2011, *J Anesth*), and heart transplantation for severe cardiac patients (Laubisch, J. E. et al., 2011, *Pediatr Cardiol* 32:1193-1195).

As noted above, SM inhalation is one cause of the rare but life-threatening disorder of plastic bronchitis, characterized by bronchial cast formation, resulting in severe airway obstruction that can lead to respiratory failure and death. Mortality in those requiring intubation is >80%. To date, no antidote exists for sulfur mustard toxicity. Additionally, therapies for plastic bronchitis are solely anecdotal, due to lack of systematic research available to assess drug efficacy in improving mortality and/or morbidity.

SUMMARY OF THE INVENTION

This Summary of the Invention is neither intended nor should it be construed as being representative of the full extent and scope of the present invention. Moreover, references made herein to "the present invention," or aspects thereof, should be understood to mean certain embodiments of the present invention and should not necessarily be construed as limiting all embodiments to a particular description. The present invention is set forth in various levels of detail in the Summary of the Invention as well as in the attached drawings and the Detailed Description and no limitation as to the scope of the present invention is intended by either the inclusion or non-inclusion of elements, components, etc. in this Summary of the Invention. Additional aspects of the present invention will become more readily apparent from the Detailed Description, particularly when taken together with the drawings.

One embodiment of the invention relates to a method to treat airway obstruction in a subject in need thereof, comprising administering to the subject a fibrinolytic agent. In another embodiment, the invention relates to a method to reduce airway obstruction in a subject in need thereof, comprising administering to the subject a fibrinolytic agent. In still another embodiment, the invention relates to a method to increase the survival of a subject having been exposed to a toxic inhaled chemical (TIC), wherein exposure to the TIC results in fibrin-containing cast formation in the airways of the subject, comprising administering to the subject a fibrinolytic agent.

In one aspect, the airway obstructions results from the formation of fibrin-containing casts in the airways of the subject. In another aspect, the subject has been exposed to a TIC. In one aspect, exposure to the TIC results in fibrin-containing cast formation in the airways of the subject. In yet another aspect, the fibring-containing cast formation in the airways of the subject results in the formation of plastic bronchitis in the subject. In still another aspect, the TIC is sulfur mustard or an analog thereof.

The fibrinolytic agent can be selected from tissue plasminogen activator (tPA), a tPA analog, urokinase plasminogen activator (uPA) and a uPA analog. In one aspect, the fibrinolytic agent is tPA. In various aspects, the tPA is administered in a dose amount of about 0.1 mg/kg/dose to about 1.0 mg/kg/dose. In still other aspects, the tPA is administered in a dose amount of about 0.4 mg/kg/dose to about 0.8 mg/kg/dose.

In still another aspect, the fibrinolytic agent is administered to the airways of the subject by a delivery method selected from inhalation, nebulization, aerosolization and intratracheal delivery.

The step of administering can include administering an initial dose of the fibrinolytic agent to the subject followed by administering an additional dose of the fibrinolytic agent to the subject. In one aspect, the step of administering of the fibrinolytic agent is conducted following the exposure of the subject to the TIC. In still another aspect, the step of administering is conducted immediately after an initial exposure of the subject to the TIC. In yet another aspect, the step of administering the fibrinolytic agent is conducted within about 0 hours to about 14 days after an initial exposure of the subject to the TIC. In still further aspects, the step of administering comprises administering an initial dose of the fibrinolytic agent following an initial exposure of the subject to the TIC and administering at least one additional dose of the fibrinolytic agent after the administration of the initial dose of the fibrinolytic agent. In yet another aspect, the step of administering the at least one additional dose is conducted about 30 minutes to about 60 minutes after the administration of the initial dose. In still another aspect, the step of administering the at least one additional dose is repeated. The at least one additional dose can be repeated about every 4 hours to about every 6 hours.

The subject in the invention can be human.

Another embodiment of the invention relates to a kit comprising a fibrinolytic agent selected from tPA, a tPA analog, uPA and a uPA analog and a device for administering the fibrinolytic agent to the airway of a subject.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. **1**A-**1**C show a description of cast scoring to assess degree of airways obstruction in plastic bronchitis. (FIG. **1**A) Map of the rat lower respiratory tract. During microdissection, extent of airway obstruction was determined at five lobar (main) branches (black lines), and at five major gravity-dependent branches (lines with arrows pointing to them). (FIG. **1**B) Nominal cast scoring chart for a given percentage of airway occlusion present. (FIG. **1**C) A branching bronchial cast present in the lobar bronchus of the right middle lobe (left panel of FIG. **1**C). Also shown is the typical appearance of a cast partially obstructing a central airway visualized en face during microdissection (right panel of FIG. **1**C). The dashed white circle (large) denotes normal airway wall perimeter, while the dotted circle (small) denotes the reduced airway lumen size due to cast attachment to the surrounding airway wall. (Image shown in FIG. **1**A was obtained from the National Alliance for Medical Image Computing.)

FIG. **2** shows the effect of tPA on mortality after sulfur mustard analog (2-Choloethyl ethyl sulfide; CEES) inhalation. Survival curves for rats exposed to CEES and given either: no treatment (NT, n=10); 'sham' treatment with isoflurane anesthesia only (Iso, n=8); placebo treatment (isoflurane anesthesia plus intratracheally administered phosphate-buffered saline (PBS, n=4); or 4) tPA treatment (isoflurane anesthesia plus intratracheally administered tPA, n=12). All three control groups had significantly lower survival than did rats given tPA treatment ($p<0.0001$ for Iso or PBS vs tPA, and $p<0.001$ for NT vs tPA, via Log-rank, Mantel-Cox test).

FIG. **3** shows the effect of tPA on tissue oxygenation in unanesthetized rats for 12 h after CEES inhalation. Noninvasively acquired oxygen saturations (SpO_2) were measured by pulse oximetry over 12 hours in rats exposed to CEES and given no treatment (NT, n=16); isoflurane anesthesia (Iso, n=10); isoflurane plus intratracheal PBS (PBS, n=4); or isoflurane plus intratracheal tPA at 0.15 mg/kg (n=6); 0.3 mg/kg (n=6); 0.5 mg/kg (n=6); or 0.7 mg/kg (n=16) doses. Vertical dashed lines indicate time interval during which the initial anesthetic, with tPA or PBS placebo, was adminis-