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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.[1] 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.[2] 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^{-1} nafamostat, 0.1 mL of 0.01 mg·mL^{-1} nafamostat, 0.1 mL of 0.05 mg·mL^{-1} nafamostat, 0.1 mL of 0.1 mg·mL^{-1} nafamostat, and 0.1 mL of 0.5 mg·mL^{-1} 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^{-1} and approximately 10^{-7}, 10^{-6}, 5×10^{-6}, 10^{-5} and 5×10^{-5} mol·L^{-1}, respectively.

There was a highly significant relationship between blood nafamostat concentration and ACT. The ACT was prolonged significantly at 5×10^{-6}, 10^{-5} and 5×10^{-5} mol·L^{-1} 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.[3] These values correspond to an appropriate nafamostat concentration of 0.6 to 1×10^{-5} mol·L^{-1}, suggesting that 10^{-5} mol·L^{-1} is required for blood to pass through the hemofilter safely. In our clinical practice, 0.5 mg·kg^{-1}·hr^{-1} nafamostat is usually injected for CHDF.[2] If the patient weighs 60 kg, 0.5 mg·kg^{-1}·hr^{-1} nafamostat injected into blood flowing at 100 mL·min^{-1} results in a concentration of 10^{-5} mol·L^{-1} nafamostat. As an alternative, nafamostat may be injected continuously to result in a circuit blood concentration of 10^{-5} mol·L^{-1}.

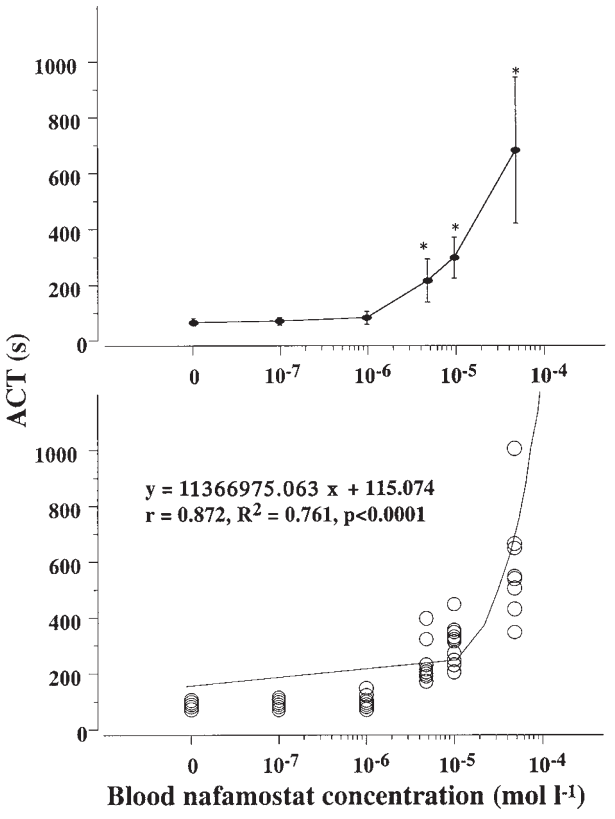

FIGURE The relationship between the blood nafamostat concentration and activated coagulation time (ACT). Upper graph shows values of mean ± SD and statistical changes (*$P < 0.05$ *vs* 0 mol·L^{-1} value). Lower graph shows scattergram and regression equation.

Hiroshi Iwama MD
Kazuhiro Watanabe MD
Shinju Obara MD
Aizuwakamatsu, Japan

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Aspiration pneumonia associated with a giant epiglottic cyst after cardiac surgery

To the Editor:
Epiglottic cysts are found incidentally during induction of general anesthesia and can hamper tracheal intubation.[1] Several methods have been reported to overcome these situations, however, to our knowledge, there has been no report of postoperative respiratory complications in patients with epiglottic cysts. We describe a patient with a giant asymptomatic epiglottic cyst who developed aspiration pneumonia after cardiac surgery.

A 71-yr-old man (height 154 cm, weight 42 kg) was scheduled to undergo coronary artery bypass grafting. During induction of general anesthesia, a giant epiglottic cyst was found (Figure). Though manual ventilation was easy, the cyst had almost obstructed the larynx and tracheal intubation was difficult. The surgery was carried out uneventfully and he was admitted to the intensive care unit for postoperative management. On postoperative day one (POD1), he was extubated and his respiratory state was stable. On POD2, he was able to drink water and the cough reflex was present. Immediately following the reintroduction of solid food, he developed aspiration pneumonia of the right lower lobe. Mechanical ventilation and administration of antibiotics proved effective and the cyst was removed surgically on POD5 under general anesthesia. The postoperative course after cystectomy was uneventful and oral intake was normal.

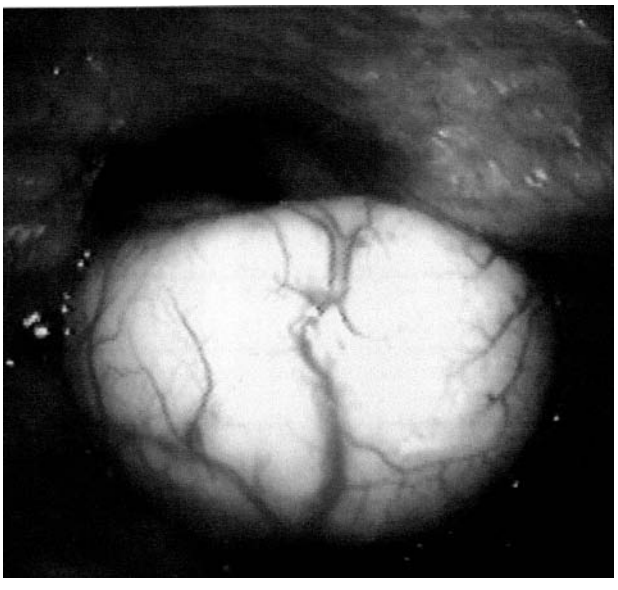

FIGURE A giant epiglottic cyst was found incidentally at laryngoscopy. The larynx was almost obstructed by the cyst.

There are several factors that increase the risk for aspiration pneumonia after surgery; namely, loss of protective airway reflexes, vomiting, pregnancy, obesity, diminished level of consciousness, anatomic distortion of the airway and a history of cerebrovascular disease.[2,3] Especially after cardiac surgery, age and duration of intubation are independent predictors of swallowing dysfunction.[4] In our patient, age, the residual effects of anesthetics, the use of transesophageal echocardiography, duration of intubation and anatomic distortion due to the giant epiglottic cyst are all possible factors explaining aspiration. We cannot tell which factor was predominant. However, the presence of this large epiglottic cyst may have resulted in postoperative epiglottic dysfunction and aspiration of solid food.

MinHye So MD
Kazuya Sobue MD PhD
Hajime Arima MD
Tetsuro Morishima MD
Masatoshi Fukumoto MD
Sayuki Tanaka MD
Hiroshi Ando MD PhD
Obazaki, Japan
Hirotada Katsuya MD PhD
Nagoya, Japan

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