LOCAL TREATMENT WITH A BISPHOSPHONATE IMPROVES TOTAL KNEE PROSTHESIS FIXATION.

PRELIMINARY DATA

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Introduction
The risk of late loosening of cemented knee prostheses is related to early fixation as measured by Roentgen Stereometric Analysis (RSA). It has previously been thought that early fixation (defined as migration by RSA during the first and second year) is a purely mechanical phenomenon. However, osteocytes next to an implant will die postoperatively because of the operative trauma or circulatory disturbance. This leads to increased bone resorption at the interface. There is also a fracture repair response to the trauma, leading to increased bone formation. Early implant fixation should therefore be dependent on the balance between these two responses. Because bisphosphonates impair bone resorption, they should lead to a more positive balance, leading to better early fixation. Indeed this is the case: We have shown that the fixation of the tibial component of a total knee prosthesis is improved by giving a bisphosphonate orally once daily for the first half year after surgery (1). The migration, measured by RSA, was reduced by one quarter during the first 6 months, and the difference between the groups persisted for 4 years (unpublished data). We now report preliminary data from a similar study, where the bisphosphonate was instead given locally during the operation.

Materials and Methods
In a double-blinded study, we randomized 50 patients, receiving a NexGen cemented knee prosthesis, to local treatment with ibandronate (Bondronate, Roche) or placebo. Immediately before cementation, 1 mg of ibandronate (1 mL) or saline was applied upon the prepared tibial bone surface. The fluid volume normally became absorbed in the cancellous bone. Patients were examined with RSA postoperatively and at 6, 12 and 24 months. Although the investigator MH is still blinded for treatment, preliminary RSA results have been analyzed by PA without knowledge about individual patients. Groups were compared with t-test.

The study was approved by the regional Ethics committee and the National Drug Agency. Patients signed informed consent.

Results
One patient was lost from follow-up. 6 months data are otherwise complete (n=49) and 39 patients have been followed for 12 months. 24 months data are too early to report.

No prosthesis migrated more than 1.0 mm.

Local ibandronate reduced migration (maximal total point motion; MTPM) at 6 months from 0.45 to 0.32 mm (p=0.006; Figure 1). At 12 months, the migration from the postoperative examination was reduced from 0.48 to 0.36 mm (p=0.03). The variance in migration at 6 months was lower in the ibandronate group (p=0.04). A similar, but not significant, decrease in variation was seen at 12 months.

Discussion
These preliminary results prove the concept that local application of a bisphosphonate during total joint surgery can decrease migration. This confirms our previous results, that early migration is dependent on osteoclast activity, and that pharmacological treatment can have a measurable impact on the mechanics of total joint replacement surgery (1). The total dose was not higher than what is accepted for a single intravenous injection, and due to the local binding to the exposed bone, the systemic dose is probably even less. The treatment takes a minute or two of the operation time. It is cheap, simple and safe.

None of our patients showed excessive migration, and consequently, perhaps none is at risk of late loosening. However, because not only the mean value, but also the variation was smaller in the ibandronate group, it is likely that excessive migration can be reduced with our treatment. Because of the strong association between early migration and late loosening (2), this would reduce the risk of late loosening.

References

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