Indomethacin for prevention of ectopic ossification in cementless hip arthroplasties

A prospective 1-year study of 100 cases

Christian Wurnig, Richard Eyb and Vinzenz Auersperg

In a prospective series of 100 patients we investigated the effect of indomethacin for 6 weeks in the prophylaxis of ectopic bone formation in hip replacements with cementless fixation. Indomethacin prophylaxis reduced ($P < 0.0001$) ectopic bone formation compared to a retrospective control group of equal size. Side-effects occurred in one-fifth of the patients, but most of these could continue the medication for at least 4 weeks.

Vienna University Department of Orthopedics, Allgemeines Krankenhaus, Währinger Gürtel 18, A-1090 Vienna, Austria
Tel +43–222 40400 4078. Fax –222 40400 4077
Submitted 92-02-02. Accepted 92-07-19

The incidence of ectopic ossifications after implantation of a total hip prosthesis seems higher in cementless than in cemented cases (Maloney et al. 1991). We report a prospective series of indomethacin-treated uncemented arthroplasties, compared with untreated, retrospective control cases.

Patients and methods

In a prospective study, 120 patients receiving a cementless total hip for arthrosis were treated with indomethacin (Gaurit®, Merckle, Vienna). Active ulcers of the gastrointestinal tract and ulcers or gastritis during the last 6 months before surgery were exclusion criteria. No other NSAIDs were allowed while the patient was on indomethacin. Indomethacin was administered orally in a dose of 2 × 50 mg from the first postoperative day on. This dosage was maintained for 6 weeks.

The patients included in the evaluation had follow-up radiographs and clinical examinations 6, 12, and 52 weeks postoperatively; for our particular question this short follow-up period seemed sufficient, since ectopic ossifications increase in size only until the sixth postoperative month (Ritter and Sieber 1985). To ascertain possible side-effects, patients were asked how they tolerated the drug.

The indomethacin group was compared with a control group of 100 patients who had a total hip replacement of the same type, also for arthrosis, but who did not receive indomethacin and also did not take any other antiphlogistic substances in the first 6 weeks after surgery. The control group was selected retrospectively in a random manner from our patient material. In the controls only the radiographs taken 12 months postoperatively were evaluated.

In all 220 patients the Zweymüller (1990) cementless total hip replacement was used (stem titanium alloy, cup pure titanium). The surgical technique was standardized and remained the same in all cases; the Bauer et al. (1986) surgical approach was used.

All patients received thrombosis prophylaxis with 3 × 5000 IU of subcutaneous heparin from the first postoperative day on; after discharge the patients usually received 1 g of acetylsalicylic acid/day (Eyb and Knahr 1983). The patients were allowed out of bed from the third postoperative day with two forearm crutches; full weight bearing was allowed from the sixth postoperative week.

For assessment of the ossification, radiographic staging by Arque (1973) was used. The chi-square test was used for statistical analysis.

The indomethacin group initially comprised 120 patients, but 20 of those had to be eliminated from the study; 13 retrospectively, since administration of indomethacin was not absolutely guaranteed, 4 stopped taking the drug after 2 weeks because of intolerance and 3 after 3 weeks. 13 patients discontinued the drug after 4 weeks but were nevertheless included in the evaluation because a sufficient effect can be seen after 4 weeks (Metzenroth et al. 1991). The remaining 87 patients verifiably received the medication during the prescribed 6 weeks. The average age of the patients was 63 years, and one half were men; the two series were equal in these respects.

Table 1. Ectopic ossification according to Arque (1973)

Grade	With prophylaxis	Without prophylaxis
0	59	19
1	35	47
2	5	27
3	1	1
Total	100	100

Table 2. Motion (degrees) 1 year postoperatively in patients with prophylaxis. Median (range)

	Grade ectopic ossification			
	0	1	2	3
Flexion	95 (60–130)	92 (70–120)	73 (40–105)	60
Abduction	21 (5–40)	20 (10–35)	8 (0–20)	10

Results

In the indomethacin group, ectopic bone formation ocurred in 41 cases and in the control group in 81 cases (Table 1). It should be noted, however, that we also included those cap-like ossifications in the area of the tip of the trochanter which are sometimes not classified as ectopic ossification (Eyb and Zweymüller 1985). If these cap-like ossifications are excluded only 6 patients in the indomethacin group had ossifications versus 34 in the control patients ($P < 0.0001$). Patients with grades 2 and 3 ossifications had impaired motion with respect to flexion and abduction (Table 2).

The side effects included dizziness, nausea and stomach pain but no bleeding ulcer. All side-effects disappeared within one week after the drug had been discontinued.

Discussion

In the literature the incidence of heterotopic bone formation varies from 5–90 percent (Nollen and Slooff 1973, DeLee et al. 1976, Kromann-Andersen et al. 1980, Errico et al. 1984, Hamblen 1984, Eyb and Zweymüller 1985, Cella et al. 1988). One reason for this wide variation is certainly the different interpretations of the radiographs (Lidgren and Nordström 1979). The reason why we chose the classification system according to Arque (1973) is that we think the correlation to the clinical result is better than in the Brooker (1973) classification system. Brooker et al. (1973) reported that they found no difference in the Harris score between groups 2 and 3. The difference between these two groups is only radiographic. In the Brooker classification there is no class 0 group, i.e., without any ossification. In our series we had in the indomethacin group 59 cases versus 19 cases in the control group without any ectopic bone formation. Based on the high ossification rates, prophylaxis is definitely justified. Most reports refer to cemented hip arthroplasties (Ritter and Vaughan 1977, Ritter and Gioe 1982, Ritter and Sieber 1985, Sundaram and Murphy 1986, Slätis et al. 1978, Søballe et al. 1988). Our results were very similar to those of Maloney et al. (1991); in their study severe ectopic bone formation occurred in one third in the group with the cementless replacements, which corresponds to the incidence in our control group. Our results would thus confirm Maloney et al.'s (1991) that cementless fixation of hip replacements carries a substantial risk of heterotopic bone formation. The effect of indomethacin may have had an effect on the bone formation process which hopefully will stabilize the prosthesis components (Keller et al. 1989). Our follow-up is too short to address this problem.

We feel that a beneficial effect of indomethacin in the prophylaxis of ectopic bone formation after cementless total hip replacement has been proven and that the rate of side-effects is justifiable. It is an open question whether administration of the drug could not be limited to 3 weeks (Schmidt et al. 1988, Kjaersgaard-Andersen and Schmidt 1991).

Acknowledgement

Randomization of the control patients was performed with help from the Department of Medical Statistics, University of Vienna.

References

Arque M. Die periartikuläre Ossifikation eine Komplikation der Totalendoprothese des Hüftgelenkes. Arch Orthop Unfall Chir 1973; 77: 108.

Bauer R, Kerschbaumer F, Poisel S. Operative Zugangswege in Orthopädie und Traumatologie. Georg Thieme Verlag, Stuttgart 1986.

Brooker A F, Bowerman J W, Robinson R A, Riley L H Jr. Ectopic ossification following total hip replacement. Incidence and a method of classification. J Bone Joint Surg (Am) 1973; 55 (8): 1629–32.

Cella J P, Salvati E A, Sculco T P. Indomethacin for the prevention of heterotopic ossification following total hip arthroplasty. Effectiveness, contraindications, and adverse effects. J Arthroplasty 1988; 3 (3): 229–34.

DeLee J, Ferrari A, Charnley J. Ectopic bone formation following low friction arthroplasty of the hip. Clin Orthop 1976; 121: 53–9.

Errico T J, Fetto J F, Waugh T R. Heterotopic ossification. Incidence and relation to trochanteric osteotomy in 100 total hip arthroplasties. Clin Orthop 1984; 190: 138–41.

Eyb R, Knahr K. The effect of prophylaxis for thrombosis on heterotopic ossification following total hip joint replacement. Arch Orthop Trauma Surg 1983; 102 (2): 114–7.

Eyb R, Zweymüller K. Periartikuläre Ossifikationen nach Implantation zementfreier Hüfttotalendoprothesen vom Typ Zweymuller Endler. Z Orthop 1985; 123 (6): 975–80.

Hamblen D L. Ectopic ossification. In: Complications of Total Hip Replacement. (Ed. Ling. R. S. M.) Churchill Livingstone, London 1984.

Keller J C, Trancik T M, Young F A, St Mary E. Effects of indomethacin on bone ingrowth. J Orthop Res 1989; 7 (1): 28–34.

Kjaersgaard-Andersen P, Schmidt S A. Total hip arthroplasty. The role of antiinflammatory medications in the prevention of heterotopic ossification. Clin Orthop 1991; 263: 78–86.

Kromann-Andersen C, Sorensen T S, Hougaard K, Zdravkovic D, Frigaard E. Ectopic bone formation following Charnley hip arthroplasty. Acta Orthop Scand 1980; 51 (4): 633–8.

Lidgren L, Nordström B. Treatment of periarticular calcification after total hip arthroplasty. Arch Orthop Trauma Surg 1979; 94 (1): 67–70.

Maloney W J, Krushell R J, Jasty M, Harris W H. Incidence of heterotopic ossification after total hip replacement: effect of the type of fixation of the femoral component. J Bone Joint Surg (Am) 1991; 73 (2): 191–3.

Metzenroth H, Publig W, Knahr K, Zandl C, Kuchner G, Carda C. Ossifikationsprophylaxe nach Hüfttotalendoprothesen mit Indomethacin und ihr Einfluss auf die Magenschleimhaut. Z Orthop 1991; 129 (2): 178–82.

Nollen A J, Slooff T J. Paraarticular ossifications after total hip replacement. Acta Orthop Scand 1973; 44 (2): 230–41.

Ritter M A, Vaughan R B. Ectopic ossification after total hip arthroplasty. Predisposing factors, frequency, and effect on results. J Bone Joint Surg (Am) 1977; 59 (3): 345–51.

Ritter M A, Gioe T J. The effect of indomethacin on paraarticular ectopic ossification following total hip arthroplasty. Clin Orthop 1982; 167: 113–7.

Ritter M A, Sieber J M. Prophylactic indomethacin for the prevention of heterotopic bone formation following total hip arthroplasty. Clin Orthop 1985; 196: 217–25.

Schmidt S A, Kjaersgaard Andersen P, Pedersen N W, Kristensen S S, Pedersen P, Nielsen J B. The use of indomethacin to prevent the formation of heterotopic bone after total hip replacement. A randomized, double-blind clinical trial. J Bone Joint Surg (Am) 1988; 70 (6): 834–8.

Slätis P, Kiviluoto O, Santavirta S. Ectopic ossification after hip arthroplasty. Ann Chir Gynaecol 1978; 67 (3): 89–93.

Søballe K, Christensen F, Kristensen S S. Ectopic bone formation after total hip arthroplasty. Clin Orthop 1988; 228: 57–62.

Sundaram N A, Murphy J C. Heterotopic bone formation following total hip arthroplasty in ankylosing spondylitis. Clin Orthop 1986; 207: 223–6.

Zweymüller K. 10 Jahre Zweymüller Hüftendoprothese. Hans Huber Verlag, Bern 1990.