RhinoChill® Intranasal cooling device for protective cooling the brain after a cerebral ischaemic event

RhinoChill® is a device which cools the brain by spraying a coolant-oxygen mixture into the nasal cavity. It is designed for use after cardiac arrest, stroke or traumatic brain injury. The device, comprising of a control unit, coolant bottle and transnasal evaporative cooling catheter, is portable and battery operated. Its portability allows initiation of preservative brain cooling during resuscitation ‘in the field’ with the use of pressurised air or oxygen prior to hospital admission. Earlier cooling may be associated with greater protection of brain function.

Background

Cerebral ischaemia occurs when there is insufficient blood flow to the brain to maintain an adequate supply of oxygen. Without an adequate oxygen supply brain tissue may die potentially causing long term disability or even death. Reduction of supply of oxygen to the brain may follow a cardiac arrest, traumatic brain injury or may occur during a stroke.

The use of therapeutic hypothermia in cerebral ischaemia is well documented but cooling is not generally used in stroke or head injury patients because of a lack of evidence for benefit. The exact mechanism by which cooling the brain leads to improved outcomes after an event is not known although hypothermia is thought to both reduce metabolism and enzyme activity thereby influencing cell death mechanisms.

It is estimated that between 17 and 66 cardiac arrests per 100,000 population occur out of hospital each year. Of these between 5 and 12% may survive. Between one and five of every 1,000 patients admitted to hospitals will have an in-hospital cardiac arrest in the UK. During 2009-10 approximately 169,000 strokes were recorded in hospitals equating to 307 per 100,000 of the population. The number of recorded deaths from a stroke in 2009 was 11,203. Traumatic brain injury occurred in about 13,000 people equating to 24 per 100,000 of the population. There were 1,180 deaths recorded due to traumatic brain injury in 2009. An average GP with a list of 2,000 patients may have six people with a new stroke each year. The same GP might see one patient in two years with a new traumatic brain injury.

Current Practice

The National Institute for Health and Clinical Excellence (NICE) recommends that after cardiac arrest comatose patients who have a return of spontaneous circulation should be cooled to a core temperature of 32-34°C. The guideline also recommends inducing mild hypothermia as soon after cardiac arrest as possible by using surface methods such as cooling blankets and ice packs or invasive endovascular techniques which may include infusing the patient with a cold liquid such as saline solution.
Clinical Studies and Research Questions

A prospective randomised trial of 194 patients, which compared pre-hospital cooling with RhinoChill® to no prehospital cooling in people who had suffered a witnessed cardiac arrest, aimed to demonstrate whether pre-hospital brain cooling with the RhinoChill® device was effective, safe and feasible. The participants were randomised to either pre-hospital brain cooling with the RhinoChill® device by an advanced life support team (93 patients) or to no pre-hospital cooling (101 patients). The mean tympanic temperature (temperature measured in the ear) was significantly lower in the RhinoChill® group compared with the control group (34.2°C vs 35.5°C, p<0.001) on arrival at the hospital, as was the mean core temperature (35.1°C vs 35.8°C, p=0.01). A tympanic temperature of 34°C was achieved in a median 102 minutes in the RhinoChill® group compared with 291 minutes (p=0.03) in the control group. There was no significant difference in the median time to core temperature of 34°C between the groups (155 minutes vs 284 minutes, p=0.13). There were no significant differences between the RhinoChill® group and the control group with respect to rate of return of spontaneous circulation (38% vs 43%, p=0.48), survival to discharge of those admitted alive (48% vs 31%, p=0.26) and neurologically intact.

New Technology

RhinoChill® IntraNasal Cooling System has been developed by BeneChill to minimise brain damage after cardiac arrest, stroke and traumatic brain injury. The portable device is made up of the control unit, coolant bottle and transnasal cooling catheter. A source of pressurised gas (air or oxygen) is required to operate the RhinoChill®.

A mixture of gas and coolant is sprayed into the nasal cavity via nasal cannulae. The nasal cavity, which has a large supply of blood vessels, is designed to warm inspired air to body temperature during normal respiration. This mechanism of warming aids in evaporating the volatile coolant. Evaporation of the liquid to a gas removes heat from surrounding tissues and cools the nasal cavity to about 2°C. Cold is transferred conductively across the thin bone at the base of the skull as well as haematogenously by the blood vessels where a circulation still exists.

RhinoChill® is portable and battery operated making it possible to use the device outside the hospital. This means that brain cooling may begin close to the time of the start of the cerebral ischaemic event and during resuscitation. Cooling the nasal cavity, which lies just below the brain, means that the device can cool the brain when there is no blood circulation. RhinoChill® is relatively non-invasive requiring only two 10cm nasal catheters. The company state that the device is not intended to be used to implement a full hypothermia protocol involving long maintenance times and controlled temperature reversal.

RhinoChill® is intended for pre-hospital use as well as use in the hospital. RhinoChill® was CE marked in April 2011 and was launched in the UK in May 2011.

These methods of cooling do not target the brain and it may be difficult to implement them out of a hospital setting.

Although therapeutic hypothermia has been used to improve outcomes after traumatic brain injury and stroke, it is not recommended for use within the NHS. A team at John Hopkins University School of Engineering has developed a portable Rapid Hypothermia induction device which delivers a chilled gas at 0°C into the nasal cavity to cool the brain but this device is not currently available commercially.

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survival at discharge (34% vs 21%, p=0.21). No significant differences were observed between the two groups in cardiogenic shock as cause of death, length of hospitalisation and days in intensive care. Nasal whitening occurred in 13 patients in the RhinoChill® group but this resolved spontaneously in all five resuscitated patients. Epistaxis (nose bleed) occurred in three patients in the RhinoChill® group and was serious in one case where the patient had an underlying condition pre-disposing then to a serious bleed. A single patient experienced periorbital emphysema 75 minutes after RhinoChill® cooling began that resolved within 24 hours.

A single arm safety and feasibility study of 84 patients who were successfully resuscitated after cardiac arrest demonstrated that RhinoChill® effectively lowers tympanic and core temperatures. Use of the device in the emergency room commenced a median of 90 minutes after the arrest and lasted for a median of 60 minutes. The lowest tympanic temperature observed after using the device was 29.4°C while the lowest core temperature was 31.2°C. Of the 34 people who survived, 26 were conscious and alert with no or moderate disability at discharge. Device related adverse events occurred in 13 patients. These included nasal discolouration, coolant in the sinus, periorbital emphysema, epistaxis and cold induced tissue damage. All the adverse events resolved spontaneously with the exception of the tissue damage which occurred in one patient and was deemed a serious adverse event.

A study of 15 patients with brain injury showed that RhinoChill® can reduce brain, tympanic and core temperature by at least 1°C after an hour’s use. The study conducted in neurological intensive care units involved individuals for whom cooling was ordered and who had experienced ischaemic stroke, intracranial haemorrhage, head trauma, aneurysm surgery or cardiac arrest. Transient hypertension (raised blood pressure), the only device related adverse event, occurred in one patient and was resolved with device removal and sedation.

A randomised controlled trial is currently underway which aims to study the effectiveness of nasal cooling with the RhinoChill® device applied in the field during resuscitation compared to cooling initiated at intensive care units in patients with witnessed out of hospital cardiac arrest.

At this time there is no trial evidence comparing the effectiveness of RhinoChill® with the current cooling methods in hospital. Randomised controlled trials and follow up studies of the use of RhinoChill® in individuals after stroke or brain injury would provide information about the safety and effectiveness of this device in these conditions. More generally research issues that need to be addressed would include the need for intensive care during cooling and the complications of cooling and re-warming.

**Potential Impact**

The portable nature of the RhinoChill® device may allow protective brain cooling to be initiated sooner than the traditional hospital based methods of cooling. Earlier brain cooling after an ischaemic event may potentially lead to better patient outcomes in terms of recovery, brain damage and disability. Trials so far have not demonstrated a decrease in ITU or hospital stay following use of the RhinoChill® device, but if such results were shown in future this may have significant impact on healthcare costs.
**References**


