Letters to the Editor

A selective COX-2 inhibitor, meloxicam, as a treatment option in patients with juvenile idiopathic arthritis and gastrointestinal side effects from naproxen

Sirs,

Meloxicam is a selective COX-2 inhibitor with a COX-2/COX-1 ratio of 10 in the whole blood assay (2). With once daily dosage, meloxicam has demonstrated efficacy in osteoarthritis and rheumatoid arthritis (3). Meloxicam in daily doses of 7.5 mg to 15 mg has been reported to be as effective as traditional nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac or piroxicam, but with a more favourable gastrointestinal adverse event profile (4).

Although nearly all children with juvenile rheumatoid arthritis (JRA) receive NSAID at some point of their disease course, up to 50% of them report gastrointestinal complaints during therapy with classical NSAIDs (5). The mechanism by which these events occur may include the inhibition of the synthesis of constitutive prostaglandins via the COX-1 pathway. During the phase I/II study of meloxicam for children with JRA, a good drug effectiveness and tolerability was observed (1). Encouraged by these results a therapeutic observation was started on January 1, 1999, using the same MX dosage (0.25 mg/kg once a day). The data was evaluated in the form of a retrospective chart review.

A therapeutic observation was carried out between January 1, 1999 and April 30, 2001. Informed consent had been obtained from all parents. Patients diagnosed with JIA were treated in the Paediatric Rheumatology Clinic, of the University Children's Hospital, Hamburg, and after August 30, 2000 the Paediatric Rheumatology Clinic moved to the General Hospital Eilbek, Hamburg.

The patients selected for participation were those who either did not tolerate naproxen or whose parents preferred a once daily dosage of MX, as a necessary nonsteroidal anti-inflammatory therapy. If side effects, independent of the severity, occurred meloxicam was stopped. Commercially available tablets containing 7.5 or 15 mg MX were used at a dosage of 0.25 mg/kg/day.

The data was evaluated in the form of a retrospective chart review.

From January 1, 1999 until April 30, 2001 meloxicam-treatment was initiated and followed up in 45 patients. Patient characteristics are described in Table I. Meloxicam was selected in 24 cases due to naproxen related side effects,in 15 of these, gastrointestinal side effects (Table II); 21 others chose meloxicam because of the once daily dosage. The mean daily dose of MX was 0.24 mg/kg/day (range 0.125 – 0.3 mg/kg/day). 8 patients received concomitant therapy, 7 of them methotrexate as a monotherapy and 1 patient methotrexate in combination with etanercept. No patient became intra-articular injection during the observation period.

Table I. Patients characteristics.

Number of patients (mean no. of involved joints/range)	45
Sex (female/male)	33 / 12
Mean age in years (range)	11.1 (5 - 19)
Oligoarticular JIA (1.6 / 1 - 3)	21
Polyarticular JIA (3.2 / 1 - 9)	5
Systemic JIA (1)	1
Enthesitis related JIA (1.6 / 1 - 5)	13
Psoriatic JIA (1.2 / 1 - 2)	5

Table II. All side effects experienced by patients.

Side effect on previous naproxen	Side effect under meloxicam leading to therapy discontinuation
Polydypsia	–
Abdominal pain	–
Dyspepsia	Abdominal pain
Headaches	–
Abdominal pain	Abdominal pain
–	Abdominal pain
Headaches	Abdominal pain
Abdominal pain	–
Headaches	–
Abdominal pain	–
–	Abdominal pain
Abdominal pain	–
Abdominal pain	–
Pseudoporphyria	Colitis
Headaches	–
–	Headaches
Abdominal pain	–
Abdominal pain	–
Abdominal pain	–
Abdominal pain	Headaches/dizziness
Hyperactivity (?)	–
Proteinuria	Proteinuria
Abdominal pain	–
Abdominal pain	–
–	Dizziness
Abdominal pain	–
Abdominal pain	Abdominal pain
Abdominal pain	–

After a mean therapy duration of 5.2 months (range 1-20 months),the number of active joints decreased from 1.7 (range 1-9) before to 0.9 (range 0-2) at the end of the observation period. In 23 patients the number of active joints decreased, in 16 stayed unchanged, and in 6 patients increased.

In 10 of the 45 patients side effects (Table II) occurred and meloxicam therapy was stopped. The mean duration of the therapy in this group was 3.4 months (0.5 - 6). 4 of the 21 patients who started meloxicam because of the once daily dosage, developed side effects. Only 7 of the 24 patients who had side effects on naproxen had also side effects with meloxicam. Therapy was discontinued in only one patient because of drug ineffectiveness.

In the preselected therapeutic observation 45 patients with JIA were treated with meloxicam, once daily at a mean dose of 0.24 mg/kg and for a mean duration of 5.2 months. The once daily application seems to be a great advantage in terms of compliance, especially in children. 11 patients experienced side effects. 5 of the 11 had abdominal pain, 3 of whom experienced gastrointestinal side effects on naproxen too. Among the 14 patients who chose meloxicam because of abdominal pain under naproxen,only 2 had abdominal pain under meloxicam. The colitis, experienced in one case, was presumably associated with the psoriatic JIA, but could be a side effect of meloxicam too. The headaches were non-specific but disturbing, the patients were sensitive to light, so meloxicam had to be stopped in all cases. Regarding comparative effectiveness to naproxen, the results of the current controlled, double blind phase III/IV study in children with JIA must be awaited.

In this preselected patient population meloxicam was well tolerated and effective in 34 of 45 (73%) patients.

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