



## A Study on Use of Indomethacin for Prevention of Heterotopic Ossification After Hip Arthroplasty

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**KEYWORDS :** Indomethacin, total hip arthroplasty, heterotopic ossification

### INTRODUCTION

Schmidt et al. (1988) showed in a prospective 1-year study a substantial reduction of heterotopic bone formation in patients receiving indomethacin for 6 weeks, after cemented total hip replacement. Administration of indomethacin for a shorter period also inhibits bone formation experimentally (Tornkvist et al. 1985) and therefore may be effective as prophylaxis against heterotopic ossification *in vivo*. In this randomized comparison, we attempted to determine the shortest course of indomethacin prophylaxis effective against heterotopic bone formation.

### CASE STUDY

In a randomized, parallel group study, we evaluated the efficacy of a 4-day versus an 8-day course of indomethacin (50 mg, 3 times per day), given as prophylaxis against heterotopic ossification formation after cementless total hip arthroplasty in 200 patients with arthrosis. Patients receiving the prophylaxis for 8 days had less ( $p = 0.03$ ) severe heterotopic bone

All procedures were primary arthroplasties in patients not previously operated on and were performed in our department

Indomethacin was administered in a dose of 50 mg 3 times per day. No other anti-inflammatory medications were administered during the treatment with indomethacin. Postoperative pain was treated with tramadol and narcotics. The surgical technique was standardized and remained the same in all cases.

Radiographs were obtained 3 months and 1 year postoperatively and evaluated for evidence of heterotopic bone formation. This follow-up period seemed sufficient, since heterotopic ossification increases in size only until the sixth postoperative month (Ritter and Sieber 1985). Patients were examined at 3 months, 6 months and at 1 year. The data were analyzed with the chi-square test, employing  $p < 0.05$  as the level of significance. 209 patients (104 in group A, 105 in group B) received the indomethacin medication, according to the study protocol. The groups were similar in age, gender distribution, postoperative bleeding, length of hospital stay and postoperative recovery time. As men are more at risk of developing heterotopic ossification than women (DeLee et al. 1976, Kromann-Andersen et al. 1980, Hierton et al. 1983, Morrey et al. 1984, Soballe et al. 1988), we looked at the gender distribution in our 2 groups and found no difference, group A 40/104 men, group B 42/105 men ( $p = 0.96$ ). No deep infection or postoperative dislocation occurred in either group.

### CONCLUSIONS

At 1 year, 61 patients in group A (59 + 9.5%, mean 95% CI) and 49 patients in group B (47 + 9.6%, mean f 95% CI) showed radiographic evidence of heterotopic ossification. These differences were not statistically significant ( $p = 0.09$ ).

However, fewer patients in group B had severe ossification (Tables 2-4). Regardless of the classification system used, the difference was always statistically significant ( $p < 0.05$ ). No patient from either group developed extensive Arcq grade III, Brooker grade IV or DeLee grade III ossification.

### DISCUSSION:

The cause of heterotopic ossification after total hip replacement is not clear. Surgical trauma and individual predisposition are the chief factors (DeLee et al. 1976, Ahrengax and Lindgren 1993). Several authors suggested the surgical approach as a cause of heterotopic ossification, but it

does not seem to be a crucial factor. Since Dahl suggested in 1975 that oral indomethacin may be effective as a prophylactic measure against heterotopic ossification, several supporting retrospective and prospective reports have been published (Ritter and Gioe 1982, Ritter and Sieber 1985, Kjrsgaard-Andersen and Schmidt 1986, Nilsson et al. 1986, Schmidt et al. 1988, McMahon et al. 1991 Kjrsgaard-Andersen and Ritter 1992). Optimal duration and dosage of indomethacin prophylaxis are still unknown. Most authors recommend treatment for at least 3 weeks. Our aim was to see whether short-term treatment with indomethacin would also be effective. Compared with results of prospective trials using indomethacin treatment for several weeks (e.g., Schmidt et al. 1988, Wumig et al. 1992), no obvious difference in the effectiveness of our %day course of indomethacin was found. Treatment with indomethacin was discontinued due to gastrointestinal side-effects in only 9 cases. No patients in either group showed clinical signs of gastric ulceration. Our findings indicate the effectiveness of short-term treatment with indomethacin (Kjaersgaard-Andersen et al. 1993) in the prophylaxis of heterotopic ossification after cementless hip arthroplasty and that the incidence of side-effects is acceptable. Although several randomized studies have shown that various NSAIDs can prevent or reduce heterotopic ossification after total hip arthroplasty (Elmstedt et al. 1985, Schmidt et al. 1988, Hoikka et al. 1990, Gebuhr et al. 1991, Wahlstrom et al. 1991, Reis et al. 1992), the question still to be solved is how short-term treatment can be used. In most of the previous studies the treatment period was 3-6 weeks, only 2 randomized studies reported shorter treatment periods; 1 with a 10-day treatment period with ibuprofen, in which there was no significant reduction in the ibuprofen-treated group, and 1 with a 5-day treatment period with tenoxicam, where the reduction in heterotopic ossification was found to be statistically significant.

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