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## Anti-fibrinolytic Agents & Lung Water in Cardiac Surgical Patients Interim results of a prospective randomised double blind placebo controlled trial

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**Introduction:** Lung injury causes the accumulation of lung water after cardiopulmonary bypass (CPB)<sup>1</sup> resulting in significant morbidity. Anti-inflammatory actions of aprotinin might be expected to reduce the amount of lung water present post-CPB. We report the interim results of a prospective randomised double-blind placebo controlled trial of aprotinin v. tranexamic acid v. placebo using a novel device that can measure impedance non-invasively to attempt to give trends in extra-cellular lung water over time.

**Methods:** 90 patients all scheduled to have cardiac surgery with CPB were recruited as part of an existing blood conservation trial and randomised in a double-blind, placebo controlled fashion to receive aprotinin 2 million units (mu) with 2 mu added to the CPB prime and an infusion of 0.5 mu/hour, or, 5 g of tranexamic acid or equivalent volumes of normal saline. Impedance across the right lung was measured at 5kHz and 200kHz using a **Dualscan 2005 (Bodystat®, Douglas, Isle of Man)**. At 5 kHz the “current” flow is related to extra-cellular water; at the 200kHz the current will be related to the total water content (intra- and extra-cellular). Measurements were taken across the right lung with the patient positioned at 45 degrees to the horizontal prior to induction of anaesthesia, immediately post-op, and at 24 hours post-op.

**Results:** Out of a total of 90 patients, 81 had a complete data set (2 lost as a result of protocol violations, and 7 from incomplete data).

Results are summarised as ratios of 5kHz to 200kHz readings with the differences between time points given as means and 95% confidence intervals (CI).

|                 | Pre-op v. Immediate Post-op | Immediate Post-op v. 24 hours Post-op | Pre-op v. 24 hours Post-op |
|-----------------|-----------------------------|---------------------------------------|----------------------------|
| Placebo         | 0.08 (0.03 to 0.12)*        | 0.03 (-0.04 to 0.10)                  | 0.10 (0.05 to 0.16)*       |
| Tranexamic Acid | 0.05 (0.03 to 0.07)*        | 0.05 (-0.01 to 0.11)                  | 0.10 (0.04 to 0.17)*       |
| Aprotinin       | 0.07 (0.03 to 0.10)*        | 0.06 (-0.01 to 0.12)                  | 0.11 (0.07 to 0.17)*       |

Table 1 – Mean differences in the ratios of 5kHz/200kHz, 95% CI in Parentheses (\*p<0.01).

**Discussion:** The results showed a significant increase in the ratio of extra-cellular water to total body water both immediately post-op and at 24 hours post-op when compared to baseline values. We could show no differences in impedance ratio between patients treated with aprotinin or tranexamic acid against those patients given placebo. With 90 patients the study has a power of 0.8 to detect a difference in impedance ratios of 10% or greater for either aprotinin or tranexamic acid against placebo.

**Conclusion: Cardiopulmonary bypass increases the levels of extra-cellular water with the changes continuing over 24 hours post-operatively. We showed no evidence to support the theory that aprotinin reduces extra-cellular water in comparison to either placebo or tranexamic acid.**

**Reference:** 1. Friedman M, Sellke FW, Wang SY, Weintraub RM, Johnson RG. Parameters of pulmonary injury after total or partial cardiopulmonary bypass. *Circulation* 1994;90(5 Pt 2):II262-II268.