GENTAMICIN CONTAINING SURGICAL BONE CEMENT

IN VITRO ELUTION CHARACTERISTICS OF PALACOS® AND PALAMED®

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ABSTRACT

Antibiotic impregnated acrylic bone cement is well accepted in orthopedics. Several brands containing the aminoglycoside antibiotic gentamicin are marketed.

To obtain information on the elution profile of the included antibiotic from the surgical cement, we studied the *in vitro* release of gentamicin from two marketed brands: Palacos® and Palamed®.

Two experimental arrangements were used to investigated the release of gentamicin from the surgical cement.

The elution of gentamicin was tracked both in a non-flowing (non-dynamic time-elapsed elution) setting and by the use of a clearly defined USP XXIV flow-through cell apparatus (#4; pg1945), through which an elution medium was pumped at a constant speed.

Weighed prepared surgical cement samples were placed in the two above mentioned settings and gentamicin release was followed in time. Elution samples were drawn from the elution medium at pre-determined time intervals.

Analysis of the gentamicin concentration in the samples was performed by the TDx-FLx Abbott method.

Palamed® gentamicin concentrations were higher at all time points than from Palacos®. In comparison to Palacos®, peak gentamicin concentrations from Palamed® were approximately three times higher in the dynamic elution setting.

In the non-dynamic time-elapsed elution setting, the elution of gentamicin from Palamed® continued for the measured 190 days in contrast to gentamicin release from Palacos®. The measured final elution concentration of gentamicin at the end of 190 days for Palacos® and Palamed® was 0,67 ± 0,06 and 3,69 ± 0,25 respectively.

KEY WORDS

Gentamicin, Implantable device, Elutionprofile, Orthopedics

INTRODUCTION

Antibiotic impregnated acrylic bone cement (PMMA) beads and surgical cement are well accepted modalities in the treatment and prevention of infection after implantation of endoprostheses.

In the 60's and early '70's the complication rate in total hip arthroplasties for postoperative infection was approximately 10%. By introducing strict aseptic techniques in the operating theatre, the introduction of pre- and peri-operative systemic antiobiotic prophylaxis and also the mixing of antibiotics with surgical cement reduced the infection level to less than 1%.

Early reports have appeared on the use and effectiveness of antibiotic impregnated bone cement (1,2).

We have undertaken an *in vitro* comparison of two bone cements loaded with the same antibiotic, gentamicin by use of two experimental settings; dynamic and non-dynamic time-elapsed leaching (3).

MATERIALS & METHODS

Dynamic elution profile

To study the elution profile of the gentamicin loaded surgical cement we used a USP XXVI defined flow-through cell apparatus. The assembly consists of a 600 ml reservoir (fig 1) containing 250 ml buffered solution; a pump for the dissolution medium; a flow-through cell (fig 2); a waterbath that maintains the dissolution medium at

37 ± 0,5 °C, a device for automatic sampling of the eluate.
Flow rate of the dissolution medium: 84 ml/hr.
Dissolution medium: buffered phosphate solution pH 7,5 ± 0,1 (KH2PO4 1.82 g/l; Na2HPO4.2H2O 9.5 g/l).
Specialties were obtained from Schering-Plough (Palacos®; Lotnr.:98D06-12/8928/97I09-46/2895) and Merck, Ortomed (Palamed®; Lotnr.: 8948 5054).
During the 190 min. test every 5 min. a sample of 250 uL was taken.

Non-dynamic time-elapsed elution profile
A final elution procedure (190 days) was studied by means of emersion of a sample of the gentamicin loaded cement in the same elution medium in an erlenmeyer (flask); appropriately diluted test samples were taken at four previously determined time points.

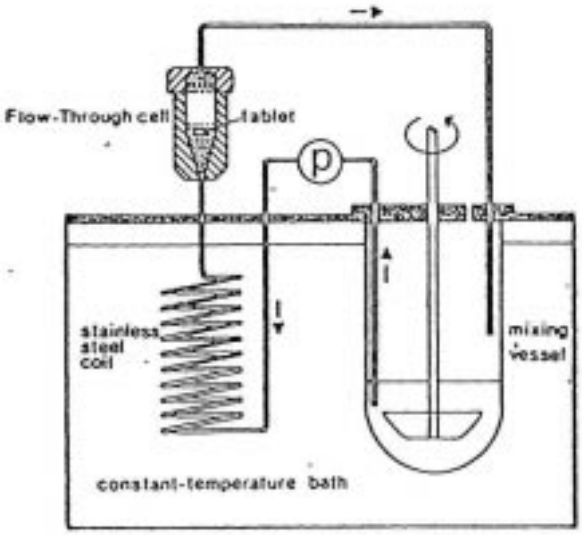


Fig.1

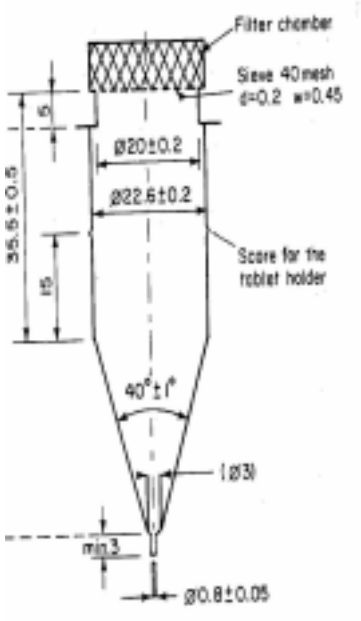


Fig.2

RESULTS
Results of gentamicin release from both Palacos® and Palamed® using the USP XXIV flow-through cell apparatus are presented in Table 1 and Fig.3.

Table 1
DYNAMIC ELUTION OF GENTAMICIN LOADED SURGICAL CEMENT DURING 190 MIN.

Specialties	n	Peak gentamicin level (mg/L); at 10 minutes	Mean gentamicin concentration from 100 minutes (mg/L)	Percentage released
Palamed®	4	93,9 ± 16,2	5,73 ± 0,38	27,1
Palacos®	5	32,0 ± 10,7	1,78 ± 0,05	8,8

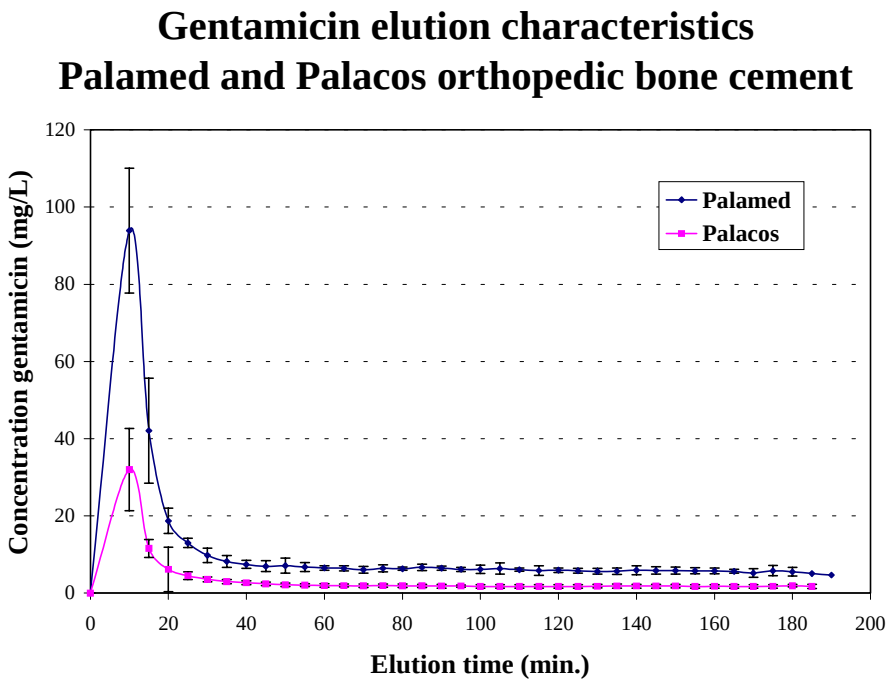
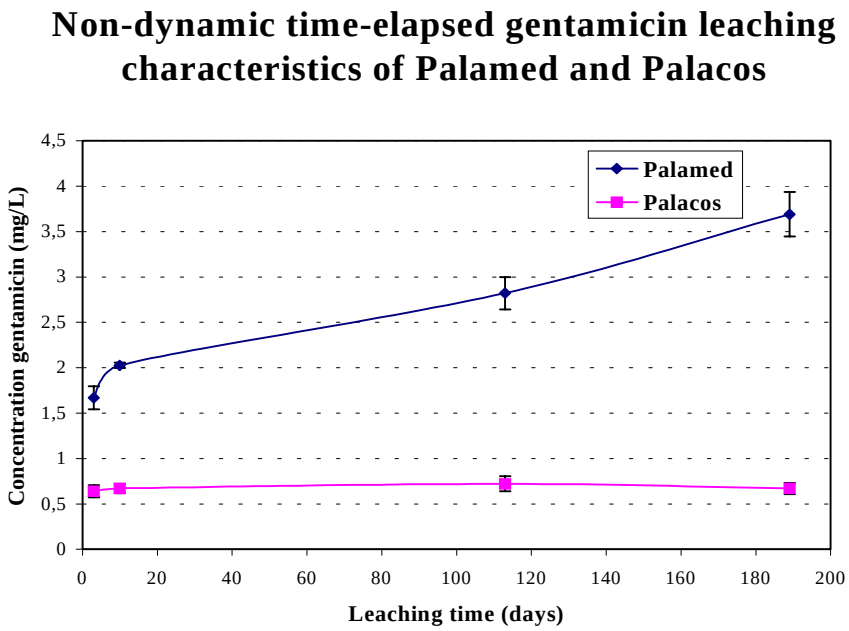


Fig.3

In the non-dynamic setting leaching of gentamicin from the bone cement was measured. Results of begin and end points are shown in table 2, whereas leaching characteristics of gentamicin during the whole time period are presented in fig.4.

Table 2
NON-DYNAMIC LEACHING OF GENTAMICIN LOADED SURGICAL CEMENT

Specialties	Gentamicin level after 3 days (mg/L)	Gentamicin level after 190 days (mg/L)	Percentage released after 190 days
Palamed®	1,67 ± 0,13	3,69 ± 0,25	69,9
Palacos®	0,64 ± 0,07	0.67 ± 0,06	13,3



DISCUSSION

Antibiotic impregnated acrylic bone cement (PMMA) beads and surgical cement are well accepted modalities in the treatment and prevention of infection after implantation of endoprostheses.

To obtain information on the elution profile of the included antibiotic from the bone cement, we studied the *in vitro* release of gentamicin from two marketed brands: Palacos® and Palamed®. Two experimental procedures, a dynamic and non-dynamic setting, were used. Several differences were noted between the two brands. First, the peak concentration of gentamicin was always higher for Palamed®. Second, the total amount of gentamicin released from the bone cement was higher for Palamed®, both in the dynamic and non-dynamic setting. Finally, in the non-dynamic experiment it became clear that leaching of gentamicin from Palacos® reached a steady-state condition, whereas from Palamed® leaching of gentamicin continued during the investigated time-period. This possibly resembles the difference in formulation between the two surgical cements. The clinical significance of the higher elution levels of gentamicin from the Palamed® will be subject of further research (4,5).

CONCLUSION

Gentamicin levels and peak concentrations are consistently higher with use of Palamed®. To interpretate these results in relation to clinical significance, further research will be necessary.

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