The therapeutic potential of hydrogen sulfide during cardiopulmonary bypass

Balancing cellular oxygen supply and demand is a key therapeutic approach to protecting organs such as the brain, kidneys and heart from ischemic injury. Permissive hypothermia and active cooling have been shown to reduce oxygen demands in patients experiencing stroke, cardiac arrest, cardiac surgery, severe trauma and other instances of ischemia and subsequent reperfusion. However, hypothermic reduction of aerobic metabolism has been associated with adverse effects, including increased rates of infection and coagulopathy. Developing other methods to acutely reduce metabolism in patients could be clinically useful.

Hydrogen sulfide (H2S) is an inhibitor of cytochrome C oxidase in the mitochondrial electron transport chain that reduces metabolism and body temperature in mice and rats. Inhalation of H2S or intravenous administration of H2S donor compounds (NaHS or Na2S) can protect rodents from hypoxia or hemorrhagic shock, improve survival rates after cardiac arrest and cardiopulmonary resuscitation in mice, and attenuate myocardial ischemia-reperfusion injury in both rodents and pigs.

Although inhaling H2S at 60 to 80 ppm reduces metabolism in mice, it has been reported that inhaled H2S does not depress total CO2 production and total O2 consumption in sedated, spontaneously breathing sheep (60 ppm H2S) or anesthetized, ventilated piglets (20 to 80 ppm H2S). On the other hand, Struve et al. reported that inhalation of H2S at 200 to 400 ppm, but not at 30 to 80 ppm, decreased body temperature in rats. Similarly, Morrison et al. showed that inhaling H2S at 300 ppm was required to decrease CO2 production in rats, in contrast to 80 ppm in mice. While these observations suggest that higher levels of H2S are likely to be required to alter metabolic rates in larger animals, the effects of higher concentrations of H2S on metabolism in larger mammals are incompletely understood.

It is well documented, however, that inhalation of high concentrations of H2S may injure the bronchial mucosa, cause pulmonary edema, and impair gas exchange. To examine the impact of delivering higher concentrations of H2S to the body without incurring the pulmonary toxicity of H2S inhalation, we administered H2S gas via an extracorporeal membrane lung (ECML). We hypothesized that high concentrations of H2S delivered via ECML in a partial venoarterial bypass system delivering blood to the aortic root might reduce the metabolic rate in sheep at rest. If ECML ventilation with H2S were found to reduce the metabolic rate in sheep, this method might provide a novel approach to balance the supply and demand of oxygen in a variety of situations, including in those patients who are supported by extracorporeal circulation during cardiac surgery or severe acute respiratory distress.
Administration of H$_2$S via extracorporeal membrane lung in sheep

Figure 1. Schematic representation of an extracorporeal circuit to deliver H$_2$S to sheep via membrane lung.

References Cited


