Conclusion We can conclude on this basis that the results confirmed most of our expectations but the experiment allowed us to refine our *a priori* hypothesis.

SAT0124 COMPARATIVE SAFETY AND EFFICACY OF TRANSDERMAL FENTANYL (DUROGESIC®) AND SUSTAINED-RELEASE ORAL MORPHINE (MS CONTIN®) IN PATIENTS WITH CHRONIC NON-CANCER PAIN: RESULTS OF A LARGE, MULTICENTER, RANDOMISED, CROSSOVER TRIAL

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10.1136/annrheumdis-2001.557

Background Opioids are the most powerful analgesics, but politics, prejudice and continuing ignorance still impede optimum prescribing.¹ Furthermore, opioids are the mainstay of cancer pain management. Retrospective and survey data have confirmed the efficacy of opioids in chronic non-cancer pain (CNCp) and found that fears of addiction were not justified in patients with no prior history of drug abuse.² While morphine, usually prescribed orally in a sustained-release formulation for the treatment of CNCp, is the standard opioid against which others are judged, severe constipation (a persistent complication of some opioids) may adversely affect some patients' quality-of-life more than their chronic pain.³ Fentanyl, delivered in a transdermal controlled-release formulation, has demonstrated analgesic efficacy in cancer pain and is associated with less constipation than morphine.⁴ Recognising the increasing importance of patient preference and choice, the authors investigated whether CNCp patients accustomed to opioids would prefer transdermal fentanyl (TDF) to sustained-release oral morphine (SRM).

Objectives

Methods A randomised, multicenter, international, open-label crossover trial assessed 8 weeks of TDF and SRM therapy. Patients previously treated with opioids with CNCp, were randomised to receive TDF and then SRM, each for 4 weeks, or the same treatments in reverse order.

Results Of the 256 patients entering the study 196 completed the trial, with 38 and 22 patients withdrawing during the TDF (n = 126) and SRM (n = 130) treatment periods, respectively. Most patients (65.1%) preferred TDF (p < 0.001), 27.8% preferred SRM and 7.1% expressed no preference. More patients considered that pain control was 'good' or 'very good' with TDF than with SRM (35% vs 23%, p = 0.002). Patients using TDF had, on average, higher quality-of-life scores than those receiving SRM. The incidence of adverse events was similar in both treatment groups; however, more subjects experienced constipation when treated with SRM than with TDF (48% vs 29%, respectively; p < 0.001). More patients withdrew because of adverse events during the TDF than in the SRM treatment periods (10% vs 5%, respectively). However, within a subgroup of 66 patients that had used neither fentanyl nor morphine prior to the study (they had used other opioids), similar numbers withdrew due to adverse effects during TDF and SRM treatments (11% vs 10%, respectively).

Conclusion Both TDF and SRM treatments were well tolerated, with good safety profiles in patients with CNCp who had previously been treated with opioids. Superior pain relief and less constipation were associated with TDF compared with SRM therapy.

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SAT0125 TRANSDERMAL FENTANYL (DUROGESIC®) PRODUCES STABLE ANALGESIA AND IMPROVED QUALITY OF LIFE IN PATIENTS WITH CHRONIC NON-CANCER PAIN. THE RESULTS OF A 12-MONTH STUDY

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10.1136/annrheumdis-2001.558

Background Persistent and misplaced fears about the risks of tolerance, physical dependence and addiction have led to the underuse of opioids for the treatment of chronic non-cancer pain (CNCp). Opioids are widely used for the alleviation of acute pain and cancer pain, and are established as the second and third steps of the World Health Organisation analgesic ladder. Evidence suggests, however, that pain is frequently undertreated even for these indications.¹ Nevertheless, several short-term, randomised controlled trials have shown that opioids can be used successfully to treat CNCp without causing undue adverse events.²⁻⁴ A previous randomised crossover trial demonstrated that, over a 2-month period, 256 patients with CNCp preferred transdermal fentanyl (TDF) to sustained-release oral morphine due to better pain control, less constipation and some improvements in quality-of-life parameters.⁵ Although these short-term data are encouraging, no prospective trials have assessed the long-term efficacy and safety of opioid analgesia in CNCp.

Objectives The objectives of this international, multicenter, open-label trial were to assess the efficacy and safety of up to 12 months' therapy with TDF in patients with CNCp.

Methods The efficacy and safety of up to 12 months' therapy with TDF was assessed in patients with CNCp who required continuous opioid analgesia. Patients' opioid preference (compared with their previous analgesic), pain control and quality of life were evaluated. TDF therapy was initiated at an equianalgesic dose to pre-trial opioids, then titrated to maintain acceptable pain control and side-effects.

Results Of the 532 patients recruited, 301 (57%) completed the full 12-month trial. A total of 530 patients were included in the safety analysis and 524 in the efficacy analysis. During the study 130 patients (25%) from the efficacy group withdrew because of adverse events and 39 (7%) due to insufficient analgesia. Weekly assessments indicated that the percentage of patients who perceived pain control as very good, good or moderate remained stable over 12 months, at an average of 67%, with 47% citing better analgesia and 27% convenience as the main reason. Global treatment satisfaction also remained stable, with 42% reporting very good or good pain control. Medical Outcomes Study (MOS) and Short Form 36 (SF-36) quality-of-life measures showed improvements after 12 months' treatment compared with baseline. The most common adverse events were nausea, somnolence, constipation, vomiting and increased sweating. One of the nine deaths during the trial was considered possibly related to TDF treatment (severe bronchopneumonia). No problems of opioid withdrawal symptoms or addiction were encountered.

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.

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

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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

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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.