the pathogenesis of calcium pyrophosphate arthropathy and osteoarthritis.

Objectives

Methods A combination of physical cloning and candidate gene approach were employed to define CCAL2. Novel expressed sequence tags (ESTs) with expression in cartilage and which mapped to the critical region were identified from EST databases of GenBank. PCR generated DNA fragments from ESTs were radiolabelled using radioactive phosphorus and used as probes in Southern blot hybridization of high density plasmid artificial chromosome (PAC) filters. PACs were identified following autoradiography of the hybridisation membranes and the selected PACs were supplied by the UK HGMP resource centre in Cambridge. The Online Mendelian Inheritance in Man OMIM cytogenetic map was used to identify possible candidate genes within or near the critical region.

Results Six novel ESTs with high cartilage expression, identified 55 PACs following Southern blot hybridization. End sequencing of the PACs allowed the construction of a contig containing 25 PACs across the critical region. Two candidate genes were identified from OMIM. The first gene TRIO codes for a transmembrane multidomain protein which promotes the exchange of GDP for GTP in the extracellular matrix. An abnormality in this pathway is likely to produce an increase in extracellular triphosphate, which has a key role in inorganic pyrophosphate metabolism. The second gene ANK has only recently been mapped to the same location and it is responsible for articular calcification with associated arthritis in mice.

Conclusion The CCAL2 region has been physically mapped and two strong candidate genes are being screened for possible disease causing mutations. This gene should provide a greater understanding of pyrophosphate metabolism and of osteoarthritis with which there is a common association.

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OP0115 POLYMORPHISM AT THE TYPE I COLLAGEN (COLIA1) AND RELATIVE RISK OF OSTEOPOROSIS AND VERTEBRAL FRACTURES IN POSTMENOPAUSAL WOMEN

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Background Twin and family studies have demonstrated that an important degree of the population variance in bone mineral density (BMD) is attributable to genetic factors.

Objectives A polymorphism in the collagen type I alpha 1 (COLIA1) gene has recently been associated with low bone mass and fracture incidence.

Methods We analysed the relationship between COLIA1 gene polymorphism, lumbar spine and hip BMD, T-score and fracture incidence in a population of 319 postmenopausal women classified by WHO standards: 98 non-osteoporotic women (NOPW) (57.4 ± 6.2 yrs), 146 osteoporotic women without fracture (OPW without fracture: OPWnF) (60.0 ± 5.2) and 75 osteoporotic women with fracture (OPW with fracture: OPWwF) (61.2 ± 6.3 yrs). The COLIA1 genotype was assessed by polymerase chain reaction and Bal I endonuclease digestion. Genotype

frequencies for the total group were 49.2% "SS" homozygotes, 39.5% "Ss" heterozygotes and 11.3% "ss" homozygotes.

Results We found significant differences in the percentage of homozygous "ss" between NOPW and OPW (6.1% and 13.6% respectively). However, the incidence of genotype "ss" in OPWnF was 6.2% and 28% in OPWwF. We observed no associations between the COLIA1 genotype and lumbar and hip BMD. However, the lumbar spine T-scores were lower in the "ss" group than in the "Ss" and "ss" group. The incidence of fractures (64 vertebral and 11 colles) varied significantly by genotype: "SS" 21.7%; "Ss" 15.9%; and "ss" 58.3% (chi-square = 15.43; $p < 0.0001$); this resulted in a fracture odds ratio of 5.96 (95% confidence interval 2.26-15.69). Logistic regression analysis of fracture prevalence showed that for prevalent fractures, the women with "ss" group had 4.17 times risk of the woman "SS" + "Ss" groups. When prevalence was adjusted for BMD and T-scores, the respective fracture risk was 2.6 and 2.94 for the "ss" group versus the other genotypes (SS+Ss).

Conclusion A slight association was found between lumbar T-score and gene COLIA1 polymorphism. Expression of the "ss" allele seems to be related with a higher incidence of fracture in postmenopausal women and was independent of bone mineral density.

SAT0099 SOFT TISSUE RHEUMATISM IN IRAQI DIABETIC PATIENTS

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Objectives To study the prevalence of soft tissue rheumatism in Iraqi diabetic patients (both IDDM and NIDDM) and to evaluate association between these sequelae and the duration of the disease.

Methods Limited joint mobility (LJM), Dupuytren's Contracture (DC), flexor tenosynovitis (FTS), frozen shoulder (FS) and carpal tunnel syndrome (CTS) were assessed in 100 Iraqi diabetics (50 insulin dependent, 50 non insulin dependent DM) and (50) non-diabetic control matched for age and sex, according to clinical examination (signs and symptoms) and electrophysiological study.

Results Prevalence of LJM, in IDDM vs. NIDDM was (56% vs. 36%), FTS (20% vs. 38%), DC(20% vs 16%), FS(22% vs 40%) and CTS(26% vs 16%).

There was significant statistical difference ($p < 0.05$) between IDDM and NIDDM, regarding LJM, FS, and FTS, the first was higher in IDDM and the last two were higher in NIDDM, while there was no significant and statistical difference regarding CTS and DC.

Conclusion Soft tissue Rheumatism occurs more frequently in both IDDM and NIDDM than in control ($p < 0.05$). Their occurrence appeared to be directly related to disease duration regarding LJM, DC and CTS. The most common sequelae in IDDM was LJM while FS was the most frequent abnormality detected in NIDDM.

Patients with IDDM had been found to be more susceptible to develop multiple rheumatic sequelae than patients with NIDDM($p < 0.05$).

SAT0100 FENOFIBRATE REDUCES SERUM URATE IN PATIENTS WITH HYPERURICAEMIA ESTABLISHED ON ALLOPURINOL

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Background Fenofibrate is an established treatment for various forms of hyperlipidaemia and is unique amongst the fibric acid derivatives due to its ability to lower serum urate. This urate-lowering effect has not, however, been assessed in patients established on allopurinol, the most widely used drug in the prevention of gout.

Objectives To assess the short-term urate lowering effect of fenofibrate in patients with hyperuricaemia and gout already treated with allopurinol.

Methods 11 patients (10M:1F), mean age 56.5 (range 38–74) with a history of either chronic tophaceous or interval gout in association with hyperuricaemia were assessed in an open cross-over study. Each had been treated with allopurinol 300 mg/day or more for at least 3 months and had been free of acute gout for a minimum of 1 month. Each patient received micronised fenofibrate 200 mg once daily for 3 weeks. Before this was commenced, the following were measured: serum urate and creatinine, 24 hr urinary output of urate and creatinine, liver function tests, creatine kinase and fasting serum lipids. These were repeated at the end of fenofibrate therapy and again 3 weeks later. Allopurinol was continued throughout the study period.

Results Fenofibrate was associated with a 24% reduction in serum urate after 3 weeks of treatment (mean 0.36 ± 0.11 vs 0.29 ± 0.07 mmol/l; $p = 0.002$). The urate-lowering effect was rapidly reversed on its withdrawal (0.29 ± 0.07 vs 0.37 ± 0.09 mmol/l). There was a rise in urate clearance of 56% (6.7 ± 3.1 vs 10.5 ± 5.6 ml/min NR 6–11; $p = 0.005$) without any significant change in creatinine clearance. The largest reductions in serum urate occurred in patients with the highest levels at baseline. Both total cholesterol and triglyceride levels in the serum fell, but this was not statistically significant in either case (5.9 ± 1.0 vs 5.3 ± 0.9 mmol/l; $p = 0.16$ and 2.34 ± 1.11 vs 1.77 ± 0.66 mmol/l; $p = 0.15$ respectively). Alkaline phosphatase activity was reduced in each patient, confirming compliance with fenofibrate (70 ± 15 vs 53 ± 12 U/l). Importantly, none of the group developed acute arthritis whilst taking fenofibrate, and the three who continue to take the drug remain free of gouty attacks.

Conclusion Fenofibrate rapidly lowers serum urate by a significant degree in patients with hyperuricaemia who are already established on allopurinol prophylaxis. No adverse effects were seen, in particular a flare of gout. Fenofibrate is a potential novel treatment for hyperuricaemia and the prevention of gout. In particular it may have a useful dual role in patients with coexisting hyperuricaemia and hyperlipidaemia.

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SAT0101 ANALYSIS OF THE EFFICACY OF CYCLOSPORIN A IN 56 PSORIATIC PATIENTS

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Background

Objectives 20% of the patients with psoriatic arthritis (PA) may develop a very severe form of arthritis. When the skin disease is extensive, it makes sense to use medications which are thought to be effective for both, the skin and joint disease. The efficacy of the cyclosporin A (CyA) on the skin lesions in psoriasis has been shown in several controlled studies. A few authors demonstrated the anti-inflammatory efficacy of the drug in the PA. The most important action of CyA is the inhibition of production of cytokines by T-cells. We have evaluated efficacy and tolerability of CyA in PA patients. 56 patients with average age of 47 (range 33–71), 21 female and 35 male have been treated with 3 mg/kg per day for 6 months. 19 patients received low doses of corticosteroids, nobody received other DMARD during the treatment.

Methods Several clinical and laboratory parameters for the assessment of joint status at the start and at the end of the study were employed: Ritchie index, duration in minutes of morning stiffness with a semi-quantitative evaluation the presence or absence of the onychopathy. We also performed at monthly interval the systolic blood pressure values and the laboratory parameters: erythrocyte sedimentation rate, CRP, serum creatinine and blood urea and liver enzymes. We measured a concentration of the drug in serum with Fluorescence polarisation immuno assay (ABOTT) method at the beginning and at the end of the study.

Results The results are shown in the following Table 1. (statistical-analysis t-student-test)

Abstract SAT0101 Table 1

Ritchie index	$p < 0,01$
Morning joint stiffness	$p < 0,05$
ESR	$p > 0,05$
CRP	$p > 0,05$

Conclusion Six of our patients drop out because of high blood pressure, all other patients finished the study. Our results show a good tolerability and efficacy on the joint pain, on the morning stiffness and on the skin lesions.

SAT0102 BONE AND JOINT PROBLEMS IN HAEMODIALYSIS PATIENTS

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Background Patient receiving maintenance haemodialysis suffer from various problems of the joints, soft tissues and tendons. These effects include avascular necrosis, osseous abnormalities, ligamentous laxity, destructive arthropathies and soft tissue calcifications. IN end stage renal disease, average bone mineral density has been reported modestly reduced.