

## References

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## Use of acute normovolemic hemodilution for blood conservation during off-pump coronary artery bypass surgery

To the Editor:

Although the premise for using acute normovolemic hemodilution (ANH) as a blood conservation modality is sound,<sup>1</sup> results for patients undergoing cardiac surgery have been controversial.<sup>2</sup> Furthermore, use of ANH for off-pump coronary artery bypass (OPCAB) has never been described. Recently, I utilized ANH in a 67-yr-old male patient (90 kg) undergoing triple vessel OPCAB. Following anesthetic induction, ANH

was performed to a hemoglobin (Hb) of 100 g·L<sup>-1</sup> (collected four units [350 mL] of autologous whole blood [AWB]; replaced with an equal volume of 6% hetastarch in lactated electrolyte solution). My strategy was to transfuse AWP when Hb levels decreased below 90 g·L<sup>-1</sup> during the OPCAB. One AWP unit was transfused after the internal mammary artery anastomosis (Table). During revascularization of the left circumflex artery (LCA) with a saphenous vein graft (SVG), occlusion of the artery produced ST segment elevation and hypotension (Table). Additional crystalloid, norepinephrine infusion and a 2.5-mm intracoronary shunt only partially reversed the ST segment changes. After documenting a Hb of 8.6 g·L<sup>-1</sup>, the second AWP unit was transfused, which was followed shortly thereafter by complete resolution of the ST segment changes. On completion of the last SVG to the right coronary artery, the remaining two AWP units were then transfused slowly (Table). Cell-saver blood (600 mL) was also reinfused producing a final Hb of 121 g·L<sup>-1</sup>. Postoperative recovery was uneventful and no allogeneic blood was transfused.

Rosengart *et al.* advocate that for ANH to be effective, the "maximal" volume of AWP should be sequestered prior to cardiopulmonary bypass (CPB).<sup>3</sup> However, CPB also produces hemodilution, which limits the volume of AWP that may be sequestered prior to initiating CPB. In contrast, in patients undergoing OPCAB, since hemodilution associated with CPB is avoided, a "maximal" volume of AWP may be collected. The endpoint for blood sequestration and the intraoperative AWP transfusion threshold or "trigger" should be clearly defined; the actual timing of AWP reinfusion should also be carefully coordinated with the surgeon's efforts. In the above patient, since the transfusion of AWP promptly reversed ST-segment changes following LCA occlusion, inadequate Hb concentration was probably contributory to myocardial ischemia, suggesting that ANH should be used with caution for OPCAB. Since considerable variation in transfusion practices still exists among cardiac surgery centres,<sup>3</sup> ANH may represent a valuable blood conservation tool for OPCAB surgery. More information is clearly needed about its safety and efficacy for OPCAB.

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TABLE Chronology of intraoperative Hb levels during ANH and OPCAB surgery

| Event                                    | Hb (g·L <sup>-1</sup> ) | Response  |
|--|-------------------------|---|
| 1st AWP unit complete                    | 128                     |   |
| 2nd AWP unit complete                    | 119                     |   |
| 3rd AWP unit complete                    | 110                     |   |
| 4th AWP unit complete                    | 101                     |   |
| IMA anastomosis                          | 89                      | 1st AWP unit administered                                       |
| L Cx anastomosis and myocardial ischemia | 86                      | 2nd AWP unit administered and resolution of myocardial ischemia |
| RCA anastomosis                          | 95                      |   |
| Post – protamine                         | 94                      | 3rd and 4th AWP units administered                              |
| Chest closure                            | 114                     | auto CS administered  |
| ICU admission                            | 121                     |   |

Hb = hemoglobin; ANH = acute normovolemic hemodilution; OPCAB = off-pump coronary artery bypass; AWP = autologous whole blood; IMA = internal mammary artery; L Cx = left circumflex coronary artery; RCA = right coronary artery; auto CS = autologous cell-saver blood; ICU = intensive care unit.

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### *In vitro relationship between the blood nafamostat concentration and activated coagulation time*

To the Editor:

The biological half-time of nafamostat (Torii Pharmaceutical, Tokyo, Japan), molecular weight 539.58, used as an anticoagulant in procedures such as continuous hemodiafiltration (CHDF) is approximately eight minutes.<sup>1</sup> Anticoagulation in the circuit is maintained adequately, whilst its concentration in the patient's blood decreases rapidly to a level which cannot cause anticoagulation, as measured by the activated coagulation time (ACT). We have routinely calculated the infusion dose of nafamostat using the patient's weight.<sup>2</sup> If the relationship between the blood nafamostat concentration and ACT is clarified, it may be possible to determine the dose of nafamostat alternatively.

After approval of our Institutional Committee, nafamostat was diluted with 5% glucose, and six plastic syringes were prepared, containing 0.1 mL of 5% glucose, 0.1 mL of 0.001 mg·mL<sup>-1</sup> nafamostat, 0.1 mL of 0.01 mg·mL<sup>-1</sup> nafamostat, 0.1 mL of 0.05 mg·mL<sup>-1</sup> nafamostat, 0.1 mL of 0.1 mg·mL<sup>-1</sup> nafamostat, and 0.1 mL of 0.5 mg·mL<sup>-1</sup> nafamostat, respectively. 1.9 mL of blood from ten healthy volunteers was aspirated in turn in the six prepared syringes from an *iv* catheter followed immediately by measurement of the ACT (ACTester™, QUEST Medical, Allen, TX, USA). The blood nafamostat concentrations were then 0 mol·L<sup>-1</sup> and approximately 10<sup>-7</sup>, 10<sup>-6</sup>, 5 × 10<sup>-6</sup>, 10<sup>-5</sup> and 5 × 10<sup>-5</sup> mol·L<sup>-1</sup>, respectively.

There was a highly significant relationship between blood nafamostat concentration and ACT. The ACT was prolonged significantly at 5 × 10<sup>-6</sup>, 10<sup>-5</sup> and 5 × 10<sup>-5</sup> mol·L<sup>-1</sup> nafamostat, showing values of 221 ± 74, 300 ± 70 and 665 ± 249 sec, respectively. (Figure).

During hemofiltration, the ACT should be maintained between 180 and 240 sec.<sup>3</sup> These values correspond to an appropriate nafamostat concentration of

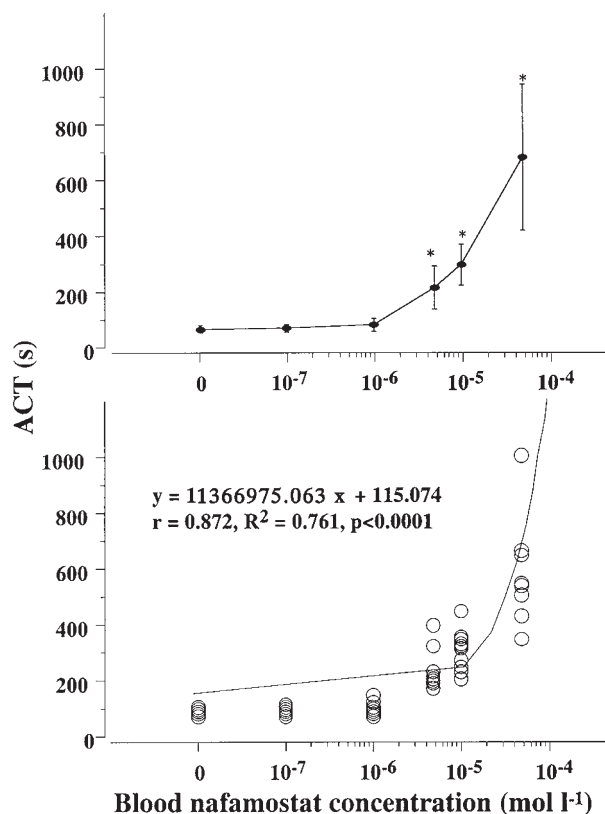


FIGURE The relationship between the blood nafamostat concentration and activated coagulation time (ACT). Upper graph shows values of mean ± SD and statistical changes (\* $P < 0.05$  vs 0 mol·L<sup>-1</sup> value). Lower graph shows scattergram and regression equation.

0.6 to 1 × 10<sup>-5</sup> mol·L<sup>-1</sup>, suggesting that 10<sup>-5</sup> mol·L<sup>-1</sup> is required for blood to pass through the hemofilter safely. In our clinical practice, 0.5 mg·kg<sup>-1</sup>·hr<sup>-1</sup> nafamostat is usually injected for CHDF.<sup>2</sup> If the patient weighs 60 kg, 0.5 mg·kg<sup>-1</sup>·hr<sup>-1</sup> nafamostat injected into blood flowing at 100 mL·min<sup>-1</sup> results in a concentration of 10<sup>-5</sup> mol·L<sup>-1</sup> nafamostat. As an alternative, nafamostat may be injected continuously to result in a circuit blood concentration of 10<sup>-5</sup> mol·L<sup>-1</sup>.

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