International Orthopaedics (SICOT) (1998) 22:171–177

International Orthopaedics

Pharmacokinetics, uses, and limitations of vancomycin-loaded bone cement

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Accepted: 30 November 1997

Summary. *We have studied the mechanical and pharmacokinetic characteristics of an industrially-prepared bone cement containing 3 g of vancomycin per 60 g cement. A low viscosity cement was selected, to increase contact between the antibiotic and the infected surfaces. Resistance of compression (95 mPa) was well above the required standard (70 mPa) and similar to that of other cements with or without gentamicin. The concentrations in blood, urine and bone were measured in mg/l and mg/kg, and compared to the break point (BP) of susceptibility tests, which must be obtained to achieve control of infection. Diffusion tests were conducted in vitro (elution in saline from rods), and in 30 sheep femora implanted with the cement in vivo. In the animal study, bone levels during the first three months were three-fold higher than the BP (i.e., were ≥12 mg/l) in 92% of specimens from all areas of bone studied and at all times since implantation; they exceeded five times the BP in 56% of specimens and were never lower than twice the BP. The mean level was four times the BP after six months and fell sharply during the next six months. A pharmacokinetic study in ten patients who had a primary total hip arthroplasty with vancomycin-loaded cement as prophylactic antibiotic therapy showed that blood levels were lower than 3 μg/ml, i.e., 30 times lower than the toxic threshold (90 μg/ml). Vancomycin was undetectable in urine after the tenth day. The levels in drainage fluids were five times the BP after 24 h and equal to it after four days. None of the ten patients treated prophylactically with vancomycin-loaded cement developed evidence of allergy, toxicity, intolerance or loosening during a two year period. No adverse events were recorded in 17 other patients treated with a vancomycin (2 g) plus gentamicin (0.8 g) loaded cement as adjuvant therapy for severe prosthetic infection.*

Résumé. *Compte-tenu de l'efficacité du ciment aux antibiotiques dans la prévention et le traitement des infections sur prothèses, nous avons étudié les caractéristiques mécaniques et pharmacocinétiques d'un ciment à la Vancomycine, car cet antibiotique est actif pratiquement sur tous les staphylocoques, même méti R. Il s'agissait d'un ciment à basse viscosité (pour optimiser le contact de l'antibiotique avec les surfaces infectées), préparé industriellement, compartant 3 grammes de Vancomycine pour 60 grammes de ciment. Les concentrations dans le sang, les urines et l'os étaient mesurées en mg/l ou mg/kg et comparées à la concentration critique (CC), qui doit être atteinte pour contrôler l'infection. Mécaniquement, la résistance en compression était de 95 mPa, et donc bien supérieure à la norme (70 mPa), et égale à celle d'autres ciments avec ou sans Gentamicine. Des études de diffusion ont été faites in vitro (élution dans du sérum à partir de bâtonnets), puis lors de 30 implantations fémorales chez la brebis. Le taux osseux était, jusqu'au 3ème mois après implantation, supérieur à 3 fois la CC (soit ≥12 μg/cc) dans 92% des prélèvements, quel que soit leur niveau dans l'os ou le délai (il dépassait 5 fois la CC dans 56% des prélèvements, et n'était jamais inférieur à 2 fois la CC). A 6 mois, le taux moyen était de 4 fois la CC, puis chutait avant un an. Pour connaître la pharmacocinétique en clinique de ce ciment, celui-ci a été utilisé comme antibioprophylaxie chez 10 premières implantations de*

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prothèse totale de hanche: cette étude a permis de constater un taux sanguin inférieur à 3 µg/ml, soit 30 fois moins que le seuil de toxicité (90 µg/ml). L'antibiotique n'était plusretrouvé dans les urines au-delà de 10 jours. On retrouvait, dans les liquides de drainage péri-prothétiques, des taux de 5 fois la CMI à 24 heures, descendant jusqu'au taux de la CC en 4 jours. Aucun incident allergique, toxique, d'intolérance, ou de descellement n'était constaté chez ces 10 cas expérimentaux d'antibioprophylaxie (avec 2 ans de recul minimum), ni chez 17 autres patients chez lesquels un ciment Vancomycine (2 g) – Gentamicine (0,8 g) avait été utilisé comme traitement adjuvant d'une infection prothétique sévère.

Introduction

The value of orthopaedic cement as a vector for gentamicin has been convincingly established [1–3, 8–10, 16, 19, 21, 24].

Nearly 50% of staphylococci responsible for prosthetic infections are now resistant to gentamicin [15], whereas virtually none are resistant to vancomycin [7, 17]. We therefore conducted a study of vancomycin-loaded cement [11, 14] in order to determine its efficacy in providing high bone levels of vancomycin and to evaluate the potential mechanical, toxic, and allergic consequences of the addition of vancomycin to the cement. After a set of in vitro experiments, the cement was studied in vivo in 30 sheep femora, and was then used for total hip arthroplasty in ten patients.

Materials and methods

The biomaterial used in our study was a low-viscosity cement (Cerafix® Osteal France) to which 3 g of vancomycin per 40 g of polymer powder had been added. This approach was in accordance with control tests which had verified that vancomycin granulometry met required specifications and that its distribution throughout the powder was uniform. The characterisation techniques had been developed in our laboratory over the last ten years for studies of gentamicin-loaded cement [4, 5, 12].

Tests for mechanical strength

We used resistance to compression and extrusion tests complying with the ISO 5833 standard. Compression tests were also performed with an antibiotic-free cement (CMW®), a standard-viscosity gentamicin-loaded cement (Palacos Gentalline®), and a low-viscosity gentamicin-loaded cement (Cerafix Genta®). We also undertook tests on the vancomycin-loaded cement after changing some of the parameters including the amount of vancomycin, amount of radio-opaque agent and irradiation.

In vitro elution was used to measure the amounts of vancomycin released by the cement. Cylindrical rods (12 mm in length, 6 mm in diameter) manufactured according to ISO standards were immersed in phosphate buffer saline (PBS) at 37° C. An automate transferred the rods from one elution bath to the next, every 4 h initially, then at longer and longer intervals, the total duration of each experiment being two months for each batch [4]. Two series of 12 rods were tested. Vancomycin assays were carried out using the EMIT® immunoenzymetric test that measures the biologically active fraction of the drug.

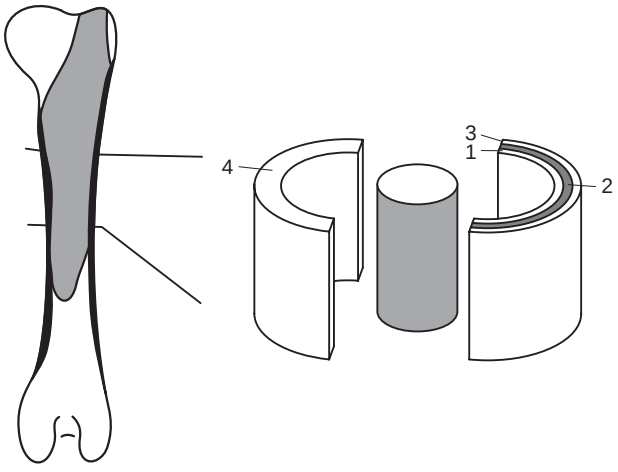

Fig. 1. Zones of sampling for the measurement of the concentration of Vancomycin in sheep femora. A cylinder of the diaphyseal bone in close contact with the cement was harvested and split in order to remove the cement core. Bone powder was obtained by filing off three layers of bone: inner cortex (*1*), intermediate cortex (*2*), outer cortex (*3*), and full thickness cortex (*4*)

Animal experiments

Because collection from human patients of cortical specimens in contact with a prosthesis or elsewhere would have been unethical, we conducted studies in our usual animal model, namely ewes with a mean weight of 60 to 70 kg, bearing femoral implants of the cement under study. The cement was introduced into a 13 mm reamed shaft, using a syringe in the top of the greater trochanter. In order to obtain data for comparisons of pharmacokinetics in humans and sheep, we determined the vancomycin levels in the blood and urine of two ewes.

A total of 38 implantations of cement into the femoral shafts of 21 ewes were performed according to the French regulations concerning animal experimentation; implantation was bilateral in 17 animals. Thirty implantations were interpretable. The remaining eight implantations were in four ewes that were sacrificed prematurely because of complications: perforation of the femoral cortex due to an S-shaped diaphysis resulted in a fracture in three, and a superficial infection occurred in one. The times to sacrifice were as follows: one day (two femora), 15 days (four femora), one month (six femora), three months (four femora), six months (four femora), one year (four femora), 18 months (four femora), and two years (two femora).

Each femur was cut longitudinally (Fig. 1) and the cement painstakingly removed from the medullary cavity. The concentration of vancomycin in bone powder obtained by filing the femur was determined by elution for six hours in PBS. To gather data on the diffusion of vancomycin in bone and to ensure that the results would not be distorted by persistence of cement in the bone samples (low viscosity cement penetrates well into bone), four different areas were studied separately: the outer cortex, i.e., the outermost millimetre, which was not in contact with the cement in the medullary cavity; the inner

cortex, i.e., the innermost millimetre adjacent to the medullary cavity; the intermediate cortex, located between the outer and inner cortices, and the "full thickness" cortex, which was filed off perpendicular to its long axis.

Implantation in human patients

We studied the pharmacokinetics of vaoncomycin after prophylactic use of vancomycin-loaded cement in a consecutive series of ten total hip arthroplasties which were at risk of infection, and which had been operated upon between October and December 1992. This part of our study was conducted in compliance with current French regulations and with the patient's informed consent. Our objectives were to evaluate the appropriateness of the cement for orthopaedic use as regards ease of handling and viscosity, its safety in relation to allergies and local and systemic toxicity, and the diffusion of the vancomycin released from the cement. We determined vancomycin levels in specimens of blood, drainage fluid, and urine collected 6, 12, and 24 h after implantation, then daily during 2 to 5 days for drainage fluid, and during ten days for blood and urine. All patients had a minimum clinical and radiological follow-up of 2 years with a maximum of 4 years.

The total number of vancomycin assays undertaken for the elution tests, animal experiments, and clinical study was in excess of 1200.

Results

Mechanical properties

Resistance to compression. We found no noticeable differences between cement loaded with 2 g or 3 g of vancomycin or between cement with or without a radio-opaque agent (2 g of ZrO_2). Sterilisation by exposure to radiation slightly decreased mechanical strength, although the difference was not significant. Based on these data, we used cement (Cerafix – Vanco) containing 3 g of vancomycin and 2 g of ZrO_2 and irradiated for sterilisation for our in vitro, animal and clinical studies.

Resistance to compression showed 95 mPa for irradiated Cerafix-Vanco, 84 mPa for Palacos-Gentalline®, 92 mPa for CMW®, and 103 mPa for Cerafix-Genta®; according to current standards, resistance to compression should be 70 mPa or more.

The viscosity of the vancomycin-loaded cement immediately after mixing was higher than that of low-viscosity gentamicin-loaded cements, but the mixture liquefied gradually to the point where it could be introduced into the diaphysis using a cement gun.

Fatigue tests showed that resistance of the study cement was 35 mPa during more than 10 million cycles.

In vitro elution

After eight weeks, 4.2% of the vancomycin in the cement had been released into the solution. Thirty per cent of the total amount eluted was released during the first 4 h after implantation, 50% during the first 24 h, and 70% during the first three days. Significant release was still occurring at the end of the two-month experiment.

Animal studies

Gross findings. Radiographs and gross examination of the longitudinally cut femora demonstrated excellent contact between the cement and the endosteum, without interposition of fibrous tissue or development of an inflammatory reaction. This can be ascribed to the low viscosity of the cement, which allows intimate contact with the bone into which diffusion of the antibiotic is sought.

Blood and urine levels. Blood and urine levels of vancomycin were determined in two ewes. Blood levels were below the detection threshold in both animals. The mean urinary concentration during the first 24 h was 10 mg/l, comparable to the levels reported in humans.

Bone levels (Table 1). Bone vancomycin levels were measured in mg/kg and as multiples of the break point of the susceptibility tests (BP) of vancomycin. When this level of 4 mg/l is obtained, the bactericidal effect of vancomycin on staphylococci is achieved. Bone levels during the first six months averaged 20 mg/kg and were not lower than 8 mg/kg in any of the bone areas studied. The mean bone level was 4 mg/kg after one year and fell below the detection threshold after 18 months. Bone levels varied between animals, from one side to the other in any animal, and from one area to another in any femur.

The average femoral vancomycin levels after 15 days were twice as high in the endosteum, the area in contact with the cement, as in the outer cortex (54 mg/kg versus 22 mg/kg), and the mean level in the full-thickness cortex was intermediate between these two values (49 mg/kg). Over time, the distribution of vancomycin became more uniform. After three months the mean levels were 48 mg/kg in the outer cortex, 39 mg/kg in the intermediate cortex, and 45 mg/kg in the full-thickness cortex. This last value, which was close to the values seen in the three other areas studied, was therefore considered to be a satisfactory index of the vancomycin level in bone.

In a given animal, side-to-side differences in full-thickness levels were generally small (e.g., 25 mg/kg on the left versus 31 mg/kg on the right after six months), although variations of up to three-fold were seen. From one animal to the next, up to two-fold variations were found. Nevertheless, the values remained consistent and varied mainly with the time since implantation. All the 64 vancomycin bone levels determined within three months after implantation (in four different areas of 16 femora) were greater than twice the BP (≥8 mg/l); 92% (59/64) were more than three times greater (≥12 mg/l), and 56% (36/64) were more than five times larger (≥20 mg/kg). The mean value for these 64 assays was 32 mg/kg and the

Table 1. Concentration of vancomycin in the femoral cortex of sheep. Vancomycin loaded bone cement was introduced in 30 femora of 17 sheep. For each femur, the bone concentration of vancomycin was measured in 4 zones: outer cortex, intermediate cortex, inner cortex, and "full thickness" cortex

Delay post implantation	Sheep Nº, side	Outer cortex mg/kg	Intermediate cortex mg/kg	Inner cortex mg/kg	Full thickness cortex mg/kg
1 day	1 L Left	26.4	9.0	8.2	12.6
	2 L	16.8	13.8	34.8	18.0
15 days	3 R Right	19.2	27.6	15.6	19.2
	3 L	24.6	32.4	61.2	45.0
	4 R	22.8	34.8	52.2	52.8
	4 L	21.6	54.6	88.2	79.8
1 month	5 L	10.2	16.2	45.6	28.2
	6 R	13.2	24.6	41.4	16.8
	6 L	72.0	27.0	15.6	42.0
	7 L	16.8	27.6	23.4	20.4
	8 R	15.6	8.4	14.4	12.0
	8 L	18.0	13.8	10.8	17.4
3 months	9 R	75.6	70.8	73.2	72.0
	9 L	87.0	66.6	72.0	55.2
	10 R	10.2	10.0	35.4	29.4
	10 L	19.8	11.4	12.6	25.8
6 months	11 R	19.8	13.8	10.8	10.8
	11 L	27.0	21.6	16.2	12.6
	12 R	10.8	11.4	19.2	31.8
	12 L	28.8	16.8	31.2	25.2
12 months	13 R	0.0	0.0	4.4	0.0
	13 L	2.8	2.8	4.4	4.4
	14 R	3.2	3.8	3.8	2.8
	14 L	2.2	0.0	4.0	0.0
18 months	15 R	2.7	0.7	2.1	2.7
	15 L	0.0	0.0	0.0	0.0
	16 R	0.2	1.6	0.0	0.0
	16 L	2.9	4.7	3.8	4.7
24 months	17 R	0.0	0.0	0.0	0.0
	17 L	0.0	0.0	0.0	0.0

range was 8.2 to 88.2 mg/kg. Bone vancomycin levels remained high until the sixth month. In the 16 femoral specimens studied at six months, the vancomycin levels averaged 19.2 mg/kg, almost four times the BP, and were consistently higher than twice the BP.

Clinical study in ten patients

Cerafix-Vanco was used for prophylactic antimicrobial therapy in ten patients receiving a primary total hip prosthesis. None of the patients had a history of allergic disease, and none had reacted abnormally to a penicillin patch test or to a test injection of vancomycin. Implantation was not associated with any haemodynamic or other abnormalities. The mean amount of cement implanted was 88 g (2.7 g of vancomycin). There was no clinical evidence of intolerance, and no laboratory evidence of inflammation due to the arthroplasty.

Blood vancomycin levels (Fig. 2) did not exceed 2.9 mg/l. Peak levels were achieved six to 24 h post-implantation. On the third postoperative day, blood vancomycin levels were below the detection threshold in four patients and averaged 0.2 mg/l in the remaining six. Ten days after surgery, none of the pa-

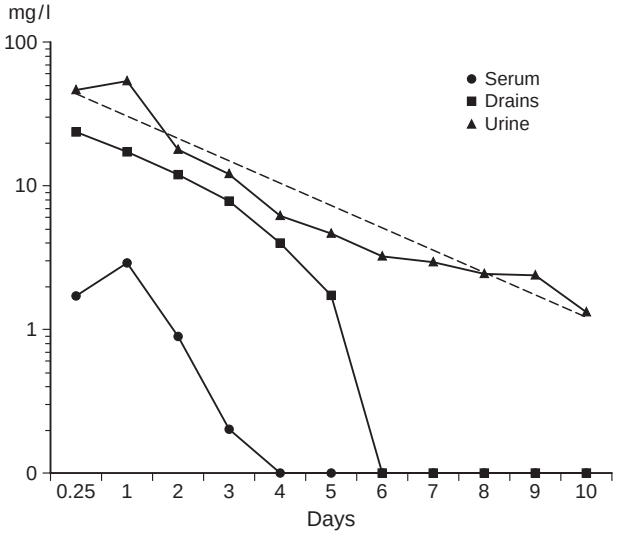

Fig. 2. Concentration of vancomycin in drainage fluids, serum and urine, in 10 patients with THR. Vancomycin concentration was measured at 6 h post operation, and every day for 10 days, after antibiotic prophylaxis of primary aseptic THR using vancomycin loaded bone cement. At the third post operative day, the concentration in drainage fluids was still more than twice the BP, whereas vancomycin could hardly be detected in the serum

tients had detectable levels of vancomycin in their blood.

Urinary vancomycin levels reached a peak of about 50 mg/l between six and 24 h after operation (48 to 53.9 mg/l) and then fell rapidly to 1.3 mg/l on the tenth day, when urinary vancomycin was undetectable in six of the ten patients.

Vancomycin levels reached very high values in the drainage fluid. The peak was achieved six to 24 h after operation and was about 20 mg/l (16.9 to 22.7 mg/l, which is five times the BP). Vancomycin levels in the drainage fluid were about 4 mg/l after four days in the seven patients who had their drain removed at this time.

All patients had a biological (ESR, C reactive protein), radiological and clinical follow up for at least two years. Seven hips had a very good result. Two hips required reoperation for a trochanteric nonunion which was cured by a hook fixation. One elderly patient had a traumatic ipsilateral fracture which was treated in another hospital. There were no signs of infection or of loosening in any THR.

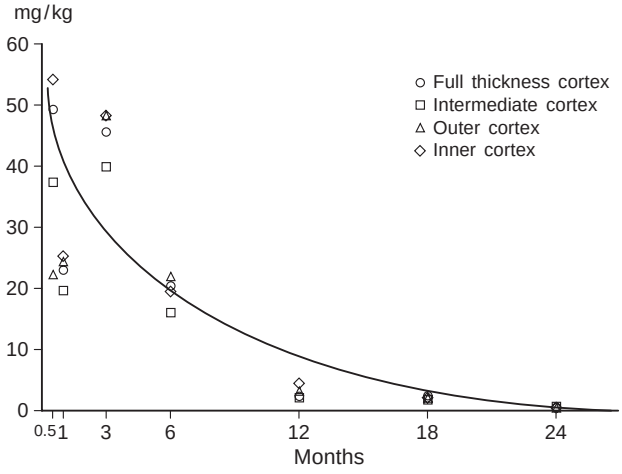

Fig. 3. Vancomycin concentration in the cortex of 30 sheep femora after implantation of bone cement. The animals were killed between 0.5 and 24 months after operation and the concentration of vancomycin was measured in 4 zones for each femur

Discussion

Our experimental and clinical data on vancomycin-loaded cement are very similar to those reported for cement containing gentamicin.

Mechanical properties

It has been demonstrated that the mechanical properties of cement can be profoundly altered by the addition of an antibiotic [12] as a solution, which may produce a 20% to 40% decrease in mechanical resistance, or as a powder in an amount exceeding 5% of the total amount of cement. The mixture we used was prepared in accordance with good manufacturing practice. Despite addition to the cement of 3 g of vancomycin per 60 g of cement and of 2 g of ZrO_2, resistance to compression (95 mPa) remained similar to that of an antibiotic-free cement (CMW®, 92 mPa) and of a cement containing only 0.8 g of gentamicin (Palacos-Genta®, 84 mPa). Whereas vancomycin-cement mixtures prepared in the operating room can only be used as temporary spacers, industrially prepared vancomycin-loaded cement exhibits mechanical properties which are similar to those of other cements and can therefore be utilised for permanent fixation of joint prostheses.

Are the pharmacokinetics of vancomycin-loaded cement suited to the clinical objectives?

The antibiotic released should not undergo denaturation due to mixture with the cement, storage, or temperature increase during polymerisation [23]. Bone levels should be greater than the BP over a six month period, which is the currently recommended duration of antimicrobial therapy for osteomyelitis. Blood and urine levels, which reflect the risk of systemic toxicity, should be low.

The BP of both gentamicin and vancomycin, corresponding to their bactericidal activity, is 4 mg/l. In vitro elution of vancomycin out of the cement was not significantly different from that of gentamicin (4.2% versus 6.2% of the amount in the cement, after eight weeks). Comparative studies were undertaken involving the use of High Performance Liquid Chromatography and the measurement of inhibition zone diameters produced by antibiotic-loaded cement cement disks placed on a culture of *Bacillus subtilis.* These investigations demonstrated that the immunoenzymetric assay used in our study measures bacteriologically active vancomycin, as opposed to the inactive crystalline degradation products of the drug.

The main characteristics of vancomycin bone levels in sheep were (Fig. 3) high levels during the first six months, regardless of the animal, the time since surgery, the bone area, and the side. Bone levels during the first three months were greater than three times the BP in 92% of the sheep, and greater than five times the BP in 56%. There was a rapid fall beyond six months, with levels of the order of the BP in only half the samples after one year (5/8), and in none after two years.

The level varied across specimens. These variations can be ascribed to the difficulty of separating the three concentric bone areas and to variations in bone cement contact and in femoral vascularisation. However, the values formed a consistent pattern with most of the variation being related to time since implantation. Furthermore, for a given femur, no marked differences were found between the endosteum and the other bone areas which were studied, indicating that there was no distortion of the results due to the presence of vancomycin-loaded cement particles in the endosteal specimens.

Our clinical study of drainage fluids, blood and urine suggests that the pharmacokinetics of vancomycin are similar to those of gentamicin. With vancomycin, the level in drainage fluids was five times that of the BP. Blood and urine levels, (2.5 mg/l within the first 6 h in blood, and 50 mg/l in the first 24-h urine collection), were about five times higher than those achieved with gentamicin bone cement, which may be due [22] to the considerably larger amount of vancomycin than of gentamicin contained in the cements (3 g versus 0.6 g). The 2.5 mg/l blood level was far below the toxic level (90 mg/l). None of the ten patients in this study developed infection.

We found marked similarities between the pharmacokinetics of vancomycin and gentamicin. The bone levels of both antibiotics exceeded four times the BP during the first three months and twice the BP throughout the first six months, and during the same period blood levels remained far below toxic values. Slight differences were found in bone pharmacokinetics, with an initial peak that was not as high for vancomycin (ten times the BP) as for gentamicin. A very high early peak is important for gentamicin but not for vancomycin since a dose-effect exists only for the former. Bone levels remained high throughout the first six months, an important characteristic for both curative and prophylactic treatment. Our data suggest that cement loaded with vancomycin may have similar efficacy on susceptible organisms to that of gentamicin loaded cement upon strains which are susceptible to gentamicin.

After the prophylactic clinical study reported in this article, we used cement containing 2 g of vancomycin and 0.8 g of gentamicin as an adjuvant to systemic antimicrobial therapy in 17 additional patients who had revisions of infected total hip or total knee replacements. Nine have been followed up for more then three years. None of the 17 patients developed intolerance. One aseptic loosening resulting from poor bone stock required further revision. Resolution of the clinical, microbiological, and radiological evidence of infection was obtained in every case. However, we cannot determine the respective contributions to the favourable outcome in these patients of surgical excision of infected tissues, systemic antimicrobial therapy, and the use of vancomycin plus gentamicin-loaded cement.

Can vancomycin-loaded cement adversely affect the patient and/or the microbial ecology?

The use of vancomycin is restricted to hospitals in France in an effort to maintain its position as a drug to which resistance among staphylococci is exceedingly rare. A number of adverse effects occurred during the first clinical studies of vancomycin (rashes, transient hypotension) [18].

Risk to the patient. We performed a penicillin-patch test to detect cross-reactions and gave an intravenous infusion of 1 g of vancomycin in 100 ml of saline over one hour in all our patients prior to use of the vancomycin-loaded cement. No abnormalities were recorded, either after the tests or after implantation of the cement.

The risk of vancomycin toxicity associated with use of the cement is very low since the peak blood level was only 3 mg/l. Peaks in the order of 60 mg/l are commonly achieved during intravenous vancomycin therapy.

Risk to the microbial ecology. Gradual development of vancomycin resistance could occur as a result of wide use of vancomycin, prolonged release in subtherapeutic doses, or the employment of large amounts. We believe that vancomycin-loaded cement should be used only for revisions of infected arthroplasties and for high risk procedures. Such cases account for less than 5% of all joint replacements. The risk of prolonged release of sub-therapeutic doses is apparently minimal, since after the tenth day vancomycin levels in urine were below the detection threshold of the very sensitive assay method used in our study. The amount of antibiotic used for conventional intravenous therapy of bone infection due to a multiresistant staphylococcus is 2 g per day for six weeks, or a total of 90 g. In our patients, the amount of vancomycin in the implanted cement was about 3 g, of which about 150 mg diffused out of the cement, 95% of the vancomycin remaining trapped in the methylacrylate. The amount of vancomycin eliminated in the urine is therefore 600 times greater after a conventional course of intravenous therapy than after use of vancomycin-loaded cement to implant a hip prosthesis.

Potential evolution of the vancomycin loaded cement

Our results with Cerafix-Vanco which contains 3 g of vancomycin, support the use of a cement containing only 2 g of vancomycin and 0.8 g of gentamicin. The 3 g dose per unit of cement is not indispensable because the activity of vancomycin is not potentiated by a dose effect. Release of vancomycin is directly proportional to its concentration in the cement, as we observed in vitro elutions. Thus, the bone and drainage fluid levels obtained with 2 g instead of 3 g of vancomycin would provide levels far greater than the BP. However, it is worthwhile to broaden the spectrum of antibacterial activity by adding an extensively studied aminoglycoside, since the spectrum of vancomycin is narrow. Addition of gentamicin provides efficacy against gram-negative bacilli, which are sometimes responsible for bacteraemia, especially in patients with urinary tract infections, and a multi-resistant staphylococcus and an organism sensitive to gentamicin are often present concomitantly in specimens from repeat revisions of arthroplasties. We have conducted in vitro studies which showed no interactions on release kinetics between vancomycin and gentamicin.

We advocate that cements produced extemporaneously in the operating room by mixing a conventional cement with vancomycin should be used only as tem-

porary spacers, since the mechanical properties of these cements are not appropriate for permanent bonding of a prosthesis.

For routine prophylactic antibiotic therapy in primary procedures and for revisions of non-infected prostheses in non-debilitated patients, the use of gentamicin-loaded cement may be currently the best compromise between prophylactic efficacy and a low risk of selection of resistant bacterial strains.

Industrially-prepared vancomycin plus gentamicin-loaded cement may be the best choice, for permanent fixation of joint prostheses, in one-stage or two-stage revision of prostheses infected with resistant staphylococci. It may also be used for arthroplasties in debilated patients such as those who need a chemotherapy [13], those who require a massive allograft composite prosthesis, or who have an immunity deficiency.

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