progressive reduction in urinary excretion of NTX, resulting from an improvement in the bone resorption. However, there was no significant change in alkaline phosphatase or osteocalcin levels. The z score of the lumbar spine improved significantly over the treatment period, suggesting an improvement in BMD, which may reflect an improvement in the balance between bone formation and resorption. We believe that these patients require an intensive and prolonged course of treatment, and a close follow-up that will help delineate the beneficial effect of the treatment.

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Competing interests: None declared.

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Accepted 15 May 2006

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Correlation of oestrogen receptor gene polymorphism with gouty arthritis

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Ann Rheum Dis 2006;**65**:1673–1674. doi: 10.1136/ard.2005.051375

Gout represents a group of diseases characterised by hyperuricaemia, arthritis, and uric acid crystal formation. Men have a higher level of serum uric acid and are more susceptible to gout than women. The lower serum urate values in women of reproductive age compared with their male counterparts have been ascribed to lower renal postsecretory uric acid reabsorption.¹ An increase in ratios of testosterone to oestradiol has been reported to be associated with hyperuricaemia.²

The oestrogen receptor gene is located at chromosome 6q25.1 and has a thymine–adenine (TA) dinucleotide repeat polymorphism 1174 bp upstream from exon 1. This polymorphism has been shown to be associated with menopausal osteoporosis,³ coronary artery disease⁴ and rheumatoid arthritis.⁵ The androgen receptor has three main functional domains that are located at Xq11–12, near the centromere of the X chromosome. Binding of the androgen receptor–androgen complex activates the expression of other genes (transactivation). This transactivation activity depends on the transactivation domain of the protein encoded by exon 1, which contains a polymorphic CAG repeat sequence. Previous studies have shown that the CAG repeat is associated with inflammatory arthritis, such as rheumatoid arthritis⁶ and ankylosing spondylitis,⁷ and severity of coronary artery disease in men.⁸

METHODS AND RESULTS

In this study, we enrolled 196 patients (181 men and 15 women) with gout according to the 1977 revised American College of Rheumatology criteria.⁹ In addition, 102 unrelated, healthy people (57 men and 45 women) living in central Taiwan served as control subjects. Informed consent was

obtained from all subjects who participated in this study. Genomic DNA was prepared from peripheral blood using a genomic DNA isolation reagent kit (Genomarker, Taipei, Taiwan). The oestrogen receptor gene TA repeats and androgen receptor gene CAG repeats in patients and controls were typed by polymerase chain reaction.

The frequency distribution of the oestrogen receptor gene polymorphism in patients with gouty arthritis and healthy controls is presented in fig 1. Patients with gout had significantly shorter oestrogen receptor gene TA repeats than their sex-matched controls (men: mean 14.9 v 17.2, $p < 0.001$; women: mean 14.8 v 17.0, $p = 0.002$; table 1). We further classified the patients and controls into groups with shorter TA repeats (≤ 18) and longer TA repeats (> 18 repeats). The frequency of the shorter TA repeats (≤ 18) was considerably higher in patients with gout than in healthy controls (data not shown).

DISCUSSION

Our findings suggest that the oestrogen receptor gene TA repeat polymorphism is associated with the risk of developing gout in both men and women. In men, the risk is more consistently correlated with decreasing length of TA repeats. The protective effect of long TA repeats increases dramatically as the frequency of TA repeats increases in men. On the basis of the reports mentioned earlier, we conjecture that longer oestrogen receptor gene TA repeats increase the transactivational activity of the oestrogen receptor, facilitating uric acid excretion and thereby decreasing the susceptibility to gout. However, the speculation will need to be confirmed by further studies.

Figure 1 Frequency distribution of oestrogen receptor gene thymine-adenine (TA) repeats polymorphism in patients with gout and healthy controls.

Table 1 Mean (SD) of the oestrogen receptor gene thymine-adenine repeats and androgen receptor gene CAG repeats for patients with gout and healthy controls

Group	Women			Men		
	n	Mean (SD)	p Value	n	Mean (SD)	p Value
OR gene TA repeats						
Control	90	17.0 (3.8)	0.002	114	17.2 (4.0)	<0.001
Gout	30	14.8 (3.0)		362	14.9 (2.1)	
AR gene CAG repeats						
Control	84	22.0 (2.8)	0.928	55	21.4 (2.9)	0.300
Gout	30	21.9 (2.9)		181	21.9 (2.9)	

AR, androgen receptor; OR, oestrogen receptor; TA, thymine-adenine.

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Accepted 11 March 2006

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Hyperimmunoglobulinaemia D syndrome in India: report of two siblings with a novel mutation

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Hyperimmunoglobulinaemia D syndrome (HIDS) is an autosomal recessive auto-inflammatory syndrome caused by mutation in the mevalonate kinase (MVK) gene.¹ It presents with febrile episodes starting in infancy with increased serum immunoglobulin (Ig)D levels.² It is

Ann Rheum Dis 2006;**65**:1674-1676. doi: 10.1136/ard.2006.054494

mostly described in people of Dutch or North European descent.³ Isolated cases have been reported from Turkey,⁴

Abbreviations: HIDS, hyperimmunoglobulinaemia D syndrome; MVK, mevalonate kinase