Drug-induced therapeutic hypothermia after asphyxial cardiac arrest in swine.

A feasibility study was performed to compare an investigational drug, HBN-1, to forced cooling to induce hypothermia after resuscitation in a translation model of asphyxial cardiac arrest in swine. Serum and cerebral spinal fluid neuron-specific enolase activity (sNSE and csfNSE) were measured after cardiac arrest as surrogate markers of brain injury. In a block design, swine resuscitated from 10 minutes of asphyxial cardiac arrest were infused intravenously with HBN-1 or iced saline vehicle (forced hypothermia [FH]) 5 to 45 minutes after return of spontaneous circulation (ROSC). External cooling in both groups was added 45 minutes after ROSC until hypothermia (T=4°C below baseline) was attained. Esophageal (core) temperature, shivering, cardiopulmonary parameters, and time to hypothermia after ROSC were monitored. sNSE and csfNSE were measured 180 minutes after ROSC. HBN-1 induced hypothermia significantly lowered temperature compared to FH 5-45 minutes after ROSC (p<0.0001). Time to hypothermia was reduced by HBN-1 (93±6 minutes) compared to FH (177±10 minutes) (p<0.0001). HBN-1 sNSE (0.7±1.9 ng/mL) and csfNSE (17.3±1.9 ng/mL) were lower compared to FH (6±1.6 ng/mL) and (49.7±32.0 ng/mL) (p<0.0001, p=0.022, respectively). There was no shivering with HBN-1 cooling while all FH cooled swine shivered (p<0.0001). The time to reach target hypothermia after cardiac arrest was reduced by nearly 50% with HBN-1 compared to the FH method of inducing hypothermia. Moreover, surrogate biomarkers of brain injury were significantly reduced with HBN-1 as compared to FH. While HBN-1-induced hypothermia shows promise for being neuroprotective, survival studies are needed to confirm these preliminary findings.

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