Pre-hospital initiation of therapeutic hypothermia in adult cardiac arrest: a literature review

Abstract

Therapeutic hypothermia (TH) following cardiac arrest is commonplace in many hospitals and intensive care units around the globe as this treatment is thought to improve survival rates and offer neuroprotective benefits. However, its use in the pre-hospital arena is still uncertain with conflicting or little evidence to support the timing, mode of delivery or potential benefit for the patient. The objective of this literature review is to collect and consider evidence and address these uncertainties with a view to offering recommendations for practice.

Methods

A systematic search was undertaken of 2 databases – EBSCOhost and Pubmed – using a Boolean search strategy. This literature review also included hand searched articles to ensure that a full and comprehensive scope of evidence was collated and included.

Papers were included if they met the following inclusion criteria:

- Studies between 2005 – 2014
- Full text
- English language
- Human subjects
- Pre – hospital studies.

Papers were excluded if they met the following criteria:

- Non – human subjects
- In – hospital studies
- Trauma
- Children
- Studies prior to 2005.

In – hospital studies were not included in this review due to the focus being specifically around pre-hospital care. It was also taken into consideration that individual hospitals would potentially have different specialities within them and also differing guidelines and protocols surrounding the implementation of TH.

Results

Three specific areas of TH were analysed – the implementation of TH during the cardiac arrest, the mode of initiating TH – either by cooling pads, by using RhinoChill or by infusion of cold fluids - and whether there were clear neurological and survival benefits for the patient.

The results from the studies analysed were unable to provide clear evidence into the benefits of the implementation of intra-arrest TH, although there was some evidence to suggest that one subgroup that received early CPR alongside early TH had improved survival outcomes. In regards to the mode of instigating TH, cooling efficacy was proved in all methods evaluated, although each method had some potential negative outcomes associated with its usage. The final area of analysis showed conflicting evidence around potential survival and neurological outcomes for the patient. Two of the three papers could not support claims that TH improved survival to discharge or improved neurological status, whilst the third paper noted a higher instance of favourable neurological outcomes.

Conclusions

From the literature reviewed, there is no unanimous evidence that prehospital TH improves patient survival or neurological outcomes. It is clear that all of the different modes of initiating TH that were evaluated were all effective in reducing patient temperature on arrival at hospital.

Key words

- Pre-hospital
- Therapeutic hypothermia
- Cardiac arrest
- Adult

Background: The role of therapeutic hypothermia (TH) in cardiac arrest

Out of hospital cardiac arrest (OHCA) in which resuscitation was attempted, accounted for approximately 28,000 call outs for the emergency medical services in 2013 in the UK. However, the survival to hospital discharge was only 8.6% - far lower than in other developed countries (British Heart Foundation, NHS England and Resuscitation Council UK 2015). Of the patients that do survive, ensuring a positive neurological outcome is difficult to attain (Arrich et.al 2012). These poor outcomes have led to research into how the prognosis of these patients can be improved and one of the ways to achieve this could be with the implementation of therapeutic hypothermia (TH) (Soar and Nolan 2007) with a particular focus on implementation in the prehospital setting (Hunter et.al 2014).

The role of TH either during or after cardiac arrest is by no means a new phenomenon – its uses were initially investigated in the 1950's but not pursued again until the 1980's when potential benefits of the treatment were explored (Marion et.al 1996). In 2002, two ground breaking human studies noted the value of TH after cardiac arrest and from these positive indications, both the International Liaison Committee on Resuscitation (ILCOR) and the American Heart Association (AHA) recommended the use of TH in adults with a return of spontaneous circulation (ROSC) in OHCA, when the presenting rhythm was ventricular fibrillation (VF) (Lee and Asare 2010). A separate review of four clinical trials in 2004 by the Canadian Association of Emergency Physicians Critical Care Committee reviewed further evidence and concluded that TH should be initiated not only in patients presenting in VF, but also when ROSC was achieved and the presenting rhythm was asystole or pulseless electrical activity (PEA) (Howes et.al 2006).

However, Arrich et.al (2013) recognise that there are conflicting views around the value of TH for the patient. Certainly, the large international, multicentre randomised controlled trial (RCT) of 950 in-hospital patients by Neilson et.al (2013) shed doubt on the perceived benefits of TH, as it was discovered that there was no clinical benefit to lowering temperature to 33°C compared to maintaining a body temperature of 36°C. The National Institute for Health and Care Excellence (NICE 2011) agree that whilst TH proves effective for some patients, the outcomes can be unpredictable and variable.

Pathophysiology

To understand why TH may prove beneficial to patients who have suffered a cardiac arrest, it is important to understand how the body is affected at the time of cardiac arrest and during the reperfusion that occurs following successful resuscitation. Certainly, whilst achieving a ROSC in OHCA is not a marker for success - this should be based on survival of the patient to discharge from hospital (Salcido et.al 2010) - there is increasing acknowledgement that organised post ROSC care can improve the chances of patient survival and decent quality of life (Peberdy et.al 2010). Arrich et.al (2013) explains that cells in the brain are damaged as soon as cardiac arrest occurs and circulation ceases. This is due to lack of oxygen and the depletion of adenosine triphosphate, a high energy compound essential for many cellular functions in the brain (Du et.al 2007). McCullough et.al (1999) cited by the Resuscitation Council UK (2010) explain that initiating TH supresses the pathways leading to these cell deaths and lessens the brain's metabolic rate for oxygen by around 6% for each single degree of cooling. There is also speculation that additional benefits may come from a decrease in intracranial pressure (ICP) – elevation of ICP is known to be neurologically damaging (Lee and Asare 2010) - and a decrease in amino acid and lactate levels (Cady and Andrews 2008). Whilst poorly understood, evidence suggests that other neuroprotective functions of TH exist when the cooling effects interfere with synaptic transmission and voltage gated ion channels which in turn reduces epileptiform activity and associated damage in the brain (Lee and Asare 2010).

Rationale behind this literature review

Assuming that TH proves advantageous for the patient, for clinicians in the prehospital environment, uncertainty remains around multiple factors. Should TH be started during cardiac arrest, which mode of cooling should be used and what are the neurological and survival benefits? The rationale behind this literature review is to look at these three specific themes regarding TH in the prehospital setting. Whilst there is uncertainty around TH it will be difficult to transfer these conclusions into current prehospital guidelines. However, it may aid greater understanding of the intervention as a whole.

Methodology

The databases PubMed and EBSCOhost were used to gather papers for this literature review and articles were also hand searched to ensure that a full and comprehensive scope of evidence was collated and included.

The construction of key words and phrases were carefully and methodically undertaken to ensure that as many hits were returned as possible and to minimise the risk of important literature being missed. 22 different key words were searched individually for each database and the results recorded for each. Some key words were included to consider that often words and phrases were known better as different names in other countries. A good example of this is that ‘paramedic’ is well known in the United Kingdom but may be often known as ‘EMS’ elsewhere in the world. From here, additional key words were added to make key phrases and Boolean operators ‘AND’ and ‘OR’ were used to refine and focus the search. Exclusion and inclusion criteria were set with the aims of the literature review firmly in mind. The purpose of this literature review was centred on the use of TH in the prehospital environment. For this reason, in-hospital studies, of which the majority of papers included, were excluded. Children and trauma were also excluded as these specialities often require different treatment protocols and as such were routinely excluded anyway by the authors of the papers that were included in the final review. A desire to include recent evidence required studies prior to 2005 being excluded and non-human subjects were also excluded as the results were not immediately transferable for practice. The inclusion criteria included full text papers which were written in the English language. Only primary research was included and duplicate papers removed. Application of these criteria led to the 60 papers from EBSCOhost being reduced down to 1 article and the 89 papers from PubMed to 2 articles. The remaining 5 articles were handsearched.

Whilst this literature review focuses on studies between 2005 – 2014, consideration has been given to more recent evidence undertaken into TH. Whilst not explored in such depth, salient evidence has been included to ensure a comprehensive review.

Discussion

Are there benefits of instigating TH intra-arrest?

As previously mentioned, one of the many unknown factor surrounding the instigation of pre-hospital TH is the actual timing of the intervention. The following analysis in this section considers firstly, the feasibility of introducing TH during an OHCA and secondly, whether the data supplied supports the hypothesis that introducing TH during an OHCA, rather than during the post ROSC phase will improve patient outcomes.

In 2010, a prospective, randomized, prehospital study by Castren et.al (2010) was conducted over 5 sites in 15 European countries. The purpose of this study was not powered to ascertain clinical outcomes, but to consider the safety and feasibility of instigating intra-arrest cooling using the RhinoChill device. RhinoChill is a method of cooling the brain via an intra-nasal cannula which delivers perfluorohexane coolant and oxygen which evaporates on contact with the cavity of the nose, thus cooling the brain (NICE 2014). This study, which was approved by the ethics committee in each participating centre, had a cohort group of 194 adults. 101 adult patients had no intervention and 93 were treated with TH to attain a target temperature of 34°C. Patients were randomized following intubation by the clinician and on confirmation that no palpable pulse or organised cardiac rhythm were present. Whilst not powered to address clinical outcomes, one of the areas of this study for scrutiny was to determine whether intra-arrest TH improved the rate of ROSC compared to the control group. However, results showed that there was no significant difference with 37.6% ROSC in the treatment group and 42.6% in the control group, despite promising data from previous animal studies. Castren et.al (2010) hypothesise that this may be because the TH was started too late in the resuscitation attempt, as that median time to initiating RhinoChill was 23 minutes after collapse. The authors acknowledge that as there were no definitive guidelines set for initiation of TH in this study due to fear of disrupting existing resuscitation protocols.

In comparison, the prospective, observational, multicentre clinical trial which was undertaken into the feasibility, effectiveness and safety of initiating TH using cold fluid by Bruel et.al (2008). This study speculated that there may be benefit to intra-arrest TH by reasoning that intra-arrest TH may lessen the duration of cerebral ischemic injury, as suggested by previous experimental models. This study, which was approved by the Institutional Ethics Committee, had a cohort size of 33 patients. During cardiac arrest, 2L of 4°C sodium chloride was infused over 30 minutes through an intravenous line. Bruel et.al (2008) explain the reasoning of a standard 2L dose was to simplify the treatment protocol, rather than using a weight based dosage. Outcomes reported showed that from the initial 20 patients who achieved a ROSC, 4 patients were alive after 6 months and 3 had a good neurological outcome. However, there can be difficulty in analysing the clinical worth of this study as that there was no control group in which to compare data with.

A much smaller randomized, controlled, observational study was undertaken by Kamarainen (2010), again into the feasibility of intra-arrest TH using cooled fluids. This study has many limitations – there is no detailed statistical data to evaluate and the sample size is small. As with the previously mentioned study by Castren et.al (2010), Kamarainen (2010) discussed that the evidence from this small study suggested that intra-arrest TH had no benefit in improving the ROSC rate.

Cooling efficacy

The study by Castren et.al (2010), reported that there was clear evidence that the treatment group reached 34°C in a median of 102 minutes, compared with 291 minutes in the control group and on arrival at hospital, the mean tympanic temperature in the intervention group was 34.2°C compared to 35.5°C in the control group, giving a P value of $P<0.001$.

The paper by Kamarainen (2010) reported that the intervention group showed temperature reduction of -1.5°C versus -0.1 in the patients in the control group $P<0.001$.

Bruel et.al (2008) reports that the median time to reach the target temperature of 34°C was 16 minutes from onset of infusion and that temperature was reduced by -2.4°C $P<0.0003$. The difference between the studies is that Castren et.al (2010) used RhinoChill to instigate TH, compared with the studies by Bruel et.al (2008) and Kamarainen (2010) who used ice cold intravenous fluids.

Results

Evidence shared by all papers reviewed for this theme is that there is no doubt that prehospital TH results in the patient being cooled to perceived optimum temperatures before arrival at hospital. However, due to the lack of control groups and comparative data in two of the three papers, it is impossible to accurately state that intra-arrest TH categorically improves ROSC and survival rates. This corroborates findings from the later study by Nolan et.al (2015) that states whether certain patients may benefit from early TH is still unknown. Interestingly, in the study by Castren et.al (2010), a subgroup of patients who had cardiopulmonary resuscitation (CPR) initiated within 10 minutes and combined with intra-arrest TH were found to have a survival rate of 56.5% compared to the same sub group with no cooling at 29.4%. This may suggest that a combination of CPR and TH could be the most beneficial treatment regime for the patient - certainly this is a recommendation by Castren et.al. Incidentally, literature by Travers et.al (2010) describe that early initiation of CPR is vital to improve the chance of survival and forms part of the ‘chain of survival’, a view shared by Murthy and Hooda (2009) who stress that ensuring adequate perfusion to the heart and brain is essential for neurologically intact survival.

Which method should be used to achieve TH in the pre-hospital environment?

The instigation of TH using cooling pads

Uray and Malzer (2008) undertook a feasibility study into the speed and safety of using cooling pads to initiate TH following ROSC. This study included a small cohort of 15 patients (with no control group for comparison) who, after successful ROSC in over 5 minutes in OHCA, had TH started with cooling pads with the aim to achieve a target temperature of 33°C. Uray and Malzer (2008) describe the pads as consisting of 12 parts which binds to the patient’s skin on application, thus ensuring efficient heat transfer. The pads cover the body and head with a total coverage of 7200cm squared and consist of a mixture of graphite and water. The pads were cooled to – 9°C and were stored in the ambulance with a combination of spare batteries and a temperature probe which would alarm in the temperature of the storage box raised above 0°C. Active warming was employed to maintain hypothermia at the targeted levels.

The instigation of TH using cold intravenous fluids

Kamarainen et.al (2009) conducted an RCT into the safety and efficacy around initiating TH using +4°C Ringer’s solution, administered intravenously, after successful ROSC in OHCA. The study by Kamarainen et.al (2009) had a cohort of 44 patients with 19 receiving TH and 18 in the control group. Following ROSC, randomization was completed using sealed envelopes. If the patient was allocated to the treatment group, rapid infusion of +4°C Ringer's solution was given at approximately 100ml/min to achieve a target nasopharyngeal temperature of 33°C. The maximum amount of fluid allowed was 30ml/kg. This study used active warming if the temperature fell below 32°C-. The control group had no intervention but nasopharyngeal temperature was recorded for comparison.

Cooling efficacy and patient benefit from each method used

Uray and Malzer (2008) report that oesophageal temperatures fell by 36.6°C to 33°C in a median time of 70 minutes, which equated to a median of 3.3°C per hour. Due to the nature of the study being a feasibility study, Uray and Malzer (2008) explain that only descriptive data and statistics are reported.

Kamarainen et.al (2009) are able to report their findings in more depth. Initial baseline temperatures were recorded as similar in both groups but on arrival at hospital, the intervention group had a significantly lower nasopharyngeal temperature recorded of 34.1°C compared with the control group at 35.2°C, $P<0.001$. The median cooling rate in the intervention group in this study was 2.0°C per hour, which suggests this mode of TH is not as rapid as the cooling pads in the study by Uray and Malzer (2008).

From the cohort of 15 patients in the study by Uray and Malzer (2008), 93% survived for 24 hours and 36% to hospital discharge. This 36% all displayed normal neurological function after 6 months from the OHCA. The purpose of the study by Kamarainen et.al (2009) was not to assess survival or neurological outcomes as a primary result, and as such, no data exists for comparison.

Difficulties associated with the mode of delivery

Uray and Malzer (2008) report that on arrival at the receiving hospital, 33-50% of the cooling pads had to be replaced as they had thawed and some pads had to be changed to enable the target temperature to be achieved, though it is stated that these particular patients had a high BMI, which suggested the need for additional pads. Data from this study also showed that active warming needed to be initiated in a majority of cases to prevent hypothermia falling below therapeutic targets. Uray and Malzer (2008) also explain that a disadvantage of this device was its weight was 13.2kg in total and that daily changing of batteries may prove laborious for medical staff. Nevertheless, Uray and Malzer (2008) are confident in stating that this method of initiating TH is quick, feasible, non-invasive and safe for the patient, but argue that there are some of the potential problems with initiating TH with cold fluids – these being that intravenous access may not be available, an additional method of maintaining hypothermia may need to be sought to alleviate rapid rewarming that may be seen with cold fluid use. This view is accepted by Kamarainen et.al (2009) who concur that cold fluid alone is insufficient to maintain hypothermia after cardiac arrest - and that pulmonary oedema may contra-indicate use. However, Kamarainen et.al (2009) did not observe onset of pulmonary oedema in their study and argue that infusion of cold fluids to initiate TH is simple and effective in the prehospital environment. Kamarainen et.al (2009) discovered that the intended infusion rate of 100ml/min was not achieved in most patients and the authors propose that transport to hospital times may restrict completion of the infusion. However, Kamarainen et.al (2009) advocate that the treatment should be continued in hospital anyway so this may not be as problematic as it appears.

Results

Whilst Kamarainen et.al (2009) and Uray and Malzer (2008) concentrate on the feasibility and safety of initiating TH using different modes – cooling pads and intravenous cold fluids – the study design of both were very different, meaning that drawing clear comparisons or deciding superiority between the two methods are impossible. Both papers achieve their objectives in confirming safety, feasibility and speed of each intervention. Certainly, patients who had TH before hospital admission had lower temperature noted which is the same conclusion drawn from the previous theme. Uray and Malzer (2008) recommend that a prospective randomised trial is performed to determine benefit of improved neurological outcome from early cooling, whilst Kamarainen et.al (2009) recommend that initiation of TH in the prehospital field should be considered in future guidelines.

Does the early initiation of TH improve survival rates and neurological status?

It has been shown in animal studies that TH in cardiac arrest has positive benefit (Azmoon et.al 2011), with suggestion that TH can also reduce the severity of resulting brain injury and improve survival rates after cardiac arrest in humans (Sandroni, Cavallaro and Antonelli 2013). From these studies, many guidelines now recommend the routine initiation of TH in the management of patients in OHCA (Dumas et.al 2011).

The purpose of this final theme is to review 3 papers, all of which use cold fluid to initiate TH during the ROSC phase of cardiac arrest, to consider whether survival and/or neurological benefits have been substantiated.

Survival rates

Kim et.al (2014) commenced an RCT with a cohort size of 1359 patients to test the hypothesis that TH initiation immediately following ROSC would improve survival and neurological outcome. Kim et.al (2014) explain that paramedics, doctors and nursing staff were not blinded to the treatment groups, but that the study personnel who collected data were not aware of study allocation. This study focused on 583 patients who presented with ventricular fibrillation (VF) and 776 who did not. Each of these groups were then divided again - in the VF group 292 were cooled, with 291 in the control group and non VF – 396 were cooled with 380 in the control group. The strength of this study is that it focuses on shockable and non-shockable patients independently which allows comparison of the ideas by Dumas et.al (2011) who suggested that patients who presented with a shockable rhythm – for example VF – and had early initiation of TH, had positive survival rates in comparison with patients presenting in asystole or PEA (who had much poorer prognosis).

Kim et.al (2014) explains that after ROSC was achieved, clinicians administered up to 2L of 4 degrees C normal saline intravenously to achieve a target temperature of 34°C. The majority received this amount but again short transport time was given as a reason if this was not the case, as mirrored in the study by Kamarainen et.al (2009). Survival rates to hospital discharge in the VF group were as follows, with the intervention group at 62.7% and control group at 64.3%. The non VF group's survival to hospital discharge in the intervention group was 19.2% with the control group at 16.3%.

In comparison to this study is the prospective observational study by Skulec et.al (2010) who again used 4°C of normal saline to initiate TH during ROSC, but in this study the therapeutic fluid dose was lower to account for difficulties previously mentioned due to transportation times. The cohort for this study was 40 patients in the intervention group with the same number in the control group. Skulec et.al (2010) reports that the majority of patients also underwent in-hospital cooling. In-hospital mortality was found to be lower in the intervention group at 37.5% compared to 55% in the control group. However, arguably these results cannot be fairly compared to the survival to discharge results supplied by Kim et.al (2014) but they are the closest data supplied by Skulec et.al (2010).

Neurological outcomes

Kim et.al (2014) found that TH in either the VF or non VF groups had no significant impact on neurological status on hospital discharge. The authors report that neurological status of full recovery or mild impairment in the VF group were as follows, with the intervention group at 57.5% and the control group at 61.9% and the non VF intervention group at 14.4% compared with the control group at 13.4%.

These results are similar to the findings of the prospective RCT by Bernard et.al (2010), who evaluate their hypothesis that prehospital initiation of TH in patients with a presenting rhythm of VF would improve neurological outcomes. The cohort size was 234 patients, with 118 treated with TH and 116 receiving no cooling until arrival at hospital. Randomisation was by sealed envelopes in allocation blocks of ten to each participating paramedic unit and if randomised, the patient was administered up to 2L of ice cold Ringer's solution to achieve a target temperature of 33°C. In-hospital cooling was initiated for all patients after bladder or oesophageal temperatures were taken. Bernard et.al (2010) recorded that 47.5% in the intervention group had a favourable outcome at hospital discharge compared with 52.6% in the hospital cooled group. A possible reason for this result is suggested by Bernard et.al (2010) in that, as in previous studies, difficulties were observed in achieving full fluid administration before hospital arrival. Bernard et.al (2010) recorded that only 48% received the full 2L, and felt that inconsistencies in amounts given may have affected outcomes.

In direct conflict to the results from these two studies in this theme, are the results on neurological outcomes by Skulec et.al (2010). The neurological outcomes in this study were analysed using the cerebral performance category (CPC), with levels 1 and 2 being favourable outcomes. Skulec et.al (2010) found that at discharge, 45% of the intervention group had a CPC score of 1 or 2 compared to 27.5% of the control group. However, it should be taken into consideration that the intervention group also had a higher instance of bystander CPR - 53.8%

compared with the control group - 23.5%. Other bearings on favourable outcomes were coupling of prehospital TH in conjunction with in hospital TH and when VF was a presenting rhythm.

Results

It would appear that there are conflicting results when reporting on both survival rates and neurological outcomes with TH initiated during ROSC. Neither Kim et.al (2014) nor Bernard et.al (2010) could support claims that TH in the prehospital environment improved survival to discharge and/or neurological status, and Kim et.al (2014) even state that their study results do not support the routine use of cooled fluid in the prehospital environment. The data from Skulec et.al (2010) disputes these claims but it is unfeasible to draw direct comparison as different data was reported regarding survival. What is clear is that both Kim et.al (2014) and Bernard et.al (2010) identify that the optimum timing for initiating TH is still unknown and all three papers call for further ongoing studies into elements of TH in OHCA.

Conclusion

Available research around the timing of the intervention was limited with only 3 papers focusing on intra-arrest TH. The results from these studies were unable to provide clear evidence of intra-arrest TH improving survival rates and indeed, the papers by Kamarainen (2010) and Bruel et.al (2008) both suggest that ongoing studies are required to analyse safety of this intervention along with any potential survival and neurological benefits. The study by Castren et.al (2010) discovered that improved survival rates were shown in the subgroup who had early CPR combined with early TH, and as such, this combination of treatment was a recommendation for practice.

In regards to the mode of instigating TH, cooling efficacy was again proved in all three modes that were evaluated, with patients who had TH in the prehospital environment recording lower temperatures than patients with spontaneous cooling. From the total literature reviewed, 1 of the papers used RhinoChill, 1 used cooling pads and 6 used an infusion of cold fluids. For the purpose of the theme regarding modes of cooling, cooling pads and cold fluid administration were considered, along with the data from the RhinoChill study. On reviewing the papers, it is clear that induction of TH using cold fluids is cheaper and simpler that with RhinoChill or cooling pads which require bulky or heavy equipment. There were also difficulties identified around cooling pads not being as effective on patients with a higher than average BMI. A potential negative to TH using cold fluid is the risk of pulmonary oedema, although this was only evident in one study and proved to be transient in nature. None of the papers critiqued focused on survival or neurological outcome as an end point, so conclusion over the benefit to the patients cannot be drawn.

Survival rates and neurological outcomes were assessed in data from the final three papers. All of these studies used cold fluid to induce TH and all in the ROSC phase of OHCA. Results from these papers showed some conflicting evidence around the benefits to the patient. Neither Kim et.al (2014) or Bernard et.al (2010) supported claims that prehospital TH influenced positive outcomes either around survival or neurologically. However, Skulec et.al (2010) felt that their data showed trends towards improved neurological outcomes when prehospital TH was combined with ongoing in hospital TH. With regards to survival to discharge, this data was not supplied by Skulec et.al (2010) so this cannot be scrutinised.

Recommendations for practice

Due to the research studies in this literature review not being undertaken in the United Kingdom, any clear recommendations for practice would be difficult to immediately implement due to several factors. Consideration must be given to the fact that pre-hospital expertise outside of the United Kingdom will comprise of differing clinical skill sets and the use of differing individual protocols regarding medication regimes. Studies undertaken in the United Kingdom are essential to give clear guidance for prehospital clinicians which take into regard their current scope of practice, as currently it is not standard practice for paramedics in the United Kingdom to administer some of the drug regimens mentioned in these studies.

Further recommendations

This literature review was unable to unanimously answer questions around the effectiveness of TH in the prehospital environment. Interestingly, more recent studies also appear to agree with this view. The meta-analysis by Villablanca et.al (2016) indicated that introducing TH in OHCA showed no increase in the survival or neurological recovery of patients, whilst the recent RINSE Trial (Rapid Infusion of Cold Normal Saline) concluded that inducing mild TH during CPR with rapid, large amounts of cold saline may actually decrease the rate of ROSC when patients present with an initial shockable rhythm (Bernard et.al 2016).

Recommendations must be around the need for further studies into the optimum timing of TH, the mode of initiation and also the potential positives for patient survival and long term neurological outcomes.

Key points

- There is still uncertainty around many elements of therapeutic hypothermia (TH) in out of hospital cardiac arrest (OHCA), such as timing, mode of delivery and benefit to the patient.
- Further studies are required to address these uncertainties and develop protocols for implementation into practice.
- Cooling pads, RhinoChill and cold fluid have all been found to be effective in reducing patient temperature on their arrival to hospital.

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