ER Journal Meeting

Present by PGY 余正元
Supervised by CR 李尚/ VS 王瑞芳
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Introduction

- Beneficial outcome of mild hypothermia
  - Animal and human studies
  - For stroke, acute myocardial infarction, and cardiogenic shock
- Aim of this study
  - To investigate the feasibility and safety of non-invasive surface cooling for induction and maintenance of mild hypothermia (32 to 34ºC) in healthy, conscious volunteers

Materials / Methods

Study Setting and Population

- 16 Volunteers (18 to 70 years old)
- Excluded criteria
  - Pregnant women
  - Cardiopulmonary disease or malignancy
  - Coagulopathy
  - Active dermatologic condition
  - Current treatment with MAOI
  - Previous or current drug abuse
  - Known allergy to the study medication
- Core temperature had to be below 37ºC at the start of the cooling procedure

Study Protocol

- **General health check** prior to enrolment
  - General PE, lab, resting ECG, and CXR
- Abstinence from alcohol, tobacco and strenuous exercise for 12 hours before the study
- A light meal before study day to minimize any potential nausea caused by Meperidine infusion

Medication

- **Meperidine** 1 mg/kg bolus, 30 mg/h IV, and **Buspirone** 30 mg PO to prevent shivering
- **Granisetron** hydrochloride 3 mg IV to prevent nausea
- **Isotonic electrolyte solution** 100 ml/h IVD throughout the cooling period
- **MgSO4** 4g bolus and 2 g/h IVD because of problems reaching the target temperature of 32 to 34°C
  - Limited to 8 volunteers

Cooling Procedure (1)

- **Cooling pads**: 20 x 30 cm, consist of multiple cooling cells filled with a patented cooling gel
  - Stored in a cooling box at -2˚C before use
- 6 cooling units were applied on the back, thorax, abdomen, and thighs of the volunteers
  - In previous studies in patients after cardiac arrest, temperature drop was observed after the removal of the cooling units; thus, in this study, the cooling units were removed when a core temperature of 35˚C was reached

Cooling Procedure (2)

- Target **core temperature** was 32 to 34˚C and maintained for 6 hours
  - If it did not drop below 34.3˚C (or started to increase), two cooling units were applied until the temperature reached 34˚C
  - If it dropped below 33˚C, a warming blanket was applied until the temperature reached 33.1˚C
- After 6 hours, the volunteers were covered with a blanket and allowed to re-warm
- Meperidine was stopped at 35˚C
  - Observation for additional 16 hours

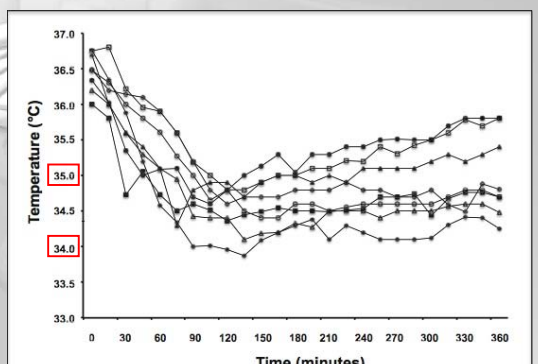
Measures

- Core temperature was measured with a probe advanced into the esophagus
- BP, ECG, HR, and SpO2 were recorded
- The comfort was measured by a 5-point scale
- Shivering was monitored by a 4-point scale
- At the end of the observational period, the skin of all subjects was examined by a dermatologist using a 5-point scale

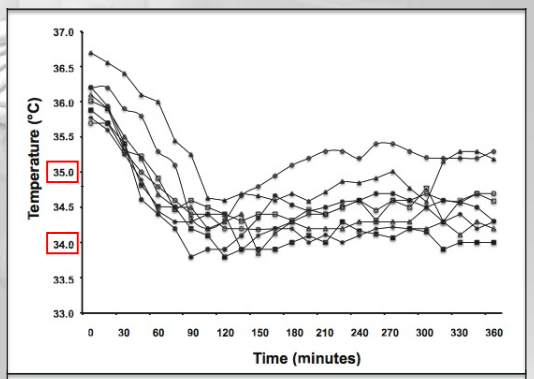
Result

Esophageal Temperature

- A target of 32 to 34ºC was only reached in 6 of the 16 participating subjects
  - Decreased to minimal temperature of 34.4˚C
  - Decreased to 34.7˚C after 6 hours of cooling
- Decreased from baseline median 36.2˚C to 35˚C within a median time of 53 minutes
  - Median cooling rate of 1.1˚C/hr
  - No correlation between BMI and cooling rate



Individual subjects not receiving magnesium



Individual subjects receiving magnesium

Magnesium Sulfate

	Receiving MgSO4	Not Receiving MgSO4	P value
Time to achieve 35° C	48 mins 38 to 93 mins	67 mins 44 to 102 mins	0.13
Minimal temperature reached	34.2 ° C 33.7 to 34.4 ° C	34.4 ° C 33.9 to 34.7 ° C	0.03
Temperatures at the end of the cooling period	34.5 ° C 34.0 to 35.3 ° C	34.8 ° C 34.3 to 35.8 ° C	0.09

Additional administration of magnesium had NO influence on cooling rate

Table 1 Vital signs

	Baseline	Cooling[a]	*P*-value
Heart rate, minute^{-1}	70	49	< 0.01
MMR[b]	55 to 96	43 to 101	
Peripheral oxygen saturation, %	98	95	< 0.01
MMR[b]	93 to 100	90 to 98	
Respiratory rate, minute-1	16	10	< 0.01
MMR[b]	10 to 21	7 to 13	
Systolic blood pressure, mmHg	134	117	< 0.01
MMR[b]	113 to 149	96 to 133	
Diastolic blood pressure, mmHg	68	58	< 0.01
MMR[b]	54 to 94	37 to 67	

[a]lowest value during cooling procedure
[b]Minimum-maximum range

- NO one complained about dizziness or signs of hemo-dynamic impairment
- NO participants report uncomfortable conditions for which termination of cooling had to be considered
- NO severe skin damage was reported

Conclusions

- Cooling to body temperature below 35˚C by using **non-invasive** surface cooling is **feasible and safe** in healthy, conscious, mildly sedated volunteers.
- Further studies are needed to investigate
  - Altered cooling protocol to achieve temperatures below 35˚C
  - The use of surface cooling pads in patients with stroke or AMI

Discussion (1)

- Patients with stroke or AMI are **awake**
  - DO NOT present in a status that necessitates intubation and neuro-muscular blockade
- Patients with an acute stroke require serial **neurological assessments**
  - Making sedation or anesthesia a contraindication
- Awake subjects have a more evident **counter-regulatory response** against cooling efforts, as compared with sedated and paralyzed patients after cardiac arrest

Discussion (2)

- **Meperidine and Buspirone** were chosen because of their previously described effects on thermoregulation in human beings
  - The efficacy of suppressing shivering have been well described
- **MgSO4** did NOT markedly improve the cooling rate or comfort
  - Might aid to achieve and maintain lower temperatures for a longer time period


Thank You Very Much!