The effect of pulsed jet lavage in vertebroplasty on injection forces of PMMA bone cement: an animal study

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Abstract Percutaneous vertebroplasty, comprising of the injection of polymethylmethacrylate (PMMA) into vertebral bodies, is an efficient procedure to stabilize osteoporotic compression fractures as well as other weakening lesions. Besides fat embolism, cement leakage is considered to be one of the major and most severe complications during percutaneous vertebroplasty. The viscosity of the PMMA during injection plays a key role in this context. It was shown in vitro that the best way to lower the risk of cement leakage is to inject the cement at higher viscosity, which requires high injection forces. Injection forces can be reduced by applying a newly developed lavage technique as it was shown in vitro using human cadaver vertebrae. The purpose of this study was to prove the in vitro results in an in vivo model. The investigation was incorporated in an animal study that was performed to evaluate the cardiovascular reaction on cement augmentation using the lavage technique. Injection forces were measured with instrumentation for 1 cc syringes, additionally acquiring plunger displacement. Averaged injection forces measured, ranged from 12 to 130 N and from 28 to 140 N for the lavage group and the control group, respectively. Normalized injection forces (by viscosity and injection speed)

showed a trend to be lower for the lavage group in comparison to the control group ($P = 0.073$). In conclusion, the clinical relevance on the investigated lavage technique concerning lowering injection forces was only shown by trend in the performed animal study. However, it might well be that the effect is more pronounced for osteoporotic vertebral bodies.

Keywords Vertebroplasty · Jet lavage · Injection force · Fat embolism · Cement leakage

Introduction

Percutaneous vertebroplasty is a procedure comprising the injection of polymethylmethacrylate (PMMA) into vertebral bodies [19]. It is an efficient method to stabilize osteoporotic compression fractures as well as other weakening lesions such as angioma or metastatic tumors. Complications related to vertebroplasty are cement leakage and pulmonary fat embolism [18, 21]. Due to the increasingly aging population and high occurrence of vertebral compression fractures related to osteoporosis, this procedure is used more and more frequently [24]. Therefore, it is crucial to increase the safety of patients undergoing vertebroplasty by investigating novel methods for preventing cardiovascular changes due to embolism and cement leakage during the procedure.

For vertebral augmentation, bone cement, currently mostly polymethylmethacrylate (PMMA), is injected into the fractured vertebral body at low viscosity. This minimally invasive technique brings great benefit to patients and leads to immediate and lasting pain relief in 80–93% of patients [16]. The analgetic mechanism is not fully explored; besides the mechanical stabilization of the

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fracture also the destruction of nerve fibers by thermal and/or toxic effect at polymerization of the PMMA cement is discussed [6, 22]. The biomechanical effect in terms of increased stiffness and strength has been documented in various studies and relates directly to the volume of injected cement [25]. Introduction of 20% cement by volume results in an increase of compressive strength of 36% and increase in stiffness of up to 174% in osteoporotic vertebrae. The effect was more pronounced in specimens with low bone mineral density (BMD) [17, 20, 25, 28]. Another study [10] using functional spine units showed an increase in stiffness of around 180% when compared to an intact osteoporotic vertebral body.

This increased local stiffness in an osteoporotic spine bears the risk of a higher incidence of fractures of the adjacent segments in the initial phase and in certain cases a prophylactic reinforcement of adjacent vertebrae with high fracture risk is advisable [10, 14, 17, 23, 25, 27, 28]. At the Orthopedic Department of the University Hospital in Bern (Inselspital, Bern, Switzerland) a prophylactic, even multisegmental vertebroplasty is performed for selected patients to prevent further collapse (up to 6 levels, monolaterally under local or general anesthesia). The clinical results are very promising, with a significant pain decrease (from 7.6 to 2.7 VAS) [18]. More impressive is the subjective report of the patients about better posture and increased force in their back, allowing them to become more active again.

Performing this prophylactic multisegmental cementation, there is also an enhanced amount of fat being displaced into the venous system. For that reason, the number of reinforced vertebrae should be limited to 6 levels per session or 25–30 cc of PMMA. This limitation was empirically determined on the basis of increasing pulmonary problems when injecting larger volumes. However, as Aebli et al. [1] demonstrated in an elaborate animal study, already smaller volumes of injected PMMA lead to measurable cardiovascular changes as hypotension, drop of cardiac output and pulmonary hypertension that can have a fatal effect in the older and pulmonary impaired patient. Aebli et al. [1] also showed a cumulative increase of fat embolism in lung biopsies in sheep after multiple level augmentations.

Another complication in vertebroplasty is cement leakage: in Hulme's review of vertebro- and kyphoplasty studies [21], a leakage rate of 41% for vertebroplasty was reported. Fortunately most of these leakages are clinically asymptomatic but especially pulmonary cement emboli that occur in 0.6% of cemented vertebrae are serious complications. Intradiscal cement leakage, which accounts for 30.5% of cement extravasation in vertebroplasty, is believed to increase the fracture risk of adjacent vertebrae [26]. Upon injection, the cement follows the path of lowest

resistance, which in the vertebrae are defects from fractures, irregular bone density patterns and blood vessels. Some studies report less cement leakage in kyphoplasty where previous to injection an intravertebral cavity is formed. This fact is most probably due to lower local resistance when filling the void created by the balloon expansion; Berlemann noted similar extravasation rates as in vertebroplasty when attempting to fill the whole vertebra but not only the cavity [8].

The accurate cement viscosity has been identified as a crucial parameter associated with the risk of cement leakage and has the potential to influence the safety of the whole procedure [3, 4, 11]. Injecting PMMA at a low viscosity leads to a scattered, fingerlike, uncontrolled cement distribution pattern and, as a consequence, an increased chance of cement leakage. By the injection of the cement at higher viscosity, a uniform and better controlled filling pattern can be achieved. During polymerization of commonly used PMMA cements, the viscosity steadily increases. Hence, the cement should be injected at the latest time point possible in order to prevent leakage and extravasation. This, however, leads to high injection forces that may not be overcome using simple manual injection systems [3].

Both issues, cement leakage and fat embolism, are addressed by a recently developed lavage technique [7], which enables the surgeon to wash out the intertrabecular bone marrow of the vertebrae before cement injection. An *in vitro* study [7], using human cadaveric lumbar and thoracic vertebrae, showed that the lavage technique leads to a reduction of cement injection forces compared to the conventional treatment. Reduction of the injection force is thought to be due to the reduced flow resistance after intertrabecular bone marrow removal. This in turn allows the injection of higher viscous cement applying equal injection forces, hence lowering the risk of cement leakage and increasing the procedure's safety [4].

To show the potential clinical impact of the lavage technique in reducing fat embolism, a large animal study was performed. The study, approved by the local animal ethics committee (204/2007), investigated cardiovascular reactions during and after conventional vertebroplasty compared to the newly developed technique using lavage prior to cement injection [15]. In order to verify the *in vitro* results on reduced injection forces using the lavage technique prior to cement injection [7], the cement injection investigation was incorporated in the mentioned animal study.

Purpose of the study presented was to investigate the cement injection into vertebral bodies *in vivo* after applying the lavage technique in comparison to injections into vertebral bodies of a control group without lavage prior to the standard vertebroplasty procedure. Monitored parameters were injection force, injection speed and cement viscosity at injection.

Methods

For the animal study 11 ewes (>3 years old) were randomly assigned to two groups to compare percutaneous vertebroplasty following lavage (group 1, 6 animals) to conventional vertebroplasty (group 2, 5 animals). In each animal three lumbar vertebral bodies (L1–L6) were treated. Accordingly 18 cement injections in the group using lavage (group 1) and 15 in the control (group 2) could be investigated.

All animals underwent surgery by a single spine surgeon (L.M.B.) in general anesthesia and under intensive cardiovascular monitoring. Since in quadruplets the facet joints and the pedicles are less sagittally oriented as in humans and because the animals cortical bone is very hard, the standard vertebroplasty technique was adapted: after a paramedian 1-cm skin incision the ideal parapedicular entry point was localized under fluoroscopic control with a 1.6-mm K-wire and opened with a cannulated 3.2-mm drill. Subsequently, the filling cannulas (8-gauge Jamshidi biopsy needles; Angiotech Medical Device Technologies, Gainesville, USA) with a length of 150 mm and outer diameter of 4.2 mm (inner volume of around 1.8 cc) were bilaterally inserted into the vertebral body. Since the ovine vertebra is very narrow in its middle part one needle was placed in cancellous bone of the cranial hemivertebra, whereas the second needle aimed for the caudal half. Finally the cannula and its opening were cleared from bony debris with a 2.7-mm diameter plunger. Vertebrae of group 1 received irrigation (ScandiMed Lavage System, Biomet Merck GmbH, Ried, Switzerland) for fat and bone marrow removal with 100 cc Ringer solution. For that purpose, the jet lavage hand unit was directly attached to the biopsy needle and Ringer solution was pulsed through the needle. The contralateral biopsy needle was used to apply a vacuum during the irrigation procedure (Medela Vario 18, Baar, Switzerland). The irrigation liquid together with the removed fat and bone marrow was retrieved through the vacuum biopsy needle during the irrigation process. The technical aspects of the lavage procedure are described in detail in Benneker et al. [7].

For the injection, a commercially available vertebroplasty PMMA cement was used (Vertecem, LOT No. 045S/0738, Synthes GmbH, Switzerland). Preparation of the cement was done according to the manufacturers instructions.

In order to perform the injection procedures in a standardized manner, the cement viscosity was monitored by rheological data acquisition. To measure cement viscosity, 3.0 cc of the freshly mixed cement were placed in a rotational rheometer (RheolabQC, Anton Paar, Graz, Austria). The rheometer is equipped with a specifically designed double gap measuring system as described by Boger et al. [9]. Real viscosity (η') and ambient temperature (T) were

Fig. 1 Photograph of the custom-made syringe holder for the instrumentation of 1.0-cc syringe

recorded directly to a PC. Data were recorded at a sampling rate of 0.2 Hz.

For the cement injection, 1.0-cc syringes (Vertecem Injection Kit, LOT F584517, Synthes GmbH, Switzerland) were attached to the Jamshidi biopsy needles. Cement injections were started at a viscosity of 35 Pa s. Injection with the instrumented syringe was carried out after complete filling of the biopsy needle with 1.5 cc of PMMA cement under fluoroscopic control to assure infiltration of the trabecular network during force and displacement measurement. This was done by the instrumentation of a syringe holder with load and displacement transducers (HBM U9B/1kN, HBM WA/100 mm and HBM MGCplus; Hottinger Baldwin Messtechnik AG, Volketswil, Switzerland) (Fig. 1) allowing recording the injection force and plunger displacement of the first milliliter PMMA applied directly to a PC. Cement infiltration into the bony structure during the measured cement injection step was guaranteed by image intensifier control.

Data were later transferred to injection force, plunger displacement and cement viscosity as a function of time. For the time period, defined by observing a continuous injection, the averaged injection force, injection speed and cement viscosity were determined as parameters. Parameters were calculated and presented as mean $\pm$ standard deviation. Following the law of Hagen–Poiseuille [11], the injection force was normalized by dividing it by injection speed and the apparent viscosity during injection.

The influence of the lavage treatment prior to cement injection versus the non-treated control group on the normalized injection force determined were statistically analyzed using a Mann–Whitney U test. Significance level was set at $P = 0.05$. Statistical analysis was carried out using SPSS V15.0.

Results

Representative curves for the injection of the first milliliter of cement into a vertebral body are presented in Fig. 2. In a typical injection process, a relatively constant force was produced using a hand-held syringe, and a constant flow rate of the cement (injection speed) was obtained.

Fig. 2 Representative data curves (control group) used to determine the cement injection. Injection force (gray line), plunger displacement (black line) and cement viscosity (circles) during cement injection

Cement viscosity at the start of the force/displacement measurements was at 46 ± 15 Pa s and not statistically different for both groups ($P = 0.54$). Averaged injection forces, ranged from 12 to 130 N and from 28 to 140 N for the group 1 (lavage, $n = 18$) and group 2 (control, $n = 15$), respectively. Mean $\pm$ standard deviations for the parameters measured and calculated are summarized in Table 1. Normality of the data was much higher for the ones received from the lavage group than for the control (Table 1). Normalized injection forces showed a trend to be lower for the lavage group in comparison to the control group ($P = 0.073$) (Fig. 3). Injection speed was higher for the lavage group ($P = 0.02$) as for the control.

Discussion

The lavage technique used for vertebral bodies showed to be feasible and reproducibly applicable to vertebral bodies of sheep.

Main purpose of this animal study was to evaluate the cardiovascular reaction during conventional vertebroplasty in comparison to the procedure using the lavage technique before cement injection. In addition to the parameters

related to cardiovascular reaction, the cement injection was also quantified using an instrumented syringe holder to collect data on injection force and injection speed. Overall purpose of the studies [7, 15] involving the lavage technique in the conventional vertebroplasty procedure was to evaluate the clinical relevance of this new technique. Clinical relevance could be achieved if the use of the lavage technique is accompanied by a lower risk of fat embolism, reduced injection forces and controlled, uniform distribution patterns of the injected cement inside the vertebral body. Reduction in the alteration of the cardiovascular parameters due to prior lavage could be shown in the animal study presented in Gisep et al. [15]. Difference in uniformity of the cement filling after lavage could be shown in the already mentioned in vitro study [7], but it was not analyzed in the herein presented animal study as cement injection was performed to a maximum vertebral body filling in both groups in order to maximize the effect on cardiovascular reactions between the lavage and control group. However, CT analysis showed that significantly more cement was injected into the irrigated vertebral bodies [15]. The results of the in vitro study [7], showing a more uniform cement filling after lavage, and the statement that intradiscal extravasations increase the risk of adjacent body fractures [28], might lead to the conclusion that lavage leads to lesser problems at adjacent levels. But this has to be shown in a biomechanical setup.

Until now, cement injection force data comparing conventional vertebroplasty to the one with prior application of the lavage technique were only available from in vitro investigations [7], which showed significantly lower injection forces when the lavage technique was applied prior to the cement injection.

Measured injection parameters herein were comparable to the in vitro study [7]. Due to significant differences in injection speed during the manual injection procedure performed in the animal study (Table 1), direct comparison of the injection forces was not possible. Thus, the injection forces were normalized, which was done by applying the law of Hagen–Poiseuille using the apparent injection speed and cement viscosity for the time period of injection.

Table 1 Mean $\pm$ standard deviations for the parameters measured and calculated: cement viscosity at injection, injection forces, injection speed and normalized injection force

Homogeneity of the data received for both groups, control and lavage group. Normality according to Shapiro–Wilk test

	Cement viscosity at injection (Pa s)	Injection force [N]	Injection speed (mm/s)	Normalized injection force [N/Pa mm]
Control group	49.6 ± 13.4	64.6 ± 37.2	6.7 ± 5.4	0.42 ± 0.723
Lavage group	44.6 ± 10.3	54.5 ± 33.9	9.3 ± 3.5	0.16 ± 0.15
Mann–Whitney test/ P values	0.401	0.361	0.02	0.73
Homogeneity in control group/ P values	0.002	0.007	0.12	0.000
Homogeneity in lavage group/ P values	0.737	0.161	0.981	0.000

Fig. 3 Normalized injections forces ($P = 0.073$). One extreme outlier in the control group of 2.96 was not displayed

However, in the presented in vivo study, lower normalized injection forces after performing the lavage technique could only be shown as a trend ($P = 0.073$) in contrast to the human cadaver study [7]. Reasons for the discrepancy may have been the high bone density (non-osteoporotic sheep model) with less content of bone marrow in comparison to osteoporotic human cancellous bone (BMD sheep, 0.40–0.48 g/cm³; BMD human, 0.10–0.27 g/cm³ [2]). However, we chose the sheep model because the size and volume of the vertebrae are comparable to humans [12, 29]. This allowed us to perform the procedure in a similar way as under clinical conditions during percutaneous vertebroplasty. We are also convinced that the differences of injection forces would be more pronounced in osteoporotic vertebrae and we were already able to show lower injection forces after irrigation in the previously conducted in vitro study [7]. Unfortunately, there is no reasonable and also ethically applicable osteoporotic sheep model available up to now. Ovariectomy alone does not induce osteoporosis without long-term steroid treatment and the associated adverse effects, especially for the immune system. Animals showed signs of infection of various degrees due to the immunosuppressive effect of the medication. Ethical considerations need to be taken into account when using these models [13].

These were the reasons for not using another animal model, e.g. rats where osteoporosis could be induced more easily.

It is our opinion that by showing a trend of lower injection forces after irrigation, even in the dense sheep vertebrae, the technique will have a bigger effect on the injection forces in osteoporotic vertebrae in vivo.

Furthermore, the in vitro measurements [7] were performed at room temperature. As a consequence, the bone marrow was of a higher viscosity compared to the in vivo

situation. This fact could lead to higher injection forces in the control group of the in vitro study compared to the in vivo situation and thus providing a significant difference between the groups. No significant result on the injection forces herein support the conclusion of a related study [5], that the intravertebral pressure and the present bone marrow only contribute a small percentage to the injection force that has to be applied on the plunger during cement injection. Higher homogeneity of the injection speed values measured for the lavage group in comparison to the control, which reflects the subjective feeling of the surgeon, may lead to the conclusion that the lavage technique leads to a more standardized procedure in cement augmentation.

Conclusion

The clinical relevance of the investigated lavage technique concerning lowering injection forces could only be shown by trend in the performed animal study. Reduced injection forces would allow the use of higher viscous cement that again would reduce the risk of cement extravasation [4].

A proven clinical relevance of the lavage technique concerning the reduction of injection forces and in turn decreasing risk of cement leakage in vertebroplasty procedures in general could only be derived from a clinical investigation. Overall clinical relevance applying lavage techniques to the conventional vertebroplasty procedures have to be further evaluated on a clinical base. This evaluation should consider the little additional surgery time and the worthwhile strategy of prophylactic augmentation to reduce the risk of new vertebral body collapse within one surgery.

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