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Small PMMA beads improve gentamicin release

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The in vivo release of gentamicin base from conventional polymethyl methacrylate 7-mm beads was compared with that from the recently introduced 3 x 5-mm minibeads. The release in 14 days from minibeads was 93 percent of their gentamicin content, while the large beads released an average of 24 percent. The volume of the minibeads is one fifth of that of the large beads. Owing to the improved release combined with the smaller size, total release from minibeads in a cavity may be some seven times that from large beads. When in smaller cavities a strong bactericidal effect is desired, minibeads are to be preferred to large beads.

The use of gentamicin-PMMA beads may be limited by their size of 7-mm diameter. The introduction of 3 x 5-mm minibeads makes it possible to use the technique in smaller cavities. The minibeads contain 2.8 mg gentamicin sulfate, equivalent to 1.7 mg gentamicin base, and 3.9 mg ziconium oxide for contrast (Table 1). In vitro studies have shown that on the first day minibeads release more gentamicin than the larger beads, whereas after the first day the release rate was lower than from large beads (Dingeldein 1983).

I have compared the release of gentamicin in vivo from minibeads with that of large beads.

Patients and methods

In 17 and 12 patients, 19 and 27 chains of large (Septopal®) and minibeads, respectively, were removed after treatment for a bone, joint, or soft-tissue infection. All the minibeads used were from the same batch. The chains were removed after 7–15 days and stored dry at room temperature.

From these chains, 44 large beads and 60 minibeads were removed in the Laboratory of Microbiology, Merck Darmstadt, FRG, Dr. E. Dingeldein. The beads were dissolved with dichloromethane, and the solution was washed four times with pH 7.4 phosphate buffer by thorough shaking. After separation the buffer was decanted and the gentamicin content was assayed. The total content of gentamicin base before use was measured in beads removed from the chains before implantation.

The amount of gentamicin released during implantation was calculated as the difference of gentamicin content of the beads before and after use. This was expressed as the percentage of the amount of gentamicin implanted.

To estimate the volume of different numbers of large and minibeads, a measuring glass was filled with beads up to variable volumes. The beads in 5, 10, 15, and 20 mL were counted. The corresponding amounts of implantable gentamicin base and of gentamicin that could be released were calculated.

Table 1. Comparison of minibeads and large (Septopal®) beads

	Size beads (mm)	Gentamicin sulfate (mg)	Gentamicin base (mg)	Zirconium dioxide (mg)
Large beads	7	7.5	4.5	20
Minibeads	3 x 5	2.8	1.7	4

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Results

In the 45 large beads, 43–96 percent of the original content of gentamicin base (4.5 mg) was present after implantation periods varying from 10 to 14 days, so they had released 57–4 percent of their original gentamicin content. From the beads that had been implanted for 14 days (36 of the 45 beads), the mean (SD) gentamicin release was 24 (11) percent of the original 4.5 mg gentamicin, i.e., 1.1 mg from each bead (Table 2).

In 60 minibeads the residual gentamicin was 6–21 percent of the implanted amount of 1.7 mg. So after a treatment period varying from 7 to 15 days, the release of the minibeads was 94–79 percent. After 14 days of implantation (13 of the 60 minibeads), the mean (SD) gentamicin release was 93 (1.4) percent, i.e., 1.6 mg from each minibead (Table 2).

The mean volume of one large bead was 0.5 mL, compared with 0.1 mL for the minibeads.

Table 2. Percentages of the implanted amounts of gentamicin, present after treatment with Septopal® beads

Beads (n)	Implanted (days)	Residual gentamicin (%)	*SD*
Large beads			
2	10	80	*0.5*
4	12	47	*2.5*
3	13	73	*1.6*
36	14	76	*11*
Minibeads			
44	7	14	*2.7*
13	14	7	*1.4*
3	15	8	*1.0*

Discussion

An in vivo study of gentamicin release gives more information of the effectiveness of a local antibiotic treatment than measurement in vitro. In an earlier study, we found a large difference between diffusion half-lives, measured in vivo compared with in vitro (Walenkamp 1983, Walenkamp et al. 1986). This study confirms the results of earlier studies in vivo, where large beads showed a gentamicin release of 20–70 percent (Walenkamp 1983) and 20–40 percent (Koeweiden and Vree 1988) in 14 days.

Minibeads were developed to overcome the technical problem of smaller cavities, as in hand and foot surgery. In cavities admitting only a limited amount of large beads, e.g., 10–20 mL, use of minibeads may also be beneficial because they improve the local antibiotic effect.

For instance, in a cavity of 10 mL, 20 large beads can be implanted containing 90 mg gentamicin compared with 100 minibeads and 170 mg gentamicin. The release in such a 10-mL cavity can be increased from 22 mg to 158 mg gentamicin by using minibeads. Thus, cavities smaller than about 20 mL should preferably be filled with minibeads if a high local gentamicin concentration is desired.

References

Dingeldein E. EMD 35650 Gentamicin PMMA Miniketten. Untersuchungen zur Gentamicinfreisetzung in vitro. Internal Report Merck Darmstadt 1983;Nr 1/3/83.

Koeweiden EMJ, Vree T B. In vivo release of gentamicin from PMMA beads: Quantitative determination of gentamicin. Acta Orthop Scand 1988;59(Suppl 227): 110–1.

Walenkamp G H I M. Gentamicin PMMA beads. A clinical, pharmacokinetic and toxicological study. Thesis, University of Nijmegen, The Netherlands 1983.

Walenkamp G H, Vree T B, van Rens T J. Gentamicin PMMA beads. Pharmacokinetic and nephrotoxicological study. Clin Orthop 1986;(205):171–83.