Mechanical characteristics of antibiotic-laden bone cement

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ABSTRACT – We studied the mechanical characteristics of cement-antibiotic combinations in vitro. Palacos R was tested without antibiotics, with gentamicin alone and with gentamicin plus vancomycin or flucloxacillin. Palacos LV was studied only with gentamicin added. CMW 1 was studied with gentamicin added, with gentamicin plus vancomycin, and with gentamicin plus flucloxacillin.

We performed four-point bending tests on beams of cement to establish bending strength and modulus, and compared the values to ISO standards. Density was also assessed. Palacos R was the strongest of the cements (bending strength 80 MPa). Palacos formulations (apart from Palacos LV) had a higher density and bending modulus than CMW 1.

Statistical comparison of various cements with plain Palacos R showed lower density in 4 of the mixtures, and lower bending strength and modulus in 6 of the mixtures. Palacos R/gentamicin plus vancomycin and CMW 1/gentamicin plus vancomycin had bending strength slightly above minimum ISO standards, suggesting that the addition of vancomycin during cementmixing may compromise the outcome in revision surgery for sepsis.

The mechanical characteristics of acrylic cement are affected by the addition of antibiotics. Liquid antibiotics have been shown to cause greater loss of compressive strength than crystalline preparations. However, losses of compressive strength and elastic modulus of less than 10% have been demonstrated when antibiotics are added in powder form (Ger et al. 1977).

Any study of the mechanical characteristics of bone cement should take into account the postcuring effect and increasing strength during the first 3 weeks especially after mixing (Lautenschlager et al. 1976), and the importance of maintaining cement samples at body temperature rather than room temperature during this period.

Gentamicin is widely used as an additive to acrylic cement, and certain formulations are associated with longer implant survival (Malchau and Herberts 1998). In these preparations, this antibiotic seems not to affect the mechanical strength of cement to any significant extent (Wright et al. 1984).

However, in contemporary joint revision surgery for sepsis, various combinations of antibiotic and cement are frequently created in the operating room, the choice of antibiotic being determined by preoperative microbiological analysis. In our experience, vancomycin and flucloxacillin are most frequently added to preparations already containing gentamicin, and therefore we were particularly interested in the quality of cements containing these combinations.

Material and methods

We compared 7 bone cements containing 1 or 2 antibiotics with Palacos R (Table 1). The manufacturers describe each cement as a 40 g mix. More antibiotics were added as 500 mg powder to the polymer powder before mixing, a concentration of about 1% in the final mix. Cements were stored

Table 1. Cement brand and mix tested

Proprietary name	Standard constituents [a]	Additional antibiotic
Palacos R	Polymer 33.80 g, Monomer 18.40 g	
Palacos R/gentamicin	Polymer 33.80 g, Monomer 18.40 g, Gentamicin 0.5 g	
Palacos R/gentamicin	Polymer 33.80 g, Monomer 18.40 g, Gentamicin 0.5 g	Vancomycin 0.5 g
Palacos R/gentamicin	Polymer 33.80 g, Monomer 18.40 g, Gentamicin 0.5 g	Flucloxacillin 0.5 g
Palacos LV/gentamicin	Polymer 33.12 g, Monomer 18.42 g, Gentamicin 1 g	
CMW 1/gentamicin	Polymer 33.89 g, Monomer 18.04 g, Gentamicin 1 g	
CMW 1/gentamicin	Polymer 33.89 g, Monomer 18.04 g, Gentamicin 1 g	Vancomycin 0.5 g
CMW 1/gentamicin	Polymer 33.89 g, Monomer 18.04 g, Gentamicin 1 g	Flucloxacillin 0.5 g

[a] besides additives including contrast

Table 2. Cement data. The mean values (SD & 95%CI) for density, bending modulus and bending strength

Cement brand/mix	Density (kg/m^3)		Bending modulus (Mpa)		Bending strength (Mpa)	
Palacos R	1281	(33 & 2.57)	3926	(225 & 5.74)	80	(6 & 7.33)
Palacos R/gentamicin	1282	(31 & 2.44)	3720	(199 & 5.36)	75	(6 & 7.58)
P-value (t-test)	0.5		0.06		0.07	
CMW 1/gentamicin	1155	(22 & 1.92)	3099	(72 & 2.33)	72	(4 & 5.12)
P-value (t-test)	<0.0001		<0.0001		0.006	
CMW 1/gentamicin/flucloxacillin	1241	(35 & 2.84)	3369	(291 & 8.65)	67	(6 & 9.55)
P-value (t-test)	0.03		0.002		0.002	
Palacos R/gentamicin/flucloxacillin	1227	(27 & 2.18)	3458	(231 & 6.67)	66	(1 & 1.96)
P-value (t-test)	0.005		0.003		<0.0001	
Palacos LV/gentamicin	1205	(36 & 2.95)	3219	(139 & 4.32)	60	(3 & 4.51)
P-value (t-test)	0.002		<0.0001		<0.0001	
Palacos R/gentamicin/vancomicin	1263	(20 & 1.58)	3526	(257 & 7.28)	56	(4 & 6.58)
P-value (t-test)	0.1		0.008		<0.0001	
CMW 1/gentamicin/vancomicin	1208	(49 & 4.02)	3263	(121 & 3.70)	53	(5 & 9.12)
P-value (t-test)	0.006		<0.0001		<0.0001	

and mixed according to ISO specifications at 23 °C ± 1% and 50 ± 20% relative humidity. We used a standard vacuum syringe-mixing method (Schering Plough) and mixing was done by an experienced orthopedic operating room nurse. The cement was poured into 6 rectangular polyethylene molds per mix to create beams measuring 10 mm × 3.3 mm × 75 mm. The molds were sealed with a metal lid slid into position. No additional pressure was applied at any stage. The beams were then allowed to cool at room temperature for 1 hour according to ISO standards to avoid sudden temperature changes, before being immersed in normal saline at 37 °C in sealed vials for 21 days.

Each of the 6 beams was then mounted on a four-point bending apparatus and fractured transversely according to ISO 5833 (Lewis 1977),(ISO 5833 1992 & Part I 1993). Density was calculated by measuring mass electronically (accuracy 0.001g), and dividing by volume, calculated by using dimension calipers to confirm the size of the beams (accuracy 0.001mm). Bending modulus and bending strength were measured by transducers on the four-point bending apparatus.The results were then compared with ISO standards, and analyzed statistically (t-test), using Palacos R (plain) as reference.

Results (Table 2)

Density was significantly lower than plain Palacos R in 4 of the mixtures. Bending modulus and bending strength were lower than plain Palacos R in 6 of the mixtures.

In relation to bending strength, values were generally satisfactorily above the minimum ISO standard (50 MPa). However, the addition of van-

comycin to proprietary Palacos R/gentamicin and CMW 1/gentamicin produced bending strengths of 56 MPa and 53 MPa, respectively, barely above the minimum ISO standards. These results compare poorly with values for plain Palacos R (80 MPa), Palacos R/gentamicin (75 MPa), and CMW 1/gentamicin (72 MPa).

Discussion

Antibiotics are frequently added to proprietary brands of bone cement during revision joint replacement surgery. The principal antimicrobial activity of such cements is thought to occur during the first 3 weeks after implantation. Although the mechanical characteristics of proprietary cements have been evaluated for many years, and the addition of gentamicin in particular has been found to result in very little in the way of mechanical disadvantage, there is increasing concern that adulteration of proprietary brands of cement with an additional antibiotic in the operating room may weaken the cement and result in early failure of the revised implant.

We found higher density and bending modulus in Palacos preparations (apart from Palacos LV) than in CMW 1, lower density in 4 cement/antibiotic mixtures than Palacos R, and lower bending modulus and bending strength in 6 mixtures than Palacos R. We consider it unlikely that the additional antibiotics in crystalline form participate in the polymerization reactions of the cement after mixing or act as a plasticizer, and the effects observed probably result from microcavitation of the cement by additional particulate material. The relatively poorer performance of Palacos LV/gentamicin and CMW 1/gentamicin may be related to the same effect as well, since both contain twice as much gentamicin as Palacos R/gentamicin in proprietary form.This may have relevance in relation to published implant survival figures, which appear to favor Palacos R (Malchau and Herberts 1998).

Of possibly greater importance is the observation that the addition of vancomycin to proprietary brands of Palacos R/gentamicin and CMW 1/gentamicin results in cement with a bending strength only slightly above the minimum ISO standards. Such cement would almost certainly be considered unsuitable for commercial release, and the consequences of the widespread use of such mixtures may become apparent over the next 5–10 years as the outcome of revision procedures for sepsis is subjected to increasing Armstrong scrutiny. Some disadvantages in relation to the addition of flucloxacillin to proprietary brands of cement have already been detected in relation to antibiotic degradation (Armstrong et al. 2000). The fact that vancomycin, an alternative to flucloxacillin, may have a negative effect on the mechanical characteristics of such cement-antibiotic mixtures is a further consideration in relation to this practice. Further assessment of alternative antimicrobial agents and their effects on bone cement will be necessary, as microbiological detection improves and the number of revision procedures increases.

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