Influence of cement viscosity on cement interdigitation and venous fat content under in vivo conditions

A bilateral study of 13 sheep

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ABSTRACT – In a sheep model permitting standardized bilateral, simultaneous cement pressurization, we studied the effect of different cement viscosities on fat and bone marrow intravasation and cement penetration in vivo. High viscosity cement (Palacos) was used on one side and low viscosity cement (Osteopal) on the other. Catheters were inserted into both external iliac veins to collect blood during bilateral simultaneous cement pressurization. After bone preparation and pulsatile lavage, both femora were filled with cement followed by simultaneous cement pressurization. A quantitative fat analysis of the blood collected was done. We used microradiographs to determine cement penetration in a left versus right comparison of both viscosity groups.

The low viscosity cement yielded lower rates of cement penetration despite adequate and sustained pressurization. Cement applied at low viscosity state seems to take the path of least resistance into the venous system before more deeper cement penetration can occur. The use of high viscosity cement ran a higher risk of fat embolism, but improved cement interdigitation.

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Under laboratory conditions, the use of cement in a low viscosity state seems to improve the penetration of cement and interface strength, particularly if cement pressurization techniques are used (Markolf and Amstutz 1976, Halawa et al. 1978, Rey et al. 1987, Bannister and Miles 1988, Bean et al. 1988, Stone et al. 1996, Reading et al. 2000). However, in the presence of active bleeding, the interface shear strength with low viscosity cements is significantly reduced, although the depth of cement penetration seems not to be affected to the same extent (Benjamin et al. 1987, Majkowski et al. 1994). The use of sustained pressure until the cement viscosity has increased to resist the displacement caused by the bleeding pressure was found to be essential (Lee and Ling 1981, Benjamin et al. 1987, Bannister and Miles 1988, Majkowski et al. 1993).

Cement pressurization, however, greatly increases intramedullary pressure (IMP) (Song et al.1994, McCaskie et al. 1997, Reading et al. 2000). Fat and bone marrow embolization may therefore occur (Breed 1974, Kallos et al. 1974, Tronzo et al. 1974, Orsini et al. 1987, Wenda et al. 1993, 1995, Pitto et al. 1998, 1999, Breusch et al. 2000b). Intraoperative fat embolism associated with cemented total hip arthroplasty is a well-known complication, but it remains unclear from the current literature whether the cement viscosity also effects the amount of fat and bone marrow intravasation.

To study the effects of cement viscosity on fat embolism and cement penetration under in vivo conditions, we used a sheep model which permits bilateral simultaneous cement application in the femoral canal and pressurization of cements of different viscosities.

Material and methods

We used a cement pressurization apparatus, which permits standardized bilateral simultaneous application of cement in the femoral canal and pressurization (Breusch et al. 2000b). A pneumatic ram

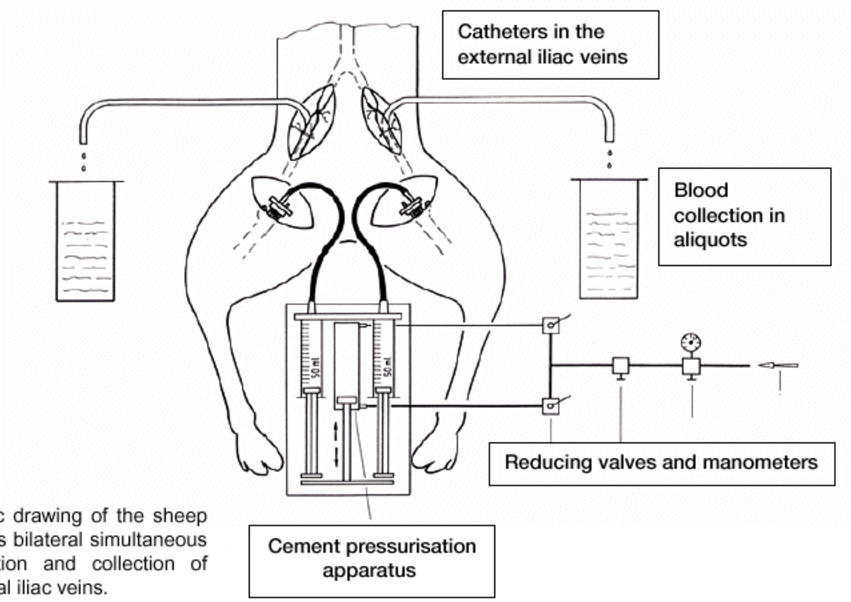

Figure 1. Schematic drawing of the sheep model which permits bilateral simultaneous cement pressurization and collection of blood via the external iliac veins.

applies a force on two syringes simultaneously which results in cement delivery at constant pressure. To prevent leakage of cement, a metal adapter was fixed with cement to a femoral neck osteotomy site before application of cement (Figure 1).

The technical set-up for cement pressurization was calibrated in vitro on cadaveric sheep femora. Three pressure gauges were placed transcortically along the femur. The pressure for the pneumatic ram was regulated in increments with a pressure reduction valve. IMP measurements were then recorded during cement pressurization.

From the findings of the in vitro study, we chose a pneumatic ram pressure of 3.8 bar, corresponding to an IMP of about 390 kPa, which accords with IMP values during cementing reported elsewhere (Song et al. 1994, McCaskie et al. 1997).

Bone cements

We used Osteopal (Biomet-Merck, Darmstadt, Germany) as a low viscosity cement and Palacos (Biomet-Merck, Darmstadt, Germany) as a standard viscosity cement. Both cements have different polymerization characteristics (Kühn 2000). Osteopal has a long phase with a lower viscosity after mixing, followed by rapid curing thereafter. Palacos has a polymerization curve with an earlier, but more continuous increase in viscosity.

To ensure pore-free filling of 60 mL cement cartridges and permit complete filling of the femoral canal via a narrow nozzle, Palacos monomer was prechilled to –20 °C to prolong its phase of low viscosity. To make quite sure of a definite difference in viscosity, Osteopal cement was prechilled to +6 °C. This prolonged its low viscosity state.

Both cements were applied 3.5 minutes after mixing and then pressurized after 8 minutes. These handling times had been selected from the results of a preceding study. With this protocol, Palacos reached a non-sticky, doughy state, while Osteopal was still in a more runny state at the time of cement pressurization.

Animal model (Figure 1)

The in vivo study was done on 15 adult female sheep after approval by the local animal-care committee. As part of a learning curve, the first 2 animals were used to standardize the surgical procedures, leaving 13 reproducible procedures for the study. All animals were aged between 2–3 years and weighed mean 75 (60–90) kg. They were anesthetized with propofol (3–5 mg per kg body weight) intravenously. A central venous line was established in the internal jugular vein after intubation and general anesthesia was maintained with isoflurane 0.8–1.5 vol%. The surgical procedure involved bilateral placement of intravenous catheters in the external iliac veins via bilateral retroperitoneal approaches. The catheters were heparinized with 1,250 IU in 5 mL 0.9% saline to prevent clotting. Using a Watson-Jones type approach, both hips were dislocated and the femoral necks osteotomized. The femoral canal was opened with an 8.0 mm drill and the intramedullary cavity prepared, using a round, semi-rigid plastic rod to preserve the cancellous architecture. This maneuver ensured mechanical removal of the firm fatty contents of the femoral cavity. Next, the femoral canal on both sides was irrigated with 250 mL 0.9% saline, using a pulsatile jet-lavage (Pulse lavage, Model L 31, Tava Surgical Instruments, USA). After intramedullary lavage, 10 mL heparinized normal saline (25,000 IU/100 mL) was injected into the femoral cavity. The metal adapters for cement application were securely fixed on both femoral necks using a separate mix of bone cement (CMW 1) to prevent leakage of cement during pressurization. Suction tubes were connected to the smaller tube of the metal adapter to vent air and blood during cement filling and pressurization. Palacos and Osteopal bone cement were placed simultaneously in the femoral canals 3.5 minutes after mixing of the cement. The early application time was necessary to permit retrograde cement delivery with narrow nozzles through the metal adapter without pressurization. Two additional cement syringes were mounted on the cement pressurization apparatus. Rubber tubes were connected securely over the larger tube of the metal adapters, using tube clamps to permit pressurization without leakage of cement. The pneumatic ram pressure of 3.8 bar was then applied 8 minutes after mixing and maintained until the cements had been completely cured. Immediately after application of pressure, both venous catheters were opened and the blood collected sequentially in 50 mL aliquots in polyethylene tubes (Greiner, Heidelberg, Germany) filled with 4 mL 3.3 % sodium citrate to prevent clotting. Intravenous fluids were given to replace blood loss and maintain adequate blood pressure and circulation. Blood collection was stopped when no macroscopically visible fat globules could be detected in the collected blood samples or the blood flow had stopped.

When the sheep had been killed by an overdose of barbiturates, both femora were retrieved and AP radiographs taken to ensure complete filling of the medullary canal with cement. Using a diamond saw, serial identical sections of every centimeter were made of the distal metaphysis of both femora and microradiographs (Faxitron machine, model 43855C, Rhode & Schwarz, Germany) taken to assess the penetration of cement in a left versus right comparison of both viscosity groups.

Analysis of blood samples

Lipid quantification. Low speed centrifugation was used to quantify the lipids—i.e., 2000 rpm for 8 min at room temperature—and macroscopically visible fat supernatant was recorded. The supernatant was washed twice with 0.9% saline and then lipid was extracted by adding 8 volumes of a chloroform/methanol (2:1) mixture, vigorously shaking and incubating until two phases were separated (Zöllner and Eberhagen 1965). The phase containing chloroform/methanol and lipids was then transferred into weighed 50 mL tubes and the solution dried under a fume hood. Lipids were quantified with an analytical precision scale. In preliminary experiments, we found that only small amounts of lipids (< 0.1 g/50 mL) could be extracted from the wash solutions containing most of the cellular elements from blood and also from sheep blood without surgical treatment. The procedure was validated and standardized by adding of 0.2–3 g of porcine fat to fresh sheep blood. Extraction procedures on these samples yielded recoveries of 88%–93%.

Cement penetration

The microradiographs were digitized, using a scanner and analyzed with image analysis software (Kontron KS 300, Kontron Elektronik GmbH, Zeiss, Germany). We deteremined the entire section area (As), the cement area (Ac) without cancellous bone (reflecting the intramedullary cavity), the cross-sectional area of cancellous bone filled with cement (Abc) and the cross-sectional area of cancellous bone not containing cement (Anc) (Figure 2). The area of cancellous bone in the cement was also measured as an indicator of bone quality. These measurements were used to calculate cement penetration (CP in %) with the formula:

$$CP\ (\%) = (Ac+Abc)/As \times 100.$$

The mean of two serial sections was used for the statistical analysis.

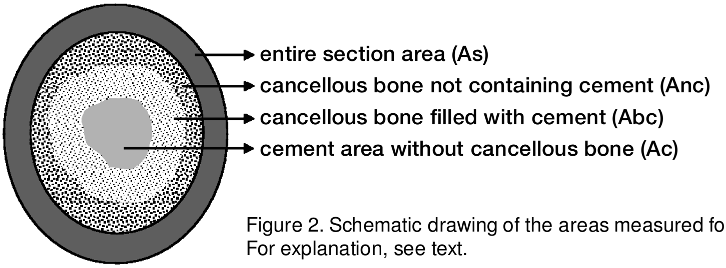

Figure 2. Schematic drawing of the areas measured for calculation of cement penetration. For explanation, see text.

Statistics

To describe the distributions of cement penetration and fat collected with the two types of cement viscosity, mean and standard deviation are presented. We calculated the intraindividual differences between the two data sets and 95% confidence intervals for the mean of these differences of both parameters. The data sets were compared using the two-sided paired t-test with an overall significance level of $\alpha = 0.05$. The nominal significance levels for the two tests were adjusted with Bonferroni-Holm's method. The correlation between the penetration of cement and the fat collected was shown by printing a scatter plot and calculting Pearson's correlation coefficient. All analyses were done with a Statistical Analysis System (SAS Institute Inc.: Cary, NC, USA).

Results

Complications

The blood loss during surgery was less than 20–50 mL in all animals. 1 animal had an episode of acute intraoperative hypotension which normalized after rapid fluid substitution and short-term inotropic support.

Of the 13 sheep in the study, 1 had to be excluded because of insufficient unilateral cement filling, thus leaving 12 animals for statistical evaluation of cement penetration. In 3 other animals, all operated on the same day, the venous blood flow stopped shortly after pressurization on the Osteopal side. This was caused by complete filling of the venous drainage system with cement, up to the level of the catheter in the external iliac vein, found by palpation during the operation and confirmed radiographically (Figure 3) and macroscopically after dissection of the surrounding soft tissue. As blood collection was incomplete, these 3 animals had to be excluded from the statistical analysis of fat intravasation.

Figure 3. Radiograph of an Osteopal specimen with extensive cement intravasation and obstruction of the venous drainage system.

Macro- and microradiographical findings

In 12 animals, cement filling of the entire femur was complete bilaterally on radiographs. In addition to the 3 animals with complete filling of the venous system, radiographs showed cement intravasation into the draining veins in 8 of 13 animals on the Osteopal side and in one on the Palacos side. On microscopic examinations, sparse blood lamellas were found directly adjacent to the cancellous trabeculae in all specimens regardless of the cement viscosity, i.e., interposed between cement and bone. The mean rates of cement penetration were

Absolute fat intravasation per sheep (in gram), mean and standard deviation (SD) and cement penetration (%) in the Palacos and Osteopal groups

Sheep no.	Fat intravasation (g)		Cement penetration (%)	
	Palacos	Osteopal	Palacos	Osteopal
1	4.81	3.56	52.4	38.5
2	2.97	2.92	11.1	9.72
3	3.26	1.53	47.3	11.5
4	4.41	2.45	35.1	14.6
5	3.23	3.27	48.2	45.1
6	1.87	1.65	26.9	32.5
7	4.02	3.35	32.0	21.3
8		[a]	33.5	23.0
9		[a]	49.1	13.1
10		[a]	32.9	8.85
11	3.19	2.79	29.2	30.1
12	4.33	2.47	27.7	7.4
Mean	3.57	2.66	35.4	21.3
SD	0.91	0.72	11.9	12.6

[a] excluded from statistics because of venous occlusion with cement during pressurisation.

21 (SD 13)% in the Osteopal group (n = 12) and 35 (SD 12)% in the Palacos group (n = 12) (Table). The difference in cement penetration between both types of cement was 14 (SD 14)% with a 95% confidence interval of 5.5–23 (p = 0.004).

Fat intravasation

During all procedures, most fat and bone marrow intravasation was collected in the first 200 mL of blood, with a rapid reduction thereafter. No cement was found in the blood samples. No thrombi occurred in the venous system (distal to the ligature), indicating effective anticoagulation.

The mean fat recovery in the Palacos group (n = 9) was 3.57 (SD 0.91) g and 2.66 (SD 0.72) g in the Osteopal group (n = 9). The mean difference between both groups was 0.9 (SD 0.81) g, with a 95% confidence interval of 0.28–1.52, (p = 0.01, Table). Pearson's coefficient (correlation between amount of fat intravasation and cement penetration) was p = 0.51.

Discussion

In our in vivo experiments, cement of higher viscosity penetrated better than that of low viscosity. Stone et al. (1996) found no difference as regards cement penetration whether Simplex was applied in a high or low viscosity state and adequately pressurized. In contrast, Bean et al. (1988) reported better cement penetration in vitro in the absence of interface bleeding when cement was applied in a low viscosity state, but no difference in the shear strength. Majkowski et al. (1993) noted that cement of higher viscosity seemed to be less susceptible to contamination with blood, but recommended that it should not be applied late because the degree of penetration might be jeopardized.

In clinical work a clear distinction between low and high viscosity cement seems difficult. All bone cements classified as of high viscosity undergo a phase of lower viscosity after mixing. Conversely, all cements of low viscosity gradually attain high viscosity. Hence, the timing of cement application and pressurization remains the most decisive factor. The handling properties of cement are extremely dependent on temperature. In our study, prechilling of both Palacos and Osteopal to prolong their low viscosity phase was necessary to guarantee complete, pore-free filling of the delivery system and the femoral canals. Prechilling is a well-recognized method (Draenert et al. 1999). The effect of monomer cooling at –20 °C on the physical properties of Palacos is not known, but it is unlikely that properties other than viscosity are affected. To ensure a "normal", clinically relevant viscosity at the time of pressurization, a long interval was necessary between cement application and pressurization. Despite this interval, blood entrapment at the interface was minimal in both groups.

Cement pressurization substantially increases IMP (Song et al. 1994, McCaskie et al. 1997). Fat and bone marrow embolization may therefore ensue (Breed 1974, Kallos et al. 1974, Tronzo et al. 1974, Orsini et al. 1987, Byrick et al. 1989, Wenda et al. 1995). The close relationship between an increase in IMP and cardiorespiratory complications has been well established both experimentally (Tronzo et al. 1974, Orsini et al. 1987, Wheelwright et al. 1993, Wenda et al. 1995) and clinically (Christie et al. 1994, 1995a, Pitto et al. 1998).

To our knowledge, this is the first study to show the interrelationship of cement viscosity, cement interdigitation and fat embolism in vivo. We found that high viscosity cement caused much more fat intravasation than low viscosity cement.

The value of pulsatile lavage in reducing medullary fat and bone marrow content has been established experimentally (Sherman et al. 1983, Byrick et al. 1989, Breusch et al. 2000a) and clinically (Christie et al. 1995b). Despite the use of thorough high-volume pulsatile lavage in our study, it may not have been effective enough to remove all marrow. This may be why the rates of cement penetration were lower with Osteopal. Cement of higher viscosity penetrates better; this could explain why greater amounts of fat extravasation occurred in the Palacos group.

Our results indicate that low viscosity cements—if applied early/runny—take the path of least resistance into the venous system before deeper cement penetration can occur. In contrast to the Palacos group, we found cement invasion of the venous system in more than half of the specimens in the Osteopal group. This phenomenon is also well recognized in clinical work as an adverse effect of pressurization with low viscosity cements (Ulrich 1995, Draenert et al. 1999, Knight et al. 1999).

Our in vivo findings do not accord with the current view that low viscosity cement penetrates better. Cements of higher viscosity yield excellent rates of cement penetration, but should be used with thorough pulsatile lavage to reduce the risk of fat embolism. The excellent clinical results with cements of higher viscosity (Havelin et al. 1995) show that such cements seem more forgiving. Which cement is used, the surgeon must be familiar with its properties to avoid adverse outcomes in cemented THA.

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