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Effects of Vancomycin, Cefazolin and Test Conditions on the Wear Behavior of Bone Cement

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ABSTRACT

Antibiotic cement has been recommended in the treatment of prosthetic infections. The purpose of this study was to investigate the mechanical behavioral changes in cement loaded with two antibiotics, vancomycin and cefazolin, in dry and liquid medium. Six groups and four study conditions were established according to the doses of antibiotic used and the ageing (immersion in phosphate buffered saline) of the samples. Properties evaluated were friction coefficient and wear. Samples in dry medium showed higher wears than in liquid. Antibiotic selection did not influence wear properties tested in dry conditions, however, in liquid medium, there were higher frictional coefficients and wear for cefazolin loaded cement after one week and for vancomycin and cefazolin after one month. The results suggest that antibiotic cements behave differently in liquid and that the molecular characteristics of antibiotics are essential for determining this influence.

The treatment of prosthetic infections remains controversial since it depends on multiple variables such as the function of the affected joint, the elapsed time since implantation and the medical condition of the patient. It has been widely documented that the two-stage revision using a bone cement spacer (polymethylmethacrylate, PMMA) mixed with various antibiotics obtain the highest success rates [1–4].

The addition of antibiotics to PMMA, particularly in liquid form, adversely affects its mechanical strength [5–7]; therefore, it is necessary to consider an antibiotic's microbiological profile, its influence on the cement and its spreading capacity, among other features. The most commonly antibiotics used are tobramycin, gentamicin, vancomycin, clindamycin and cephalosporins [2,8]. Since the introduction in the market of cement with gentamicin for infection prophylaxis in primary arthroplasty, various microorganisms with acquired resistance to gentamicin [9] have been described. This necessitates the search for new antibiotics and combinations thereof to increase the antimicrobial spectrum without compromising the characteristics of PMMA.

There are multiple studies that assess and compare the effect of different antibiotics on the resistance of PMMA to bending and compression. Most of these studies have been performed in vitro, based on ISO and ASTM standards for testing acrylic cements [10,11]. The extrapolation of in vitro results to clinical practice is controversial since these studies disregard the changes undergone by antibiotic-mixed PMMA with the liquid medium of the physiological environment. It is also important to note that the influence of these antibiotics in the breakdown of bone cement has not been well defined; this wear is closely related to the osteolysis observed in medium/long term in patients undergoing joint replacements that occasionally leads to an aseptic loosening of the implant [12,13].

The aim of this study is to investigate the mechanical behavior changes of two antibiotics with different biochemical properties on the process of in vitro wear of commercial acrylic bone cement preloaded with gentamicin. Therefore, this study will determine if the results are similar in relation to test condition and if they are maintained after being immersed in physiological saline solution for a period of 7 and 30 days, thus simulating physiological conditions.

Material and Experimental Method

Preparation of the Antibiotic-Loaded Bone Cement

The cement under study was Palacos R + G (Heraeus Medical GmbH, Wehrheim, Germany) containing 0.5 g of gentamicin. The selected antibiotics were Normon EFG vancomycin (Normon,

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Table 1
The Study Groups and the Amount of the Antibiotic Relative to the Mass of the Cement Powder (in w/w).

	Cefazolin	Vancomycin
Group 1 (Control)	-	-
Group 2	2.5%	-
Group 3	-	2.5%
Group 4	2.5%	5%
Group 5	-	5%
Group 6	-	10%

Table 2
The Test Type and Aging Conducted for Each of the Tested Conditions.

	Test	Ageing
Condition 1	Dry	Without ageing
Condition 2	Immersed in saline solution	Without ageing
Condition 3	Immersed in saline solution	1 week in saline solution at 37 °C
Condition 4	Immersed in saline solution	1 month in saline solution at 37 °C

Madrid, Spain), an antibiotic with a high molecular weight (1449.3 g/mol) and low water solubility, and cefazolin Normon EFG (Normon, Madrid, Spain), an antibiotic with a low molecular weight (454.51 g/mol) and high water solubility. Depending on the antibiotic selected and the dose used, 6 study groups were established. The amounts and combinations of the tested antibiotics are shown in Table 1.

The antibiotic was added manually by adding the same amount of polymer powder as antibiotic to obtain a homogeneous sample, as recommended by Frommelt et al [14]. The cements were prepared by manually mixing the powdered PMMA with the liquid monomer methylmethacrylate in a bowl with a spatula according to the manufacturers' instructions. The resulting mix of liquid cement was then poured into a silicon mold that contained six holes of 30 mm in diameter and 4 mm in height. The mold with the samples was pressurized on a metal foil for 30 minutes with a load of 100 N. After the cement hardened, the cement discs were removed from the mold and stored under dark, at room temperature. Each disc had a total surface area of 7.07 cm^2 and a weight of 3.5 $\pm$ 0.3 g. During the preparation of the samples, the temperature and relative humidity were kept constant at 23 $\pm$ 2°C and at 35 $\pm$ 5%, respectively. In all cases, the samples were mixed in air (without vacuum) and stored for 24 hours prior to testing or conditioning

Sample Conditioning

Four different test conditions were established (Table 2). Condition 1 specimens were tested in dry condition. Condition 2 was tested in the liquid medium (phosphate-buffered saline; PBS) without ageing. Samples from conditions 3 and 4 were tested in the liquid medium after ageing.

Exposure to ageing environment was achieved by immersion of antibiotic-loaded cement discs in 250 ml of PBS at a constant temperature of 37°C.

Wear Study (Mechanical Wear Tests)

The mechanical wear tests were carried out in a Pin on Disk Tribometer from Microtest (Madrid, Spain), with a 6 mm diameter AISI 304 stainless steel pin.

The wear tests were performed according to the ASTM G99-05 [15] on cylindrical specimens. The tests were conducted a speed at of 0.1 m/s with an applied load of 15 N, and the sliding distance was 1000 m. Three samples from each group were tested at each condition (18 samples per condition), yielding a total of 72 tested samples. For the samples tested in the liquid medium, a circular beaker (50 mm radius $\times$ 30 mm height) was fixed to the tribometer with 100 ml PBS for direct testing in the liquid medium. For each group and ageing condition, the coefficient of friction and wear was evaluated.

The average friction coefficient was obtained by the tribometer, whereas the lost volume and the wear of each sample were obtained by a geometric relationship [15] using a Nikon Profile Projector V profilometer -20 (Nikon Instruments Inc, Melville, NY), defined in $(mm^3/nm)\cdot 10^{-4}$.

Scanning electron microscope

After the mechanical wear test, the wear tracks were studied using a XL-30 Scanning Electron Microscope (SEM) from Philips (Eindhoven, Holland), to determine the mechanism of wear. The samples were prepared using gold coating in a high-resolution Polaron SC7610 sputter coater from VG Microtech (Uakfield, United Kingdom) to

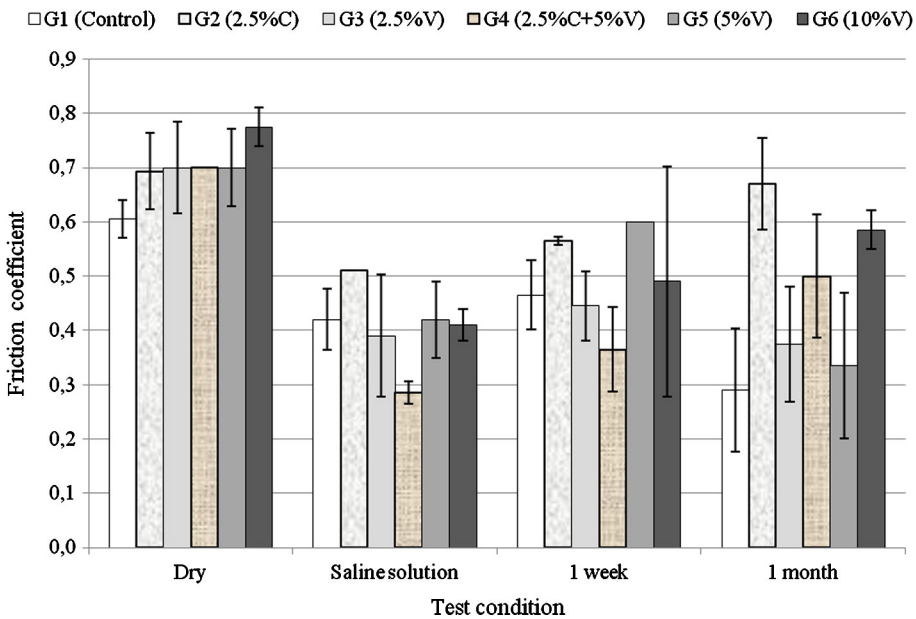

Fig. 1. The friction coefficients of each groups under each test condition.