SCIENTIFIC ARTICLE

Adding vancomycin to bone cement: research on its influence on mechanical and fixation strength using rabbit femoral prostheses

Yu-hui Yang MD, Jin-cheng Wang MD, Yan-ling Pei MD

Department of Rehabilitation, China-Japan Union Hospital, Jilin University, Changchun, China

Objective: To compare the influence of different methods of adding vancomycin on the strength of bone cement used for fixing rabbits' femoral prostheses.

Methods: Eighteen New Zealand white rabbits (36 femora) were allocated to three groups of six rabbits (12 femora) each: a control group, an experimental group 1 and experimental group 2. The bone cement used in the control group was mixed manually without vancomycin; in experimental group 1 it was mixed manually with 5% (2 g/40 g) vancomycin; and in experimental group 2 it was mixed in a vacuum with 5% (2 g/40 g) vancomycin. The cement combinations were then used to fill the marrow cavity of rabbit femurs to fix prostheses. An electronic universal testing machine (EUTM) was used to test the pullout force of the prostheses with bone cement 48 hours later. Student's paired *t*-test was used for statistical analysis.

Results: It was found that the maximum load of pullout force was 559.3 ± 82.3 N in the control group; 523.6 ± 86.5 N in experimental group 1; and 645.1 ± 105.9 N in experimental group 2. Statistical analysis showed there was no significant difference between the control group and experimental group 1 ($P > 0.05$). However, there were significant differences between the control group and experimental group 2 ($P < 0.05$); and between experimental group 1 and experimental group 2 ($P < 0.05$).

Conclusion: When bone cement and vancomycin were mixed manually in a low concentration (<5%) vancomycin had no influence on the strength of the bone cement. However, bone cement and vancomycin mixed at the same concentrations in a vacuum did have a statistically significant effect on the strength of the bone cement.

Key words: polymethyl methacrylate; prostheses and implants; rabbits; vancomycin

Introduction

With ongoing development in materials and surgical procedures, prosthetic joint replacement has become the commonest and most effective treatment for end-stage joint disease¹. Infection is a serious complication and can result in treatment failure. Local delivery of antibiotics by using antibiotic-loaded bone cement to fix a replacement prosthesis has become a recommended practice for the management of infected prosthetic joints. *Staphylococcus aureus* is the main bacterium that causes infection of arthroplasties. Because this organism is resistant to common antibiotics (such as penicillin, gentamicin and tobramycin), vancomycin has become the only effective

antibiotic for treatment of *S. aureus* infection². Vancomycin acts by altering the composition of peptidoglycan, thus leading to effective antibiosis³. On the other hand, much *in vitro* research has shown that antibiotics have a negative effect on the strength of bone cement⁴. However, there is controversy regarding the concentration of antibiotics required, and there has been little research on the influence of different methods of cement mixing. We researched the effects on mechanical strength of using different methods to add vancomycin to bone cement before using it to fix prostheses in rabbits.

Materials and methods

Experimental materials

A commercial radiopaque bone cement (Surgical Simplex, Stryker, Kalamazoo, MI, USA) was chosen as control, and as the basic material with which the antibiotic was mixed. This product contains liquid and powder

Address for correspondence Yu-hui Yang, MD, Department of Rehabilitation, China-Japan Union Hospital, Jilin University, Changchun, China 130033 Tel: 0086-431-84995380; Fax: 0086-431-84995380; Email: yangyuhuime@163.com

Received 15 June 2011; accepted 2 August 2011

DOI: 10.1111/j.1757-7861.2011.00155.x

Figure 1 Test of the maximum load of pullout force. (a) Before testing. Arrow 1 indicates the Steinmann pin and arrow 2 the rabbit femur. (b) Testing of the maximum load of pullout force. Arrow 1 shows the shaft of the femur and arrow 2 the anchoring to the electronic universal testing machine.

components. The liquid component includes methyl methacrylate 19.5 mL, N-Dimethyl-p-toluidine 0.5 mL (to prevent early polymerization) and hydroquinone 19.5 mg. The powder component includes methyl methacrylate styrene copolymer 30.0 g, polymethyl methacrylate 6.0 g and barium sulfate 4.0 g. Vancomycin ($C_{66}H_{75}Cl_2N_9O_{24}HCl$, Eli Lilly, Japan) was added in the experimental groups.

Experimental methods

The experimental procedures were in accordance with the guidelines of the Ethics Committee of the China-Japan Union Hospital of Jilin University. The experiments were carried out on 18 male New Zealand rabbits 3–4 months of age and weighing 2.5–3.1 kg. The rabbits were divided into three groups of 6 rabbits (12 femora) each: group 1 (the control group), experimental group 1 and experimental group 2. The rabbits were anesthetized with 3 mL of 3% pentobarbital via marginal ear vein injection. The superior extremities of both femurs were then exposed and their medullary cavities thoroughly prepared. According to the ISO5833 standards, the bone cement was mixed with vancomycin under aseptic conditions using a self-restraint powder mixer in a thermostatic chamber at a temperature of $(23 \pm 1)^\circ\text{C}$ and humidity of 40% ~ 60%. The bone cement used in the control group was mixed manually without vancomycin, that used in group 1 was mixed manually with 5% vancomycin and that used in group 2 was mixed in a vacuum with 5% vancomycin. The marrow cavities were filled with bone cement while inserting the prostheses (2.2 mm diameter Steinmann pins) into the centres of the marrow cavities of the rabbit femurs. An electronic universal testing machine (EUTM, AG-10TA, Shimadzu Corporation, Kyoto, Japan) was used to test the pullout force of the prostheses with bone cement at a speed of 20 mm/min 48 h later (Fig. 1).

Statistical analysis

Statistical software SPSS 14.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. All data were expressed as mean and standard deviation and evaluated by using Student's *t* test. Significance was set at $P < 0.05$.

Results

The control group and experimental group 1 each included one failed case caused by non-uniform cement filling, which led to femoral fracture when pulling out. The other femora were split in half after the experiment had been completed and it was confirmed that the bone cement had filled the cavities without gaps. The maximum load of pullout force occurred at the moment that the prosthesis was pulled out. The maximum load of pullout force was 559.3 ± 82.3 N in the control group, 523.6 ± 86.5 N in experimental group 1, and 645.1 ± 105.9 N in experimental group 2 (Table 1). Statistical

Table 1 The maximum load of the specimen in each group (N)

Specimen No.	Control group	Experimental group 1	Experimental group 2
1	640	592	679
2	448	472	419
3	552	592	557
4	448	635.2	694
5	608	627.2	771
6	704	551.2	654
7	480	456.8	598
8	432	404	684
9	512	596.3	801
10	456	667.2	605
11	480	522.5	552
12	—	—	727
Mean $\pm$ SD	559.3 ± 82.3	523.6 ± 86.5	645.1 ± 105.9

analysis showed there was no significant difference between the control group and experimental group 1 ($P > 0.05$); however, there were significant differences between the control group and experimental group 2 ($P < 0.05$) and between experimental group 1 and experimental group 2 ($P < 0.05$).

Discussion

Bacterial infection is a significant and devastating complication of total joint arthroplasty because it increases the prosthesis failure rate. Antibiotic-loaded bone cement was first used in revision joint arthroplasty in the 1970s. Release of antibiotic from this cement produces an antibiotic concentration in local tissue that is much higher than the blood concentration. Furthermore, the antibiotic can permeate into the prosthesis-bone and cement-bone interfaces. Since the 1980s, antibiotic-loaded bone cement has been commonly used in revision joint arthroplasty and has improved the cure rate of infection. On the other hand, the mechanical property of bone cement is a critical factor in regard to this treatment. Many researchers have investigated whether the mechanical properties are affected by antibiotic mixing^{4–6}. Although many studies have been done on different mixtures and proportions, no consistent conclusion has been reached. There have been no comprehensive studies of the effect of different mixing methods on antibiotic-loaded bone cement. Gram positive cocci are the major pathogenic bacteria (about 85%–95%) that cause post-operative infection, most of them being *S. aureus*^{2,7}, one of the commonest pathogenic bacteria to cause acquired infection in hospitals and communities globally⁸. Because *S. aureus* is resistant to many common antibiotics (penicillin, gentamicin and tobramycin, etc.); vancomycin has become the only effective antibiotic for *S. aureus* infection¹. So far, many *in vitro* studies have been done on antibiotic-loaded bone cement. Here we report *in vivo* research on the effects of different mixing methods on the mechanical properties of antibiotic-loaded bone cement.

By measuring the maximum load of pullout force in each group, we found that there is no significant influence on the strength when the bone cement contains about 5.0% vancomycin, which is in accordance with Klekamp's research⁹. We also found that, at the same vancomycin concentration, vacuum mixing increases the maximum load compared both to manual mixing and to the control group. These results lead us to the conclusion that the mixing method is the critical factor in regard to the mechanical properties of antibiotic-loaded bone cement. Since manual mixing is not a homogeneous mixing

method and is very variable, it can lead to bubbles in the cement. Because the mechanical strength of manually mixed cement depends on the expertise of the operator, the research on total joint arthroplasty has inconsistent results. In contrast, vacuum mixing is a well-developed technique that is more consistently reproducible and does not depend on the skill of the operator. In conclusion, we recommend that vacuum mixed antibiotic-loaded bone cement should be routinely used in total joint arthroplasty and in revision surgery of arthroplasty due to infection.

Disclosure

The authors did not receive any outside funding or grants in support of this research for, or preparation of, this work. Neither they nor a member of their immediate families received payments or other benefits, or a commitment or agreement to provide such benefits, from a commercial entity.

References

1. Xiong H, Dai M. RANK/RANKL/OPG system in aseptic loosening of artificial joints (Chin). *Int J Orthop*, 2011, 32: 48–50.
2. Smith TL, Pearson ML, Wilcox KR, *et al.* Emergence of vancomycin resistance in *Staphylococcus aureus*. Glycopeptide-Intermediate *Staphylococcus aureus* Working Group. *N Engl J Med*, 1999, 340: 493–501.
3. Zhao JQ, Chen Q, Zheng Q. Vancomycin release of vancomycin-calcium sulfate and vancomycin polymethylmethacrylate in animal study. *Clin Edu Gener Prac*, 2010, 8: 167–169.
4. Persson C, Baleani M, Guandalini L, *et al.* Mechanical effects of the use of vancomycin and meropenem in acrylic bone cement. *Acta Orthop*, 2006, 77: 617–621.
5. Armstrong MS, Spencer RF, Cunningham JL, *et al.* Mechanical characteristics of antibiotic-laden bone cement. *Acta Orthop Scand*, 2002, 73: 688–690.
6. Ying M. Antibiotic-loaded bone cement in joint prosthesis surgery (Chin). *Orthop Biomech Mater Clin Study*, 2005, 2: 2–3.
7. Yao HQ, Zou F, Dai M. Post-arthroplasty common complication and prevention (Chin). *J Tradit Chin Orthop Trauma*, 2004, 16: 56–58.
8. Li YM, Xu ZZ, Xu ZB. Research on *Staphylococcus aureus* lower susceptibility to vancomycin. *Prog Modern Biomed*, 2011, 11: 194–198.
9. Klekamp J, Dawson JM, Haas DW, *et al.* The use of vancomycin and tobramycin in acrylic bone cement: biomechanical effects and elution kinetics for use in joint arthroplasty. *J Arthroplasty*, 1999, 14: 339–346.