychological dysfunction in patients with Behçet's disease (BD) was examined. The influence of current or past clinically overt central nervous system involvement, disease activity, corticosteroid use, HLA B51 allele, and anxiety and depression levels were evaluated.

Methods Twenty-two BD patients fulfilling the criteria of the International Study Group for Behçet Disease, and twenty-two healthy controls, similar for age, gender and education were included in the study. Patients and controls underwent to a standardised battery of neuropsychological and psychological tests. Disease activity was assessed by using the Behçet Current Activity Index (BCAI). The current daily dosage of prednisone (mg/day) was recorded.

Results Cognitive impairment was identified in 41.0% (9) of patients with BD ($p < 0.0008$ vs. control). A significantly greater proportion of patients with BD than controls was impaired in tasks assessing attention, episodic memory, semantic and visuospatial abilities (P from < 0.05 to < 0.005). As concern psychological distress BD subjects were significantly more anxious ($P < 0.005$) and depressed ($P < 0.01$) than healthy controls. The presence of current or past clinically overt central nervous system involvement, current steroid medication, disease activity, HLA B51 positivity, and psychological distress could not account for these findings.

Conclusion Cognitive dysfunction is a common finding in BD patients. Our series suggest that BD can be associated with a specific pattern of cognitive deficit, involving mainly long-term verbal and visuospatial abilities.

SAT0129 ANTALGIC EFFECTS OF U69593, A KAPPA AGONIST, DO NOT IMPLICATE ADENOSINE RELEASE

T Pham, JC Peragut, H Rochat, P Lafforgue, R Guieu. *Rheumatology, CHU Timone, Marseille, France*

10.1136/annrheumdis-2001.562

Background There is evidence that endogenous adenosine (ADO) is implicated in the modulation of opiate action in central and peripheral nervous system, via both A1 and A2A receptors.

Objectives However, little is known about the interaction between opioid receptor agonist subtype and ADO release at the supraspinal level. We sought to answer two questions: first, what subtype of opioid receptor is more particularly implicated in the

modulation of ADO uptake by the supraspinal central nervous system cells? Second, is there a relationship between the modulation of extracellular ADO concentration by opioid agonist-subtype and the analgetic effects?

Methods We evaluated the effects of caffeine, a non specific ADO receptor antagonist on the hot-plate and tail pinch test latency increase that is induced by i.c.v. administration of oxymorphone hydrochloride, SNC 80 or U69593 (respectively μ , δ and κ agonist).

We also evaluated the effects of these opioid receptor agonists on the uptake of ADO by whole brain synaptosomes (HPLC).

Results Tail-pinch test and Hot-plate latencies

Opioids and ADO agonists induce an increase both in tail-pinch test and hot-plate latencies in a dose dependant manner and in the rank order as follows: Oxymorphone hydrochloride $>$ CCPA $>$ SNC80 $>$ CGS21680 = U69593. No increase in tail-pinch test and hot-plate latencies was observed ten minutes after i.c.v injection whatever the drug tested.

Opioids and ADO agonists have synergistic effects when coinjected. The rank order was: CCPA + Oxymorphone $>$ CCPA + SNC80 = CGS21680 + Oxymorphone $>$ CCPA + U69593 = CGS21680 + SNC80 $>$ CGS21680 + U69593. The increase in latencies induced by Oxymorphone and SNC80 (but not U69593) was partly reversed by coinjection of caffeine. Caffeine alone had no effect on latencies.

ADO uptake

ADO uptake was evaluated by measuring the decrease in adenosine concentration in the supernatant as a function of time. Oxymorphone hydrochloride at 10 μ M increased ADO concentration by a mean of 16, 21 and 25% at times 5, 30, and 60 s respectively. SNC80 (10 μ M) increased ADO concentration by 17, 16 and 40% at times 5, 30 and 60 s. At 100 μ M, SNC80 increased ADO concentration by 26, 24 and 60% at times 5, 30 and 60 s. U69593 did not significantly modify ADO concentration in the supernatant whatever the dose used. Finally, none of the opioids tested had a significant effect on ADO uptake at 1 μ M concentration.

Conclusion In summary, we found that oxymorphone and SNC80, but not U69593 (respectively μ , δ and κ agonist) inhibits ADO uptake by brain cells. Furthermore, caffeine which is a non specific ADO receptor antagonist, failed to reverse analgetic effect obtained with U69593 in a acute pain model.

These results suggest that the analgetic effects of κ opioid agonist does not implicate ADO release.

SAT0130 TOXIC PSYCHOSIS RELATED WITH HYDROXYCHLOROQUINE

P Barbosa, M França*, I Almeida, F Farinha, C Vasconcelos. *Department of Internal Medicine, Hospital Geral de Santo António, Porto, Portugal*

10.1136/annrheumdis-2001.563

Background Hydroxychloroquine is one of the commonest anti-rheumatic drugs, being well tolerated and traditionally safe.

Objectives

Methods The authors report a case of a 52-year-old woman with a 8 week symmetric polyarthrititis, involving the hands, feet, knees and elbows and morning stiffness lasting for more than 60 min. The rheumatoid factor was positive and the X-rays findings were normal.

At the time of the first appointment she already had been treated with different NSAID without clinical improvement.