INTRODUCTION

Embolization of bone marrow fat during orthopedic surgery can lead to intraoperative cardiovascular deterioration. Cardiovascular changes are characterized by an increase in pulmonary arterial pressure, systemic arterial hypotension and a decrease in cardiac output. These changes are often transient but may be fulminating, resulting in cardiac arrest and even death. Even though surgical techniques have been improved, incidences still occur during total hip and knee arthroplasty, intramedullary nailing and spine surgery (e.g. vertebroplasty). Anesthetic management aiming at maintaining arterial blood pressure and cardiac output may be challenging in the presence of increased right heart after-load and decreased left heart pre-load. Aggressive volume support will deteriorate right heart overload. Furthermore, systemic vasoconstriction and administration of positive inotropic drugs may not be effective. A better understanding of the pathophysiology of these complications would therefore assist in developing effective therapeutic measures.

The severity of cardiovascular deterioration after fat embolization cannot be explained by mechanical blockage alone, unless activation of the coagulation cascade increased the number of pulmonary emboli. Alternatively, vasoactive mediators released from the bone marrow cavity or as a result of lung injury after embolization may cause pulmonary vasoconstriction. Increased plasma levels of endothelin-1 (ET-1), the most potent pulmonary vasoconstrictor known to date, have been reported after pulmonary air embolism.1

The role of ET-1 and coagulation in the development of acute cardiovascular deterioration after fat embolization was thus investigated.

METHODS

Investigations were carried out using an animal model of vertebroplasty containing the pathophysiological complexity of an orthopedic intervention.2 Furthermore, it allowed studying cardiovascular responses to multiple events of fat embolization in the same animal. Thus in 6 skeletally mature mixed-bred ewes of approximately equal size, polymethylmethacrylate (Mendec, Tecres, Italy) was injected into three lumbar vertebrae (L2–L4) and any subsequent cardiovascular changes were recorded until 60min after the last injection (approved by local Animal Ethics Committee).

Anesthesia was induced with propofol and maintained with isoflurane in oxygen (50%) under positive pressure ventilation. Arterial blood pressure (ABP), central venous pressure (CVP) and pulmonary arterial pressure (PAP) were recorded continuously. Heart rate was derived from the electrocardiogram. Cardiac output, arterial and mixed venous blood gas parameters, ET-1 and multiple coagulation parameters (n=6, i.a. D-dimer, thrombin-antithrombin complex) were measured at selected time points. Subsequent cement injections followed 20min after the previous one, so that cardiovascular values could reach a new steady state. Post mortem, lung tissue samples were taken from each lobe (n=5) for analyzing the presence of intravascular fat (oil red O).

Cardiac index, systemic and pulmonary vascular resistance (PVR), physiologic dead space and intrapulmonary shunt were calculated. Data was calculated as mean ± SD. One-way ANOVA for repeated measures was used to test for differences between pre- and post-injection values. Post hoc analyses were achieved using Scheffé’s test.

RESULTS

On average, 4.7 ± 0.7ml bone cement were injected over a period of 31 ± 11s. There was no difference in the cardiovascular responses to the three injections. The data were therefore pooled. Cement injection resulted in a sudden (1min post-injection) increase in mean PAP (approx. 107%) and CVP (approx. 40%) as well as a decrease in mean ABP (approx. 35%). The increase in mean PAP lasted for 10min whereas mean ABP and CVP were no longer different from pre-injection values 2min after injection. There was also an increase in PVR and pulmonary dead space 1min after injection.

Plasma levels of thrombin-antithrombin complex (pre-injection: 3.0 ± 0.7µg/L, 60min: 4.5 ± 1.3µg/L, p=0.97) and D-dimer (pre-injection: 0.87 ± 0.9mg/L, 60min: 1.0 ± 0.96mg/L; p=0.86) demonstrated an increasing trend. However, there was no significant change in any measured coagulation parameter. Plasma levels of ET-1 increased from 4.8 ± 0.2pg/ml at pre-injection to 5.1 ± 0.5pg/ml at 1min post-injection (NS, p=0.99). Values increased further over time (Fig. 1) and were significantly (p=0.02) elevated 60min after injection (6.1 ± 0.8pg/ml).

Intravascular fat and bone marrow cells were present in all lung lobes.

Figure 1: Plasma levels of endothelin-1 prior to and after cement injections. * Significantly (p=0.02) different from pre-injection value.

DISCUSSION

The cardiovascular response to bone marrow fat embolization was characterized by a sudden (1min post-injection) and dramatic (>100%) increase in mean PAP and a decrease in mean ABP (35%). There was no significant change in any coagulation parameter. Endothelin-1 levels were significantly elevated 60min after injection.

Vasoconstrictive effects of ET-1 or additional thrombo-embolism did not contribute to the acute cardiovascular deterioration after fat embolization. However, other vasoactive mediators, such as serotonin or thromboxane, may play a role. Alternatively, reflexive pulmonary vasoconstriction may be initiated by the event of embolization.

Present results are in accordance with previous studies demonstrating an increase of ET-1 after pulmonary air embolism.1 Endothelin-1 may be involved in the development of postoperative cardiovascular and respiratory complications after fat embolism. Present investigations should therefore be extended beyond 60min after injection.

Vertebral filling was higher compared to the clinical situation. However, it was crucial to inject similar volumes of material compared to the clinical situation, replacing similar volumes of bone marrow fat. Endothelin-1 and thrombo-embolism did not contribute to the acute cardiovascular changes after bone marrow fat embolization. However, ET-1 may cause postoperative cardiovascular and respiratory complications after fat embolism.

ACKNOWLEDGMENTS

Technical assistance by Boris Leskosek and financial support by Wesley Foundation, Brisbane, Australia and AO Foundation, Davos, Switzerland.

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53rd Annual Meeting of the Orthopaedic Research Society
Poster No: 0957