Case report

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Management of hemorrhagic shock with severe brain hypoperfusion: Application of targeted temperature management

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Abstract

***Background*: Hemorrhagic shock is one of the leading causes of death. It is attributable to half of death in the trauma setting and can be iatrogenic such as the one that happened during surgery. (1) Despite prompt management, morbidity, and mortality remain high, because of brief response time. (2)**

***Case presentation*: This is a case of 27 y.o male, admitted to the Intensive Care Unit (ICU) due to hemorrhagic shock that occurred during surgery. The patient was admitted to the ICU with a high dose of inotropes and vasopressor and showed no signs of brainstem reflexes including dilated pupils, despite lack of use of atropine intra-operatively and beyond the duration of action of muscle relaxants. He was managed with massive transfusion protocol and mechanical ventilation, combined with targeted temperature management in order to limit brain damage. Later on, he developed disseminated intravascular coagulation (DIC), which was managed accordingly.**

***Conclusion*: Aggressive management is required in hemorrhagic shock. In cases where the patient exhibits signs of severe brain perfusion impairment, targeted temperature management might be a feasible strategy despite its controversy as part of the triad of death.**

Key words: Hemorrhage, hemorrhagic shock, targeted temperature management, hypothermia, brain hypoperfusion, suspected brain death.

Introduction

Hemorrhagic shock is the second highest cause of death in trauma settings, with more than 50% of patients dying prior to hospital admission and another 25% die within 24 hours of admission. High mortality warrants search, improvement, and evaluation of protocols used in the management of hemorrhagic shock. Targeted temperature management in form of controlled hypothermia (TTM-CH) might be an option. (1)

Controlled hypothermia is controversial in bleeding patients, as hypothermia is a part of the triad of death. Other components of the triad of death include metabolic acidosis and coagulopathy. In research by Bozorgi in 2019, even one of the triads is a predictor of mortality in multiple trauma patients. (3) But TTM-CH might help in tissue protection. A decrease in body temperature decreases metabolic rate, oxygen consumption, apoptotic pathway, and inflammation. (4)

Case report

A 27-year-old male was admitted to the Intensive Care Unit (ICU) post exploratory laparotomy to remove a progressively enlarging abdominal mass. Prior to surgery, the patient was classified as American Society of Anesthesiologists (ASA) II with anemia (hemoglobin level 10.5 g/dl). There was no prior history of neurologic anomalies or coagulopathy. With a body weight of 55 kg and an ideal body weight of 68 kg, the maximum allowable blood loss

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was 1213 ml with a transfusion trigger of hemoglobin 8 g/dl. During surgery, there was a total of 10.8 liters of blood loss causing hemodynamics to collapse. He was resuscitated with adequate fluid combined with vasopressors and inotropes. He was transferred to ICU intubated and supported with norepinephrine 0.3 mcg/kg BW/min, dobutamine 15 mcg/kg BW/min, and epinephrine 0.5 mcg/kg BW/min.

Initial ICU assessment revealed unstable hemodynamics with mean arterial pressure (MAP) of 54 mmHg despite support, with capillary refill time (CRT) >3 seconds, and cold extremities. The patient was unconscious (Glasgow Coma Scale [GCS] 3) despite ample time having passed since the last dose of hypnotic sedatives and muscle relaxants. Pupils were dilated and there was no response to light. There was no history of atropine use intraoperatively. The core temperature was 33 ºC. Urinary output was maintained during surgery (100 ml/hour).

Upon admission, the patient was hooked to controlled ventilation. Invasive blood pressure and central venous and jugular blub (**Figure 1**) access was inserted. Vasopressin 0.03 IU/min was added. Initial arterial blood gas (ABG) showed that the patient was acidotic (pH 7.181) with type 4 respiratory failure (serum lactate 12.5 mmol/l). Initial central vein oxygen saturation (ScvO2) was 61.1 and jugular vein oxygen saturation (SjvO2) was 50.7 (**Table 1**). Initial hemoglobin was 6.9 g/dl and thrombocyte was 71000 cells/ul (**Table 2**). The massive transfusion protocol was started with 4 units of packed red cells (PRC), fresh frozen plasma (FFP), and thrombocyte concentrate (TC).

The patient was managed with concern for the prevention of secondary brain injury, as the patient already exhibited signs of primary brain injury due to hypoperfusion. End-tidal carbon dioxide (ETCO2) was maintained to prevent a decrease in cerebral blood flow (**Figure 2**).TTM-CH strategy was employed. The core temperature was raised to 35 ºC with a water-based warmer blanket, then maintained at 34-35 ºC. A bag of ice was placed behind the patient's neck to further reduce brain temperature. He was sedated with ketamine 2 mg/kg BW/hour IV and atracurium 30 mg/hour IV to prevent shivering. Ventilator-associated pneumonia (VAP) bundles and central line bundle was observed at all times. Ceftriaxone 2000 mg IV BID was given as infection control. Tranexamic acid 500 mg IV and vitamin K 10 mg IV TID was given as hemostatic agents.

The patient had coagulopathy with prothrombin time (PT) of 18.1 seconds, activated partial thromboplastin time (aPTT) of 50.2 seconds, and international normalized ratio (INR) of 1.79 (**Table 2**). Due to the possibility of consumptive coagulopathy, prothrombin complex concentrates with a dose of 1 ml/kg BW was given. Upon resuscitation evaluation, lactate improved to 2.4 mmol/l, ScvO2 63.7, and SjvO2 54.2 (**Table 1**). After a blood transfusion, hemodynamic was stable and support was tapered-off and discontinued on the 2nd ICU day.

Disseminated intravascular coagulation (DIC) was evaluated with a DIC score by the International Society of Thrombosis and Haemostasis. D-dimer was 1.28 ng/ml with INR of 1.79 and thrombocytopenia (71,000 cells/ul) (**Table 2**), even without fibrinogen level, the DIC score for DIC is fulfilled. Subcutaneous enoxaparin 0.4 ml BID was added to management.

On the 2nd day, there was an increase in leucocyte count (20,000 cells/ul) and an increase in procalcitonin (94.04 ug/l) (**Table 2**). Due to the nature of the illness, which originated in the abdomen, metronidazole 500 mg IV TID was added. The patient started to show improvement in the neurologic examination, the pupil was not dilated and with positive light reflex. ScvO2 was 69.6 and SjvO2 58.2. Sedation vacation was initiated and TTM-CH was discontinued. The core temperature was raised by not more than 0.2 ºC/hour. During TTM-CH, the patient blood sugar was within 110-180 mg/dl, no further intervention was given. The patient was found to be alert and followed commands and had stable vital signs (**Table 3**). He was then weaned from mechanical ventilation and was extubated on the 4th day. The patient was transferred to the ward on the 6th day due to an improvement in clinical condition and a decrease in procalcitonin level to 46.31 ug/l (**Table 2**).

Discussion

This was a case where a patient underwent hemorrhagic shock, severe enough that it caused impairment of cerebral perfusion causing loss of signs of brain function. In this kind of patient, aggressive high-quality intervention is warranted to regain homeostasis while providing attention to brain protection. The brain can be protected from secondary injury by: (5)

1. Hemodynamic stabilization and optimization
2. Management of cerebral metabolism
3. Maintenance of adequate cerebral perfusion pressure (CPP)

The main armaments in an attempt to reduce cerebral metabolic rate are pharmaceutical interventions. But it was not feasible in this case as the patient was hemodynamically unstable, since any at-

tempt to use an adequate dose of sedatives might cause hemodynamic compromise. (5) This limitation triggered an attempt to control cerebral metabolism through other means.

It was well known that hypothermia causes a noticeable decrease in cerebral metabolic rate. For each celcius decrease in core temperature, there was a 6-8% decrease in cerebral metabolic rate. This is accompanied by a reduction of free radical formation and inflammation, along with improved of organ tolerance to ischemia. Furthermore, the degree of coagulopathy correlates well with the degree of hypothermia. At a core temperature of 33-35 ^{o}C, only mild platelet dysfunction is observed. Clotting factors are not affected until the core temperature falls below 33 ^{o}C. (4) During initial ICU admission, there were no signs of active bleeding. Hence, the patient became an ideal candidate for the TTM-CH strategy. Later on, the patient was assessed with hypothermia, coagulopathy, and metabolic acidosis, a complete set of the triad of death.

A review by Moffat in 2013 stated that the triad of death must be controlled, or it will become a vicious cycle that causes death. Hemostatic agents might be added to control coagulopathy that might be associated with hypothermia. The benefit of added golden hour far outweighs the risk of bleeding. (6) In our patient, we suspected the presence of consumptive coagulopathy, hence aside from tranexamic acid and vitamin K, we added prothrombin complex concentrate. But then during a further assessment, we found that the cause of coagulopathy was excessive intravascular coagulation due to DIC. So, we stopped the hemostatic agent and provided an anticoagulant instead.

Other components of the triad of death were also actively controlled. Metabolic acidosis was caused by hypoxia due to inadequate resuscitation causing the formation of lactate. Increased lactate in critically ill patients does not necessarily a bad incident since lactate is an energy substrate. A decrease in lactate after resuscitation proves that ongoing lactatemia is a compensatory condition, where cells that utilize lactate as an energy substrate receive enough supply to reduce the need to form lactate. (7)

Upon transfusion of blood components, oxygen delivery increased, and lactate production decreased. Hypothermia itself was managed actively using a water-based warmer blanket. This patient was placed under the TTM-CH strategy, which mainstay was to control hypothermia. Controlled hypothermia must be differentiated from uncontrolled hypothermia, where oxygen supply-demand mismatch took place. During TTM-CH, muscle relaxant was used to prevent shivering to control oxygen demand. (8)

Although being actively controlled, TTM-CH has its own risk. Four main risks that might happen are arrhythmia, infection, fluctuation of blood glucose, and reduced gut function. (4) During early admission, the patient was placed under clear fluid infusion via nasogastric tube (NGT) to preserve gut mucosal integrity. Enteral nutrition was started at a low dose to ensure proper tolerance. Arrhythmia and fluctuation of blood glucose were monitored by electrocardiogram (ECG), measuring serum electrolytes, and regular blood glucose monitoring. In this patient, none of the 3 risks took place.

But the patient had increased leucocyte count accompanied by increased procalcitonin level. This might be secondary to reduced immune system response to infection. During hypothermia, there was a decrease in leukocyte migration and phagocytosis and a decrease in proinflammatory cytokine synthesis. This will decrease the pro-inflammatory response, which may protect against damaging neuroinflammation, but increase the risk for infection. (4) This was managed with additional antibiotics that covered the most likely source of infection. In this patient, abdominal organs were suspected as the source of infection, hence additional antibiotics that covered anaerobe bacteria.

Conclusions

Targeted temperature management with controlled hypothermia might be an option in the management of patients with hemorrhagic shock accompanied by requirements to protect the certain organ from further deterioration. The benefit outweighs the risks, but nevertheless, close monitoring is required to prevent and manage potential complications.

Disclosure

There is no conflict of interest between the authors and the pharmaceutical or device company whose products were used in this case report.

Table 1. Blood gas analysis trend

Parameter	02 Nov 2021 (Day 0)	03 Nov 2021 (Day 1)	04 Nov 2021 (Day 2)
pH	7.181	7.484	7.38
PCO2 (mmHg)	44.5	29.8	43.5
PO2 (mmHg)	107.9	189	252.4
SaO2 (%)	96.3	99.2	97.2
HCO3 (mmol/l)	19.3	22.6	25.9
Base excess (mmol/l)	-11.8	-1	+3.0
P/F ratio (mmHg)	107.9	236.2	315.5
ScvO2 (%)	61.1	63.7	69.6
SjvO2 (%)	50.7	54.2	58.2

Legend: PCO2=partial pressure of carbon dioxide; PO2=partial pressure of oxygen; SaO2=arterial oxygen saturation; HCO3=bicarbonat; P/F ratio=the *ratio* of arterial oxygen partial pressure to fractional inspired oxygen; ScvO2=central vein oxygen saturation; SjvO2=jugular vein oxygen saturation.

Table 2. Blood laboratory trend

Parameter	02 Nov 2021 (Day 0)	03 Nov 2021 (Day 1)	04 Nov 2021 (Day 2)	08 Nov 2021 (Day 6)
Hemoglobin (g/dl)	6.9	7.8	9.2	9.8
Hematocrite (%)	21	25	29	30
White blood cell (/mm^3)	22,900	17,900	20,100	14,100
Platelet (/mm^3)	71,000	119,000	153,000	173,000
PT (seconds)	18.1	-	13.8	-
INR	1.79	-	1.36	-
aPTT (seconds)	50.2	-	29.3	-
D-dimer (ug/ml)	1.28	-	-	-
Ureum (mg/dl)	-	31	-	71
Creatinine (mg/dl)	-	0.69	-	1.21
SGOT (U/l)	-	243	-	153
SGPT (U/l)	-	163	-	104
Total bilirubin (mg/dl)	-	0.94	-	-
Procalcitonin (ug/l)	-	-	94.04	46.31
Na (mmol/l)	-	148	139	-
K (mmol/l)	-	4.3	4.5	-
Cl (mmol/l)	-	104	112	-
Lactate (mmol/l)	12.5	2.4	1,7	-
Albumin (g/dl)		2.1	2.7	-
Blood sugar (mg/dl)	126	111	115	110

Legend: PT=prothrombin time; INR=international normalized ratio; aPTT=activated partial thromboplastin time; SGOT=serum glutamic oxaloacetic transaminase; SGPT=serum glutamic pyruvic transaminase; Na=natrium; K=kalium; Cl=chloride.

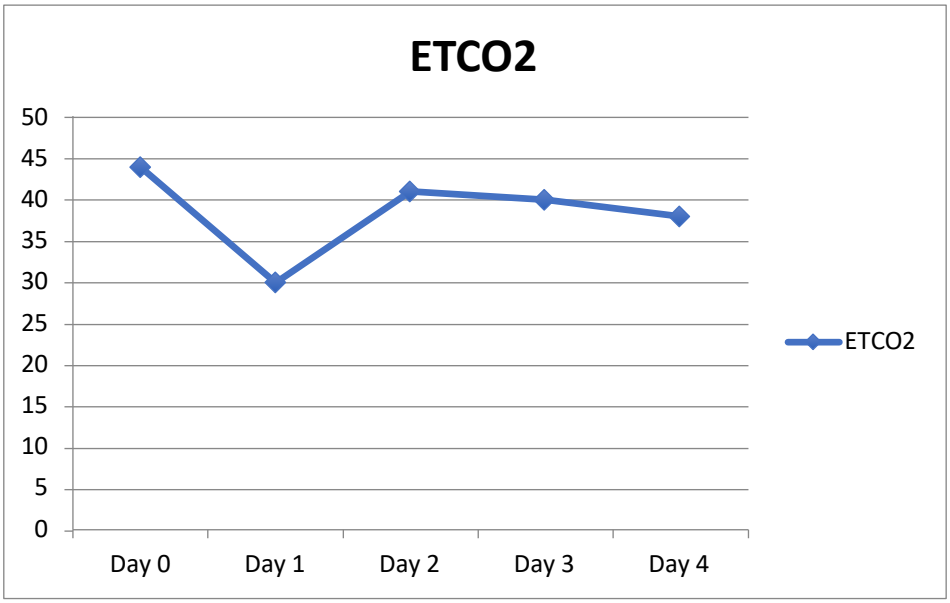
Table 3. Vital signs, central venous pressure, and urine production

Day	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	HR (bpm)	CVP (mmHg)	Urine (ml/hour)
0	80-100	30-60	50-68	125-140	2-8	20-30
1	95-110	50-60	65-72	110-120	6-8	30-40
2	95-110	55-70	65-80	100-115	6-8	40-60
3	100-130	65-85	65-104	75-95	4-6	30-50
4	105-130	65-85	65-104	70-85	3-5	60-70
5	100-130	65-85	65-105	70-85	3-5	60-100
6	100-130	65-85	65-105	70-85	2-4	150-200

Legend: SBP=systolic blood pressure; DBP=diastolic blood pressure; MAP=mean arterial pressure; HR=heart rate; CVP=central venous pressure.

Figure 1. Catheter tip confirmation at jugular blub

Figure 2. The trend of ETCO2 during ICU admission



Legend: ETCO2=end-tidal carbon dioxide; ICU=intensive care unit.

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