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REVIEW ARTICLE

Hypothermia in trauma

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ABSTRACT

The number of polytrauma patients in high energy accidents brought to trauma centers is increasing day by day. For their management we require a multidisciplinary team capable of performing lifesaving maneuvers following the sequence of resuscitation protocols. The physiological response in a patient with trauma is usually hypovolemic shock. The compensatory mechanisms are activated to improve redistribution of the flow and maintain systemic vascular resistance. During the transitional period rational and goal-directed fluid therapy and prevention of inadequate tissue perfusion and impaired metabolic exchange at the microcirculatory level take precedence.

Trauma kills by acidosis, hypothermia and coagulopathy- together called the "mortal triad"- which develop as a consequence of the metabolic changes induced by polytrauma. Hypothermia as part of the triad in the polytrauma patient is an indicator of injury severity and is associated with an increase in mortality. In the case of trauma patients, the presence of hypothermia is related to inability of the body systems to maintain temperature in the face of increased heat loss, decreased production and/or alterations in thermoregulation. The hemodynamic response to the decrease in temperature begins with peripheral vasoconstriction, myocardial dysfunction and electrical instability develops as a consequence of the metabolic changes induced by polytrauma.

The complications of hypothermia include activation of the coagulation cascade, triggering of acidosis, endothelial dysfunction, inflammatory cascade activation, consumption coagulopathy, hypoxia, cell death, multiple organ dysfunction etc. This review highlights the main aspects of the pathophysiological derangements occurring as a result of trauma.

Key words: Trauma; Polytrauma; Hypothermia; Thermoregulation; Shock, hypovolemic; Resuscitation

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INTRODUCTION

Hypothermia in the patient with trauma must be differentiated from accidental or exposure hypothermia and that induced for therapeutic purposes. Hypothermia may increase the susceptibility of patients to infection in the surgical wound by peripheral vasoconstriction and impaired immunity. Vasoconstriction reduces the partial pressure of oxygen in the tissues. There is a decrease in microbial death, because the production of oxygen radicals is dependent on tissue oxygen tension. Mild hypothermia may alter immune response mechanisms such as chemotaxis, granulocyte phagocytosis, macrophage motility, and the production of anticonvulsants.

At the time of trauma, in the golden hour and during all phases of resuscitation, there are several factors that contribute to the production of hypothermia;

including exposure, hypovolemia, hypoperfusion and aggressive administration of intravenous fluids.[1] To correct the lethal triad, the goals of resuscitation in the traumatized patient continue to be the subject of ongoing debate and there is no universal consensus at present; however, the delay in initiating resuscitation goals correlates with the increase in complications. Anesthesiologist must consider these factors in a polytrauma patient during damage control surgery (DCS). All these measures of resuscitation are time dependent and together mean series of simple procedures intended for physiological and hemodynamic stabilization of the polytrauma patient as urgently as possible. Those surgical lesions that threaten the life are addressed, leaving the definitive repair for a latter day. If the triad of death: hypothermia, acidosis and coagulopathy are not corrected in a timely manner, the surgical control of bleeding alone will not succeed.[2]

It is important to know the pathophysiology of trauma, as it allows us to quickly identify the patients in a state of hemorrhagic shock so that a rapid control of the source of hemorrhage and resuscitation can be achieved. It also helps to take into account the appropriate anesthetic decisions, their clinical management and the numerous controversies regarding the management of resuscitation goals.[3]

Goal-directed resuscitation in the trauma patient includes use of intravenous fluid and blood derivatives, as well as ventilatory strategies to correct the death triad. This resuscitation should be timely and efficient, in order to maintain an adequate balance between the delivery, transport and consumption of oxygen, and correction of hypoperfusion state.[4] Inadequate blood and blood products transfusion therapy directly affects blood pressure and an inadequate perfusion pressure in the microcirculation.[5]

The physiological response to the presence of hypovolemic state resulting from a decrease in the effective circulating volume is triggered. Compensatory mechanisms are activated, including the metabolic response to trauma to compensate for blood volume. The measurement of lactic acid or base difference allows us to control the evolution of the state of hemorrhagic shock. The availability of O_2,[4,5] which is equal to the product of minute volume by the arterial oxygen concentration, cannot be maintained for a long time and ultimately it leads to acidosis and cell death by hypoxia. Organs affected by hypoxia differ in their response to the hypoxia; out of all tissues heart, lung and brain can only sustain for 4 to 6 min. Abdominal organs tolerate between 45 and 90 min and skin and muscle tissue from 4 to 6 hours.[6] There is an increase in systemic vascular resistance to maintain blood pressure, causing a redistribution of the flow to vital organs (brain, kidney, heart) and an increase in sympathetic activity and cardiac contractility with decreased vagal activity.[7] So the blood pressure is maintained by increased vascular resistance and cardiac output. It is a cyclical process that causes insufficient supply and inadequate distribution of oxygen, causing serious alterations that produces the state of microcirculation insufficiency.[8] Decreased blood volume as a result of acute hemorrhage can produce shock due to decreased preload. At least 30% loss of intravascular volume is required to cause it. Massive hemorrhage results when the blood loss is greater than 40% of the total volume. It is due to major vascular injury or massive intra-abdominal visceral bleed.

PHASES OF HEMORRHAGIC SHOCK

Phase I: Vasoconstriction or ischemic anoxia due to arteriolar narrowing (both pre and postcapillary sphincter closure) and opening of arteriovenous shunt, which causes reduction of capillary hydrostatic pressure.

Phase II: Cell metabolism passes from aerobic to anaerobic type, with accumulation of lactic acid and potassium in the interstitial space.

Phase III: The decrease in the pH and increased blood viscosity favors intravascular coagulation with consumption of coagulation factors and release of lytic enzymes leading to autolysis.

Phase IV: Irreversible shock and secretion of fibrinolysins leading to necrosis with multiorgan failure in relation to the extension of the process.[9]

A few years back Benjamin Trump described a model of ischemia / anoxia that once triggered the events secondary to tissue ischemia will take place seven stages; the first three stages are reversible and, after a transition stage, the last three become irreversible and accelerate death of the cells. The hypoperfusion results into a decrease in ATP synthesis with increase in ADP/ATP; therefore there is activation of anaerobic glycolysis with decreased pH, presenting a deficient sodium pump activity producing mitochondrial edema, increased permeability of the cell membrane and calcium influx. This ion invades mitochondria and forms deposits of calcium phosphate, lysosomes increase inside with destruction of cellular structures. The deterioration is progressive and the process ends in stages V, VI and VII that

consolidate cell death.[10]

There are several blood tests that can detect hypoxia, e.g. arterial blood gas (lactate, pH, DO_2 / VO_2, SvO_2, delta PCO_2). These are very useful in various conditions of the polytrauma patient but fail to detect regional hypoxia, which requires other indices. For example gastric tonometry, regional blood flow measurements, polarographic oxygen electrodes, infrared spectrometry, NMR spectroscopy and positron emission tomography. The resuscitation of the patient in a state of shock must be sufficiently effective to restore VO_2 in the shortest possible time.[9,10]

For the aforementioned, we must take into account that blood pressure and heart rate in patients with trauma are not adequate indicators of shock. Some patients with trauma may have a "compensated shock" state. Here the blood pressure or heart rate figures are within normal limits, however, the patient's tissue perfusion is low.[11]

HYPOTHERMIA ... A COLD REALITY

The fatal triad: Acidosis, hypothermia and coagulopathy (which some authors postulate as "Lethal Pentad" including hypoxia and hyperglycemia). It is associated with a higher mortality regardless of the type of trauma.

The presence of hypothermia results from the reduction of oxygen available at the tissue level secondary to hypoperfusion as well as the exhaustion of the systems to maintain the temperature. Hypothermia is a cause of platelet dysfunction through a depression of thromboxane B2-dependent temperature production and altered enzyme kinetics [12]. It slows the onset and propagation of platelet aggregation, inhibits several enzymes involved in both the intrinsic and extrinsic pathways of the coagulation cascade, and elevates prothrombin time as the partial time of thromboplastin at the cascade level of coagulation (extrinsic). The damaged cerebral endothelium activates the platelets and the intrinsic pathway of the coagulation cascade causing vascular thrombosis, with the consequent depletion of platelets, fibrinogen and other factors of coagulation.

In the polytrauma patient, from the moment of the accident and during the different phases of resuscitation, there are different risk factors that favor the development of hypothermia. It is worsened by exposure and the replacement of previously unheated fluids and blood products. This creates an unsustainable situation for the body and ultimately causes the death of the patient traumatized by refractory hemorrhagic shock.[14]

Hypothermia is defined as a body temperature below 35 ?C (95 ?F)

Light: Temperature is between 32 and 35 ?C

Moderate: Between 30 and 32 ?C

Grave: Temperature is below 30 ?C

This classification had been initially designed for individuals who had an accidental exposure to the cold, for example freezing.

CLASSIFICATION OF HYPOTHERMIA IN PATIENT WITH TRAUMA

This classification was redesigned in 2008, in the eighth edition of the Advanced Trauma Life Support (ATLS). It set temperature at 36 ?C.for patients with hemorrhagic shock due to increased heat loss secondary to tissue hypoperfusion and decreased oxygen exchange and the progressive loss of heat production secondary to hypovolemic shock. 15

Classification

Light: 36-34 ?C.

Moderate: 34-32 ?C.

Severe: Below 32 ?C.

Severe < 28 ?C.

Degree IV: Tª between 28 and 24 ?C.

Degree V: Tª between 24 and 15 ?C.

Grade VI: Tª below 15 ?C.

In the acute phase of cooling, the increase in metabolic activity increases the heat generated by the shivering mechanism is the body's most important mechanism for generating heat (thermogenesis).[16]

The loss of heat is produced by 4 mechanisms: radiation, evaporation, conduction and convection. Radiation, consisting of the transfer of heat between two surfaces with different temperatures without contact between them, represents 50-70% of the heat losses in the awake patient. The exposure of the traumatized patient to temperatures lower than the corporal favors the decrease of the temperature by this mechanism. Evaporative heat loss occurs on the skin, respiratory tract and exposed thoracic or abdominal viscera[17].

The rate of thermal change in the viscera is proportional to the bloodstream and the caloric loss is

direct by thermal conduction of organs located more than five centimeters from the skin. The loss of heat from the deep organs is through bloodstream, a loss of 12-16 kcal / hour, although it can reach 160-400 kcal / h with direct and linear relationship between body temperature and oxygen consumption. [15,16]

This amount of heat lost by conduction is in direct relation to the contact surface. This mechanism increases by airflow (convection), and there is loss of heat by exposure of the patient at low temperatures both in the prehospital and hospital phase. Such as the use of solutions for the preparation of the skin or the massive restitution of liquids, blood and derivatives of fluids and blood products.[17]

At the beginning, as a compensatory mechanism response to hypothermia, there is a metabolic response to trauma where the autonomic-adrenal axis releases catecholamines. This causes an increase in vascular resistance due to the release of epinephrine and norepinephrine, increasing vascular resistance with fluid sequestration at the precapillary sphincter closure, water and sodium retention. Dependence on oxygen consumption requiring greater contribution, generates tissue oxygen flow characterized by hyperglycemia, proteolysis and gluconeogenesis. Increases in the basal metabolic rate, therefore, causes chills. Later the response is inhibited with temperatures lower than 31 ?C and a state of complete poquiletry is reached[18]. The expression of the vascular space before the trauma in Phase II the need for cellular oxygen determines the opening of the capillaries, this lowers circulating blood leading to a decrease of the central venous pressure and therefore decrease of cardiac output. Cellular metabolism goes from aerobic to anaerobic; starting the accumulation of lactic acid and potassium in the interstitial space. The resulting prolongation of electrical activity and increased systemic vascular resistance ultimately produces arrhythmias.[19] In 2004 Parkinson EJ et al. describe Biological zero, which is 'the cessation of the functional activity of an organ according to body temperature'.[16,20]

SYSTEMIC EFFECTS

Hypothermia has gradually worsening effects as the body temperature is lowered down from the normal range.

34 ?C: Reduces factor activity by 10% for each degree that decreases the temperature.

32 ?C: Inhibits the interaction between von Willebrand factor and platelet glycoprotein.

30 ?C: The production of thromboxane decreases.

30 ?C: Platelets are the most susceptible to the decrease of body temperature with absence of adhesiveness.

28 ?C: Factor VII retains its activity by only 50%.

26 ?C: Adrenals cease their activity.

25 ?C: Respiratory function slows.

25 ?C: Loss of photomotor and osteotendinous reflexes.

24 ?C: Pontine-bulbar system suspends its activity.

18 to 20 ?C: Electrical silence on the EEG.

20 ?C: Medullary level

19 ?C: Glomerular filtration and intestinal absorption are lost.

15 and 16 ?C: Cardiac activity stops.

There is a decrease in oxygen consumption by 6% for each degree drop in temperature.[16,21]

There are numerous systemic effects of hypothermia.

1. Metabolic

Hypothermia causes impairment of systemic vascular resistance due to the release of catecholamines, vasopressin and angiotensin II. This lowers the organic perfusion that can progress to a potentially irreversible state of shock and death is the end result. There is increased metabolic and muscle activity during mild to moderate hypothermia.[21] Consistent cellular hypoxia leads to anaerobic metabolism, resulting in increased production of lactic acid leading to metabolic acidosis and reduced adenosine triphosphate production. ATP depletion reduces the substrate for energy-dependent metabolic processes and results in dysfunction of the cell membrane.[22] The release of lysosomal enzymes may also contribute to membrane damage and proteolysis.

Decreases in temperature induce a decrease in basal metabolism to which some authors have attributed a protective role.[23]

Increased muscle activity with tremor results in increased oxygen consumption with progressive development of anaerobic metabolism and acidosis, altering the metabolism of various drugs. The effect of benzodiazepines and neuromuscular blockers is prolonged up to 50%. The presence of hyperglycemia, common in trauma patients, increases during hypothermia as insulin production decreases and peripheral resistance increases.[24]

2. Cardiovascular

Loss of blood results in a decrease in circulating blood volume and reduces systemic venous pressure and cardiac filling, decrease in venous return (preload) and primary cardiac dysfunction.[9,12,25]

There is a reduction in vagal tone and a reinforcement of the sympathetic tone that causes tachycardia and a positive inotropic effect on the atrial and ventricular myocardium, resulting in a decrease in cardiac output and expense, increased systemic vascular resistance and irreversible left ventricular dysfunction. The hypovolemic and hypothermic patient is very irritable and there is increased susceptibility to atrial or ventricular fibrillation. At temperatures below 25 ?C asystole occurs.[9,12,26]

At 35 ?C myocardial excitability is modified, causing an autonomic imbalance. Suppression of the parasympathetic and activation of the sympathetic nervous system is common[9]. There is a risk of atrial fibrillation, atrioventricular block, prolongation and alteration of PR, QRS and QT.

The Osborn J-wave deflection at the junction of the QRS complex with the ST segment occurs in 80% of the hypothermic and hypovolemic patients. However, it is not considered a pathognomonic finding. There are also abnormalities in repolarization with changes in the ST segment and in the T wave.[27]

3. Renal Function

Hypothermia has been shown to cause renal vasoconstriction and decreased renal blood flow. The decrease in temperature causes an increase in diuresis by altering the enzymatic activity in the distal tubule with decreased sodium and water reabsorption, activation of the atrial natriuretic peptide and decreased antidiuretic hormone and its "cold-induced diuresis" receptors. Later, thrombosis can occur in the glomerulus, with oliguria manifesting in a renal compromise. Hypothermia alters local vasoregulatory mechanisms, which normally act to maintain tissue perfusion, by provoking tubular ischemia, cytokine damage and free radical release. There is decreased glomerular filtration rate and worsening sodium absorption altering blood pressure by altering vascular smooth muscle tone.[28]

Cortical renal perfusion decreases while medullary perfusion increases; this alteration results in a decrease in glomerular filtration. Prolonged hypoperfusion usually leads to acute renal insufficiency. As for electrolyte balance, hypothermia produces an intracellular potassium ions shift that can lead to hyperkalemia with overheating if this shift is not taken into account in potassium replacement.[29] With rapid correction of blood volume and hypothermia, renal perfusion is increased.

4. Pulmonary Function

The pulmonary response to shock is found in 1 to 2% of these patients who had a normal previous lung and is characterized by acute respiratory insufficiency. It is called 'shock lung' and 'post-traumatic wet lung'. Changes in lung function are common in shock ranging from compensatory changes in response to metabolic acidosis to a respiratory failure called Respiratory distress syndrome (non-cardiogenic pulmonary edema). Hypothermia causes deviation of the hemoglobin dissociation curve by oxygen and consequently tissue hypoxia. Hypoventilation causes suppression of the cough reflex and mucociliary reflex. Thereby predisposing to the development of atelectasis and pneumonia, leading to hypoxemia, hypoperfusion and tissue hypoxia.[29,30]

For every degree centigrade decrease in the temperature, oxygen consumption drops by 5% -15%. There is preservation of acid-base balance in mild and moderate hypothermia, but in severe hypothermia the metabolism becomes anaerobic, with intracellular accumulation of lactate and metabolic acidosis. There is central nervous system depression predisposing to respiratory acidosis and alveolar hypoventilation. Increased filling pressure in the left ventricle leads to increase in pulmonary capillary permeability. The resulting leakage of proteinaceous fluid from the intravascular space to the alveolar interstitium causes alveolocapillary damage. Temperatures below 28 ◯C cause congestion and pulmonary edema and produce a clinical picture of sodium and water in an attempt to restore blood volume. As for CO_2, there is a 5% decrease in its production for each degree of decrease in temperature, $PaCO_2$ in blood gas measurements must be corrected according to temperature since hypothermia increases the solubility of CO_2.[30,31]

The effects of hypothermia on the inflammatory response are decreased and there is production of an immunosuppressive anti-inflammatory profile, which favors the presentation of infectious complications.[31]

There are some theories regarding the behavior of the Microcirculatory and Mitochondrial Distress Syndrome (SDMM). This entity may appear in the course of systemic inflammatory response syndrome (SIRS) and the fundamental thing in it is the presence of tissue hypoxia that persists despite the normalization of the variables of the macrocirculation

(cardiac output, arterial oxygenation, hematocrit value, saturation of hemoglobin, etc.). Cytopathic or cytotoxic hypoxia that is not corrected by oxygen transport optimization (TO_2), is associated with a defect in oxygen utilization and an inability to produce energy in the mitochondria.[32] In the patient with trauma, there are large concentrations of cytochrome C oxidase protein in the mitochondria, mainly because of hypoperfusion, hypothermia and acidosis that precipitate the release of cytochrome C, stimulated by reperfusion of ischemic tissues, reducing transport of oxygen (50%) causing cellular ischemia in early stages of the apoptotic process triggering the production of c-reactive protein. In advanced stages there is a decoupling of the electron transport chain and alterations in the production of cytochrome C.[33]

5. Cerebral Ischemia

Cerebral blood flow decreases by 7% with each degree of decrease in body temperature causing a progressive decrease in the level of consciousness as cerebral metabolism decreases. When the mean arterial pressure is less than 50 mmHg, there is increase in cerebral blood flow as a result of reactive vasodilation. O_2 consumption is increased by elevated uptake capacity, decreased pH and increased CO_2. Marked and prolonged hypothermia and hypotension result in hypoxic encephalopathy or brain death. Patients with severe hypothermia can present in a coma with loss of ocular and deep tendon reflexes and a marked decrease in electroencephalographic recording.[34,35]

6. Gastrointestinal

Oztürk (2009) states that the response to vasoconstriction is the development of ileus and gastric distension. Hepatic damage may occur due to apoptosis of hepatocytes probably due to hypoperfusion, ischemia and reperfusion injury.

The liver then initiates the acute phase response and decreases the production of proteins, albumin, pre-albumin, transferrin and retinol-bound protein.[37]

a. Intestinal Ischemia and Necrosis: Intestinal ischemia is produced by microthrombosis and low-flow states; increasing the proinflammatory response in the liver. Intestinal ischemia and hemorrhagic necrosis can occur if hypotension is prolonged. Depending on the severity of hypotension and hypothermia, hemorrhages of the intestinal submucosa, ileus, and rarely intestinal perforations may occur.

b. Hepatic Function: Elevation of blood glucose is common in shock, primarily due to glycogenolysis and lipolysis by sympathetic stimulation. Liver function is often affected by prolonged hypothermia. The reduced blood supply leads to ischemia, metabolic dysfunction and hepatocellular necrosis.

Hepatic dysfunction in a patient with trauma may be the result of primary damage of the liver parenchyma, after severe tissue injury or shock. A systemic inflammatory response is triggered which may progress to a state of hypermetabolism. It affects liver function, limiting the ability to produce clotting factors. In the pancreas there is enzymatic hydrolysis of cellular proteins with a negative effect.[38,39]

7. Hematological

Hypothermia causes a decrease in the enzymatic activity of clotting factors, the production of thromboxane B2 and fibrinogen. There is a consequent decrease in platelet aggregation. Hypothermia causes an increase in fibrinolysis and thus promotes the formation of microthrombi and platelet aggregates. It initiates intravascular coagulation, resulting in obstruction of arterioles and capillaries. Platelet and fibrinogen consumption causes decreased platelet activity even with adequate replacement. There is increased prothrombin time and partial thromboplastin time due to platelet sequestration in the portal circulation and inhibition of numerous enzymes in both the intrinsic pathway and the extrinsic pathway of coagulation.[40]

GOALS FOR THE CONTROL OF HYPOTHERMIA

The presence of hypothermia is related to the severity of the lesion and hemorrhage. The aims of management in the patient with trauma and the control of hypothermia are early identification of hypothermia, rational restoration of intravascular volume, prevention of lethal triage, and optimization of oxygen transporters. In traumatized patients with hypothermia, there is a 17% increase in transfusions for each degree of temperature drop.[41] When the temperature drops below 30 ?C, the risk of mortality is very high. There is a relationship between the presence of the mortal triad and the severity of the lesion, which is assessed by the lesion severity index (ISS). The patients who presented the death triad have scores of 30 or more on ISS. The presence of the mortal triad was associated with a higher mortality regardless of the type of trauma. Serum lactate and pH are key factors to consider in achieving resuscitation goals. Inadequate delivery of oxygen to tissues leads to

anaerobic metabolism. The degree of anaerobiosis is proportional to the severity of the hemorrhagic shock in the traumatized patient. An effective method of monitoring the acid-base balance is by determining the arterial gases. These are modified according to the temperature: for each degree centigrade drop in temperature, the PaO_2 decreases by 7.2%, the $PaCO_2$ decreases by 4.4% and the pH increases by 0.015.[42] Body temperature below 36 ?C (96.8 ?F) requires invasive monitoring methods, including esophageal thermometer, rectal probes and urinary catheters.

a. Reheating Phase. It is necessary to ensure slow temperature increase to normal range, for tissue preservation. Reheating may be paused to avoid electrolyte disturbances resulting from the movement of fluid between the intra and extracellular compartments. As well as to reduce insulin sensitivity and the risk of hypoglycemia. It is very common that hyperthermia occurs after the reheating phase. Normothermia should be achieved to maintain normal brain tissue by decreasing the lactate/glucose, lactate/pyruvate and glycerol levels.[43]

   Use of active external reheating measures can lead to complications such as 'rewarming shock' and 'rewarming acidosis'. This occurs because of peripheral vasodilation and subsequent return of acid metabolites of distal vascular territories. For this reason active external warming should not be used in lower limbs. Blood rich in lactic acid products reaches the heart and increases the risk of ventricular arrhythmias.[42,43]

b. Passive External Reheating: This prevents and controls mild hypothermia by improving environmental conditions, by means of fields and intravenous solutions of 39 ?C to 40 ?C. Administration of thyroid hormone is controversial and reserved for patients with a strong suspicion of hypothyroidism to increase endogenous heat production.

c. Active External Reheating: In cases of severe hypothermia vasoconstriction can make it difficult to raise the central temperature. Active external reheating methods are used. They consist of applying different types of heat sources to the body surface. Hot air heaters are most effective because they maintain a continuous flow of hot air in addition to transferring heat, creating a thermo-neutral microenvironment that favors the production of endogenous heat.

d. Active Central Reheating: This is effective technique to increase the central temperature by having direct access and avoiding blockage of heat transfer by vasoconstriction.[43]

   Warming of intravenous fluids and blood products, washing of body cavities with warm liquids, heating by inhalation (through intubation and administration of hot and humid oxygen), renal replacement techniques and extracorporeal reheating techniques resulting in a reheating rate of 2.5 to 10 ?C per hour.

   Continuous arteriovenous renal replacement techniques and cardiopulmonary bypass are indicated for patients with cardiovascular instability and severe hypothermia. Cardiopulmonary bypass is contraindicated in patients with temperatures higher than 32 ?C, potassium levels of 10 mmol/lit and associated severe traumatic lesions.

e. ECMO (Extra Corporeal Membrane Oxygenation) has good results in the rewarming of patients with cardiac arrest. Because it requires a lower level of anticoagulation than the extracorporeal circulation pump, it could be a good alternative for the management of severe hypothermia in the traumatized patient.[44]

THERAPEUTIC HYPOTHERMIA

The use of hypothermia for therapeutic purposes was initially carried out on the basis of the first observational studies that attributed its beneficial effects solely to decrease of metabolism. Several studies have shown that in addition to decreasing metabolism and O_2 needs, it modulates inflammation, prevents mitochondrial dysfunction, regulates cellular apoptosis and decreases free radical production, oxidative stress and vascular permeability. It is useful in preservation of tissue and to improve survival in ischemia-reperfusion events. Its beneficial role has been established in cardiac, vascular and neurosurgery and recently it is considered of possible benefit in neonatal hypoxic encephalopathy, cardiac post-arrest and in ischemic stroke. The role in trauma is controversial. The main protective effect is to reduce brain injury and brain metabolism through multifactorial effects. The first form of its application is use as a neuroprotective measure applied prior to surgery. In second form it is used as a measure of cerebral resuscitation, when it is induced to treat already established lesions. The reduction of the cerebral temperature to 32 to 34 ?C in the zones of cerebral ischemia, provokes a neuro-protector effect and significantly diminishes residual

cerebral lesions.

The treatment is divided into four different phases:

1. The induction phase: The goal is to get the temperature below 34 ?C.
2. The maintenance phase: The objective is to strictly control the central temperature, with no or small fluctuations of maximum 0.2 and 0.5 ?C.
3. The reheating phase: Slow and controlled reheating with temperature increments of 0.1 and 0.2 ?C per hour.
4. Controlled normothermia phase: Maintenance of temperature from 36 to 37.5 ?C to avoid deleterious effects of temperature increase.[44,45,46]

Therapeutic hypothermia is currently recommended by the American Heart Association (AHA) as a neuroprotective treatment in post cardiac arrest. In theory it is indicated for the treatment of complications associated with traumatic brain injury such as intracranial hypertension (> 20 mmHg) and status epilepticus, but it is not considered as the first line of treatment for traumatic brain injury in the USA. However, it is in use in 47% of the neurotrauma centers in Japan. According to the guidelines of the Brain Trauma Foundation/American Association of Neurological Surgeons, the optional and cautious use of therapeutic hypothermia in adults with traumatic brain injury is a level III recommendation.[46] The induction of hypothermia has been considered as a cellular protection strategy to allow time for surgical repair.

Uncontrolled bleeding is the leading cause of preventable trauma mortality. Hemorrhagic shock and ischemia produce tissue injury, but it is the reperfusion of the tissues that causes oxidative stress with production of reactive O_2 species, activation of the inflammatory cascade and cell death. ?In the field of clinical research, two strategies have been proposed for the use of hypothermia in traumatic hemorrhagic shock: use of mild hypothermia in low-flow states and use of deep hypothermia in cases of cardiac arrest secondary to massive bleeding. Studies have been performed in such cases and the first clinical trial was not approved until 2011. Most evidence of the neuroprotective effects of mild to moderate therapeutic hypothermia in patients with traumatic hemorrhagic shock derives from research with animal models. Its clinical role in humans is still undefined.[46,47]

Therapeutic hypothermia can lead to various complications, including increased risk of infection, electrolyte disturbances such as hypokalemia, hyperkalemia, increased coagulation time, thrombocytopenia, neutropenia, acute renal failure, sepsis, decreased pulse rate, decreased cardiac output, hypoventilation, CNS depression, hyporeflexia or arreflexia, bradycardia, atrial fibrillation, acute pulmonary edema, ventricular fibrillation and even asystole.[48, 49] Therefore, human studies are needed to clarify its safe therapeutic effect and use.

CONCLUSION

Trauma is now an everyday reality. It has become the leading cause of death in many countries, either due to road traffic accidents or man-made conflicts and wars. Clinicians have the responsibility to attend every trauma patients and prevent his or her drift into fatal triad: acidosis, hypothermia and coagulopathy (include hypoxia and hyperglycemia to call it "Lethal Pentad"), as it is associated with a higher mortality regardless of the type of trauma. All these factors have been shown to be inter-dependent and the cycle needs to be broken for a favorable prognosis. Every available means must be utilized to maintain physiological homeostasis, while providing the medical and surgical treatment as per requirement.

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REFERENCES

1. Narang U, Narang P, Gupta O. Organophosphorus poisoning: A social calamity. J Mahatma Gandhi Inst Med Sci 2015;20:46-51 [Free full text]
2. *Chintale KN,* Sanjay V P, Sanjay S.C. Clinical profile of organophosphorus poisoning patients at rural tertiary health care centre. *Int J Adv Med. 2016;3(2):268-274* [Free full text] DOI: http://dx.doi.org/10.18203/2349-3933.ijam20161074
3. Goldfrank LR. Goldfrank's Toxicologic Emergencies. 7th ed. New York: McGraw Hill, 2002;1346-1360.
   World Health Organization. WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2000- 2001. WHO/PCS/01.4. Geneva: World Health Organization, 2001. [Free full text]
4. Altintop L, Aygun D, Sahin H, Doganay Z, Guven H, Bek Y, et al. In acute organophosphate poisoning the efficacy of hemoperfusion on clinical status and mortality. J Intensive Care Med 2005;20:346-350. [PubMed] [Free full text]
5. Okonek S. Probable progress in the therapy of organophosphate poisoning: extracoporeal hemodialysis and hemoperfusion. ArchToxicol 1976;35:221-227. [PubMed]
6. Karalliedde L, Senanayake N. Acute organophosphorus poisoning in Sri Lanka. Forensic Sci Int. 1988;36:97–100. [PubMed] [Free full text] DOI: http://dx.doi.org/10.1016/0379-0738(88)90220-4
7. Kamenczak A, Jasi?ska-Kolawa K, Targosz D, Szkolnicka B, Sancewicz-Pach K. Acute pesticides poisoning in the Krakow Department of Clinical Toxicology in 1986-1995. Przegl Lek. 1997;54:671–6. [PubMed]
8. Stefanos NK, David CC. Acute chemical emergencies. New Eng J Med. 2004;350:800–8. [PubMed]
9. du Toit PW, Muller FO, VanTonder WM, Ungerer MJ. Experience with intensive care management of organophosphate insecticide poisoning. S Afr Med J. 1998;60:227–9. [PubMed]
10. Srinivas R, Venkateswarlu V, Surender T, Eddleston M, Nick AB. Pesticide poisoning in south India: Opportunities for prevention and improved medical management. Trop Med Inter Health. 2005;10:581–8. [PubMed] [Free full text]
11. Safdar A, Saeed A, Muhammad NR. Organophosphorus poisoning: Emergency management in intensive care unit. Prof. 2003;10:308–14.
    Ahmed SM, Das B, Nadeem A, Samal RK. Survival pattern in patients with acute organophosphate poisoning on mechanical ventilation: A retrospective intensive care unit-based study in a tertiary care teaching hospital. *Indian J Anaesth* 2014;58(1):11-17. [PubMed] [Free full text] doi: 10.4103/0019-5049.126780.
12. Muley A, Shah C, Lakhani J, Bapna M, Mehta J. To identify morbidity and mortality predictors in acute organophosphate poisoning. *Indian J Crit Care Med* 2014;18(5):297-300. [PubMed] [Free full text] doi: 10.4103/0972-5229.132488.
13. Aygun D, Doganay Z, Altintop L, Guven H, Onar M, Deniz T, et al. Serum acetylcholinesterase and prognosis of acute organophosphate poisoning. J Toxicol Clin Toxicol 2002;40:903–10. [PubMed]
14. Singh J, Kapoor D, Singh M, Anand LK. Plasma cholinesterase levels in acute organophosphorus poisoning: a plausible marker for weaning? Anaesth Pain & Intensive Care 2016;20(4):477-479 [Free full text]
15. Hiremath P, Rangappa P, Jacob I, Rao K. Pseudocholinesterase as a predictor of mortality and morbidity in organophosphorus poisoning. *Indian J Crit Care Med* 2016;20(10):601-604. [PubMed] [Free full text]
16. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. *Lancet* 2008;371(9612):597-607. [PubMed] [Free full text]