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Research Article

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The Effects of Intraoperative Hypothermia Review of the Molecular Mechanisms of Action in Therapeutic Hypothermia

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Introduction

During surgery the patient may lose heat during and after surgery through the contribution of several factors: ambient temperature, cold fluid infusion, the position on the operating table, surgical skin preparation methods, type of surgery, conventional surgery or laparoscopy, and the loss increase of the heat by opening the serous cavities, thoracic or abdominal [1]. They add other factors, depending on patients: the elderly are more prone to heat loss, sex; women lose less heat, the existence of associated diseases, as peripheral vascular diseases, endocrine diseases, cachexia, physical constitution or presence of pregnancy. Temperature of the patient's body lowers in relation to prolonged patient stay in a cool room of resuscitation. The heat loss of the skin tissue in the operating room is important and is expressed at approximately 100 W [2]. More important than the relationship between temperature of the operating room and patient's skin, the microclimate, which is established between operators fields and patient. Another important factor is body surface area exposed having significant area reported at weight. Hypothermia is aggravated by cold fluid administration, abdominal or thoracic wounds. The use of cold solutions in urologic surgery exposes the central temperature drop, which is more marked if intervention is performed under epidural anesthesia [3]. In epidural anesthesia, hypothermia is due to redistribution of heat between the center and periphery, the thighs being established to intense vasodilatation and heat loss [4, 5]. All measures taken to prevent heat loss are important for prevention of coagulation disorders. Hypothermia reduces oxygen release in half, reducing the liver's ability to metabolize citrate and lactic acid and cause arrhythmia. The existence of hypothermia in surgical patient reflects failure thermoregulatory mechanisms [1-3].

Material and Method

In the prospective study of 131 patients we tried to identify factors that induce the patient's body temperature drops during surgical intervention from considered normal to temperature 36.6 0C ± 0.38 0C. For measuring the temperature of the operating room, and in different areas of the patient's body, the temperature of fluids infused, the peritoneal cavity, during surgical intervention, was used remote infrared thermometer, model O1500N1, approved by Ministry of Health and which records temperatures between 1 °C and 55 °C, for any object besides uman body. The severity of physiological changes that occur as the temperature falls, classifies hypothermia in four grades: mild hypothermia between 35 °C and 32.2 °C, moderate between 32.2 °C and 28 °C, severe, between 28 °C and 20 °C, and deep, between 20 °C and 14 °C. In the prospective study of 129 patients, data were recorded in two categories of patients: 62 patients operated for abdominal surgical diseases or of the extremities and 69 hypothermic patients coming from the polytrauma group of 1456 patients. In the group of 62 patients data were followed at different surgical interventions in the peritoneal cavity: stomach (n = 5), gallbladder (n = 7), bowel (n = 2), colon (n = 7), appendix (n = 2), rectum (n = 3), sigmoid volvulus (n = 2), lumbar sympathectomy (n = 2), retroperitoneal hematoma (n = 3) or the extremities: chest - mastectomy (n = 2), eventration in abdominal wall (n = 3), inguinal hernia (n = 5), arteritis (n = 7), hydrostatic varices (n = 8).

Results

Because skin temperature is different in various parts of the body surface, we recorded the temperature at the forehead, the carotid region, the anterior wall of the chest, the abdomen in the umbilical region, in inguinal regions, chest and pelvic limb in its different areas. The measurement of temperature in several places allows assessing the average skin temperature, necessary to calculate the thermic balance. The average body temperature was calculated based on core temperature (Tc) and peripheral skin temperature (Tp), in which skin temperature was calculated using the formula: T skin = 0.3 (T chest + T arm) + 0.2 (T thigh + T calf).

If is measured extremities temperature and compares two regions between them, such as forearm - fingers, is obtained a gradient proportional to the digital blood flow and it is a measure of the degree of vasoconstriction. Vasomotricity Index (IVM) is defined by the temperature of the eardrum or esophagus for core temperature (Tc), the palm side of the third phalanx of the index for extremity temperature (Te) and ambient temperature measured at the head level of the patient (Ta), ie expressed mathematically:

I.V.M. = (Te - Ta) / (Tc - Ta).

Registration forehead temperature is approximately equal to the core temperature, because this area is related to temporal artery that receives blood from the aorta by the carotid artery, blood flow being effective. On the other hand, the forehead is the only region of the cranial extremity without hair and is by the anatomic elements in direct contact with the surface of the brain. "Thermo focus" allows to record temperature at a distance of 3 cm, without being implanted. Being equipped with sophisticated microprocessor, "Thermo focus" allows comparability with oral or rectal temperature and ambient temperature. Thus, recordings made on the forehead have found differences up to 1° C between preoperative temperatures of the forehead, with the intraoperative and immediate postoperative.

Normal thermoregulation involves a dynamic balance between heat production and heat loss control, which ensures a constant central temperature. Temperature control is done by hypothalamic centers that integrate the physical and chemical processes for production or decrease in temperature. Hypothalamic centers, much like a thermostat with a reception and execution mechanisms, respond automatically to prevent positive or negative fluctuations in body temperature. The hypothalamus, in addition to the role of thermostat has thermo reception function. Central hypothalamic thermo receptors are stimulated by circulating blood changes and by feedback mechanisms maintain constant temperature. Vasomotor effector mechanisms temperature makes the skin circulation rehabilitation. Adjusting skin blood flow depends on local and systemic factors.

Exchanges of heat at extremities level, whose surface is 50% of body surface area, is covered mainly by shallow flow adaptation. In areas exposed to cold, blood supply is direct via arteriovenous anastomoses, which shorts hot arterial blood in the veins. Superficial blood flow may go from 200 ml / min. to 3ml/min and blood flow in fingers can vary from 0.5 ml / min to 120 ml / min / 100cm^3 tissue. Exposed to low ambient temperature, the body will consume oxygen reserves, then it will stabilize the core temperature, protect the central organs: brain, heart, kidneys and will sacrifice peripheral perfusion producing vasoconstriction in areas affected by cold. Harmful action of cold is facilitated by adjuvant factors, especially the sensitivity of the individual, general and local. General sensitivity can occur with abnormal responses to cold. Local action is favored by cold adjuvant factors and especially individual predisposition, explaining why, in the same thermal conditions, the answers vary from individual to individual. In conventional thermal conditions, the body loses heat by radiation (50%), convection (15%), raising the inspired air temperature to body temperature (2-3%) and urine and feces (2-3%). Conduction occurs when the body is in contact with a cold object: air covering skin, clothing, breathing air that is heated in the airways and lungs, the patient contact with the operating table. Evaporation removes heat from the skin and respiratory tract. One gram of water consumes 0.6 kcal when passes from liquid to vapor state at a temperature of 33°C in physiological conditions.

Loss of body heat occurs through physiological mechanisms at the level of skin and respiratory system. The volume of the heat lost depends on the extent of surface, respiratory system, surface humidity, air temperature and relative humidity, as well as current speed air on that surface. This explains why a fat person who has a larger area, loses a large amount of heat more than a thin person. Changes in surface temperature on the human body are made by three different physiological mechanisms:

Surface temperature is determined largely by the ease with which heat is transported from depth to the body surface. Water present in the blood, approximately 80% by volume, has a high thermal capacity. In the cutaneous circulation, the heat is usually ceded by blood. The total amount of heat from one area is conditioned on the speed of blood flow in that area. Body surface temperature varies by region, being lower in the limb than in thorax. In a room with 12°C, temperature in the nose peak is 24°C, at the menton is 28°C, 28°C on the cheeks, 21°C on chin and on the scalp, and skin under clothing is 30°C. If the temperature rises to 28°C, the temperature of clothes increases from 19°C at 26°C, and the skin under clothes at 33°C. Between central and peripheral temperature there is a temperature gradient of 2° – 4°C due to vasoconstriction in the peripheral circulation imposed by sympathetic tonus with hypothalamic origin where the thermoregulatory centers are located.

Surface temperature depends on the ease with which heat is transferred by the body to environment and backward. Conduction or radiation may be delayed by interposing a thermo – insulating material. The clothes may have this role.

Surface temperature is changed by humidity of surface. In man, a quantity of water, about 50ml / h, is lost through breathing membranes or skin, because they are wet, a phenomenon known as "insensitive water loss".

The temperature loss in surgical patients occurs because of several factors, which are related to: room temperature, the patient, the patient's position on the operating table, the methods of preoperative skin preparation, the use of unheated infusion solutions, type of anesthesia, type of surgery - classic or laparoscopic, serous cavities opening - thoracic or peritoneal cavity, the use of large amounts of cold liquid washing peritoneal cavity.

General anesthesia induced endogenous determine an alteration of thermoregulatory hypothalamic centers, which can lead to a temperature difference of 0.2° - 4°C. Induction of general anesthesia will cause peripheral vasoconstriction due to sympathetic tonus of arteriolar system, with a redistribution of heat from the center where blood is warmer to the periphery, where blood is colder. In the final stages of general anesthesia, skin temperature continues to drop by ambient heat dispersion, by convection, irradiation, evaporation and conduction. Skin temperature is stabilized, the plateau phase, where it creates a dynamic balance between production and heat loss, such as during general anesthesia, skin temperature may record losses of 2.8 ± 0.5°C.

In loco regional anesthesia, central block by subarachnoid and epidural anesthesia causes a reduction in the central temperature similar with that from general anesthesia, but with a longer duration. Loco regional anesthesia determines hypothermia centrally by the hypothalamic nuclei, but has also peripheral effect by sympathetic system. As with general anesthesia, in loco regional anesthesia the essential cause is represented by the redistribution of temperature between center and periphery. The main cause is the peripheral loss by blocking nerves and ensures arteriovenous shunts tonus of the lower end of the body, so this difference may reach 2°C.

For example will consider two patients with surgery for varicose veins of the left lower limb, one operated under general anesthesia, the other under spinal anesthesia

Case 1: Male, 68 years old, 93 kg, height 174 cm, surgical intervention was under general anesthesia (duration: 9^{30}hours – 11^{10}hours)

Recorded temperature	At the start of operation	At the end of surgery
Operating room	28.7°C	29.0°C
Perfusion bag	26.8°C	26.9°C
Forehead	36.9°C	36.9°C
Precordial	35.6°C	36.0°C
Left inguinal region	36.4°C	36.6°C
Left thigh	35.5°C	35.0°C
Surgical wound	35.0°C	34.6°C
Mechanical ventilation tube	32.0°C	32.8°C

Case 2: Male, 58 years, 76 kg, height 170 cm, under spinal anesthesia, surgery (duration: 10^{05} – 12^{10}), crossectomy with left safenectomy

Recorded temperature	At the beginning of the operation	At the end of surgery
Operating room	25.4°C	25.8°C
Perfusion bag	24.7°C	24.7°C
Forehead	36.1°C	36.3°C
Left inguinal region	37.5°C	37.7°C
Right inguinal region	37.7°C	37.9°C
Lower third of left leg	35.5°C	35.9°C
Lower third of right leg	35.9°C	36.1°C
Dorsal side of left foot	35.1°C	35.6°C
Dorsal side of right foot	35.6°C	36.4°C

In patients who require abdominal surgery, peritoneal exposure is the predominant factor of heat loss. The thermic balance results from the difference between heat production and heat loss. For heat, the measurement unit is calorie (cal.) or joule (one calorie = 4.187 J). The amount of heat exchanged between two bodies per unit time is expressed in Watt (1W = 1J / sec.) or in calories per hour (1 k = 1.163 J). Basal metabolism produces an average of 80 W. So 80 W is 1652 kcal / day. Metabolism may be expressed by "oxygen consumption" (VO_2). Knowing the caloric coefficient of oxygen, which is equal to 4.485 kcal / l of oxygen to the protein, 4.686 kcal / l to the fat, by 5047 kcal / l to the carbohydrates, can make the necessary calculations.

For temperature measurement, was simulated on a computer mathematical model to calculate the heat loss during celiotomic intervention in a patient with a duodenal ulcer in hemorrhagic shock, weight 70 kg, body surface area 1.7 m2, located in operating room at a temperature of 210C, the specific heat of the human body 0.83 kcal / kg /1°C and body temperature changes every 1°C by 58kcal. Crystalloids and blood temperature was in administration, 360C. Were given 4 liters of blood and 4 liters crystalloid solutions. Bleeding control showed lower bleeding from 100ml / min. to 50 ml / min. At 70 kg patient, the peritoneal surface of 0.76 m^2 was exposed to only half, that is 0.38 m^2. The body temperature resulting from heat gained and heat lost, or expressed mathematically: body temperature = body temperature + (heat gained + calories intravenously infused liquid - heat lost). The heat gained is derived from metabolic heat, plus the heat generated by external means of heating the patient. The anesthetized patient, metabolic heat production decreases logarithmically with body temperature. Heat from external heat transfer is considered to be the water to 40°C, which has a heat transfer coefficient of 7 kcal / m^2 / hour, in a contact surface of the body, the material being heated on the operating table, the surface being 0.5 m^2 or formula:
Heat gained = (metabolic caloric production + heat brought by external heating) / 58, in which, 58 kcal occurs in the thermal balance for each change of body temperature by 1°C. Calories of intravenous fluid = (blood calories + calories of crystalloids) / 58. Heat gained by heating the inspired air is insignificant.

The patient that is operated, heat is lost from the skin by bleeding and by exposing the peritoneal cavity, which is expressed in the formula: heat lost = (skin loss + loss by bleeding + loss through peritoneal surface). During surgery the total heat loss from the skin resulting from the multiplication of constant cooling of the skin, which is 5 kcal. / h / m^2, with the difference between skin temperature and the temperature in the operating room and exposed skin area, which estimated to be half of the body surface, 0.85 m^2, which is expressed mathematically : lower skin temperature = (core temperature - 5) - surgery room temperature x skin cooling constant x exposed skin. External heating of the patient is calculated by the formula: external heating of the patient = 3.5 (43 - core temperature - 5). Heat loss by hemorrhage depends on the amount of blood lost, the difference in temperature between the body core temperature and ambient temperature and specific heat of blood, which is 0.83 kcal / m^2/ 1°C. Rate of heat loss from bleeding = bleeding rate x 0.83(core temperature – room of operation temperature). Calories lost by hemorrhage = blood volume lost x 0.83 x (blood temperature - the body core temperature). Blood and crystalloids are administered at a temperature of 36°C. Calories lost by crystalloids = crystalloids volume x (crystalloids temperature - the body's core temperature).

Heat loss from the peritoneum is by conduction, convection, radiation and evaporation and is 300 kcal / hour / m^2. From the area of 0.76 m^2 per 70 kg patient, only half, that is 0.38 m^2, are exposed during surgical exploration. Total heat loss through the peritoneum exposure is calculated by multiplying the difference between core temperature and ambient temperature, temperature of 21°C and product of peritoneal cooling constant, 42.2 kcal / hour / m2/ 1°C and exposed peritoneal surface, 0.76 m^2, or : peritoneal heat loss = (core temperature - ambient temperature) x peritoneal cooling constant x peritoneal surface exposed.

An example is the patient aged 51 years, in hemorrhagic shock by bleeding duodenal ulcer, who recorded these external and internal temperatures:

- External temperatures: operation room walls temperature = 25°C, the bag of infusion fluid temperature = 25°C; mechanical ventilation tube temperature = 31.2°C;
- The patient's body temperature on the forehead = 36°C;
- Internal temperatures determined intraoperatively:

- External wall of the stomach temperature = 36.7°C;
- Inner wall of the stomach temperature = 34.6°C;
- External face of the liver temperature = 36.0°C;
- Jejunum outer face temperature = 34.4°C.

This patient also had these biological constants during surgery: hemoglobin = 4.4 g / dl, white blood cells = 10200 / mm^3, ESR = 38mm / h, urea = 97mg / dl, glucose = 128mg / dl, sodium = 138 mmol / l, potassium = 3.4 mmol / l, chloride = 108 mmol / l, Quick time = 11.7 sec., APP = 98%, INR = 101.02, fibrinogen = 277 mg/dl, blood group: AB (IV), Rh + (positive).

Heat loss calculations shows that the peritoneum is the largest, which requires increasing ambient temperature and more rapid closure of the peritoneal cavity, in 60-90 minutes, which prevents the installation of the triad "hypothermia - acidosis-clotting". Heat loss is adding to the rapid development of coagulopathy in massive transfusion, haemodilution and hypotension. From inadequate tissue perfusion results acidosis, with negative effects on contractile function of the myocardium. In the acidic environment of the body normal clotting mechanism suffers. Triad "hypothermia-acidosis, coagulopathy" creates a vicious circle that requires its discontinuation.

Discussion

Normal temperature implies a dynamic balance between heat production and heat loss control, which ensures a constant central temperature [2]. The body temperature means the temperature of internal organs, the central environment temperature that is composed of: brain, thoracic organs and abdominal organs. These represent core temperature. Superficial levels temperature, which are forming the "central core shell", consisting of: skin, subcutaneous tissue, skeleton, muscles, chest and pelvic limbs is lower with 3°C to 5°C than the core temperature. At the extremities, the temperature is dependent on external temperature and thermal regulation mechanisms [6]. Animal warm-blooded, man possesses mechanisms to maintain body temperature unchanged against changes in ambient temperature. Maintaining a constant central temperature and a gradient between center and periphery is regulated by the hypothalamus via two processes, including thermo genesis and thermolisis. Temperature of warm-blooded beings represents the balance between heat produced in tissues and the heat produced in environment. At an ambient temperature between 28°C and 30°C to the men, and between 27°C and 33°C to the women, the body without clothes can maintain its temperature effortless, what is called "comfort zone". For recording temperature we used remote infrared thermometer. The advantages of using "Thermo focus" are: comfort, in the sense that it can be used at the patient anesthetized, measured values are displayed immediately, do not require disinfection, because the temperature is recorded at a distance of 3 cm from the area studied, therefore, without need to be introduced into the body cavity, such as esophageal probe is inserted, the probe in the pulmonary artery, tympanic probe, rectal probe or probe bladder. Other advantages of using "Thermo focus" are the possibility to scan the body temperature in different temperature zones and even internal organs during surgery, and to anything outside the human body temperature, the limit for registration is between 1°C and 55°C, thus, can measure temperature of any object in the operating room, infusion solutions, and operation room temperature. Heat loss through accidental exposure to cold induce spontaneous adaptation unable to maintain a balanced body heat or by inadequate consumption of heat, either through inefficient heat production. Heat loss is recorded and during surgery or afterwards. Numerous studies have been undertaken to assess the heat loss during major surgery (1-6). Through multiple logistic regression analysis in SPSS 10.05 system has been identified as predictive factors of intraoperative hypothermia: 2 = 15.014 + 0.097 x (age) + 0.263 x (weight) - 0.323 x (weight) - 0.055 x (preoperative systolic blood pressure) - 0.121 x (preoperative heart rate). Using this model, the probability of hypothermia is estimated by the formula: probability = 1 / 1 + e^{-2}. If is estimated that the probability of hypothermia is > 0.5, the prediction of sensitivity is 81.5% and specificity is 83% (3). Surgical interventions that promote heat loss are those that open the serous cavities, chest or abdomen, such as shown in this study. Heat loss during surgery may be accompanied by intra- or postoperative complications (7-12). Among intraoperative complications reported to be produced were recorded the followings: metabolic disorders represented by alterations in protein metabolism, impaired tissue oxygen use, alter or delay of the late absorption of metabolism of anesthesia, the curare and drugs, peripheral vasoconstriction, coagulation abnormalities, increased blood loss or biological changes due to transfusions, cardiac arrhythmia, myocardial ischemia, cardiac arrest, hyperthermia and tachycardia.

Heat loss and decreased oxygen in the postoperative period may cause myocardial ischemic injury or other nature. There has been an increased incidence of sepsis and increased production of proinflammatory factors, increased incidence of stress ulcers, deep venous thrombosis growth, the growth of blood loss, postoperative metabolic disorders, multiple organ dysfunction, prolongation of awakening after general anesthesia, extension postoperative pain, complications leading to more time spent standing in the intensive care service, extending the period of postoperative discomfort, all accompanied by rising medical costs [10-13].

Therapeutic hypothermia (TH) is one of the wonders of medicine. The use of TH in modern clinical medicine has been documented over the past 200 years. Hypothermia was widely used in ancient times [14]. TH is nowadays one of the most important methods of neuroprotection [14, 16].

Studies show that the mechanisms of hypothermia are varied. Therefore, the mechanisms and effects of hypothermia have been studied in the following situations:

Mechanisms of Action of Therapeutic Hypothermia

Understanding the mechanisms of action through which TH provides neuroprotection will allow a better understanding about the indications for this therapy, search for other therapies when used in conjunction with hypothermia will provide a therapeutic synergistic effect and the emergence of more clinical trials demonstrating the utility of this therapy in other diseases as well [15]. Hypothermia significantly reduces extracellular levels of excitatory neurotransmitters, including dopamine and glutamate. The release of these neurotransmitters is temperature dependent, and it was demonstrated that even mild levels of hypothermia exerts an inhibitory effect [16-18].

Hypothermia and Apoptosis

Two types of cell death exist: necrotic cell death and programmed cell death, also known as apoptosis. Necrosis is a form of cell death where edema and cellular inflammatory response occur, leading to sudden death. Apoptosis is caused by a connection between intracellular enzyme pathways; it is the culmination of an interaction between pro-apoptotic and ant apoptotic proteins [19]. It is a programmed intracellular process which leads to cell death. TH inhibits apoptotic neuronal death because decreases p53 protein levels in the brain, a cellular transcription factor which activates genes of apoptosis and pro-apoptotic proteins, including Bak, Bax, and PUMA [19-21]. Another pathway that also triggers the process of apoptosis is the

TNF pathway. TNF through its receptors can initiate several routes (such as caspases) and culminate in apoptosis. These receptors are the Fas ligand (FasL), Fas (CD95), the complex of TNFR1 and 2, and many others [22]. The induction of TNF apoptotic pathway has been described in TBI and is one of the most important pathways mediating neuronal apoptosis. TNF receptors can trigger apoptosis because of an activation of pro-apoptotic transcription factors such as NFkB and AP-1 [23]. There are experimental studies in where TH has demonstrated to block the TNF pathway of apoptosis, its receptors such as FasL, Fas, TNFR1, and the following events that culminate in cell death [24]. Hypothermia exerts also has a mechanism of action on one of the most important pathways in the process of apoptosis, the caspases pathway. This pathway is the point in where many of the other vias meet, caspases are the final pathway which directly "executes" the cell. There are two principal apoptotic pathways mediated by caspases: Intrinsic and Extrinsic pathway. The intrinsic pathway is known to be activated by cellular stress such as radiation, hypoxia, and substrate deprivation. When the cell is subjected to one of these stressors, the substrate MMP is formed, this substrate acts at the mitochondria allowing the release of Cytochrome C, which interacts with another substrate, the Apaf-1, eventually leading to the activation of caspases 9 and 3, culminating in cell death [25]. Other pathways and proteins cause apoptosis without directly involving the caspases, for example, a protein called apoptosis inducing factor (AIF) located in the mitochondrial membrane. When this protein is released by the mitochondria, travels to the nucleus and performs a DNA fragmentation culminating in cell death [26].

Hypothermia and Metabolism

After the cerebral blood flow decreases, metabolism turns in to anaerobic metabolism and intracellular levels of hydrogen, phosphate, and lactate increase creating intra and extracellular acidosis. In the absence of ATP, there is mitochondrial dysfunction and cell death [27]. Brain metabolism decreases in range of 5–6% or even up to 10% for every degree decrease in temperature [28]. Hypothermia can also improve brain glucose metabolism and preserves glucose reserves in the brain, so they can be used even days after brain damage.

Hypothermia, Oxidative Stress, and Inflammation

Free radicals are oxygen derived compounds [29]. Free radicals can come from arachidonic acid, nitric oxide, catecholamines, glutamate, and activation of NMDA receptors. Examples of these radicals are hydroxyl radicals (OH–), superoxide (O2–), and hydrogen peroxide [30]. Hypothermia decreases the production of inflammatory cytokines, leukotrienes, and inflammatory cells function such as macrophages [31].

Recommendations for Future Studies

Some therapies have been tested previously in experimental models. For example the combination of TH with neuronal growth factors, especially BDNF. This combination therapy has shown impressive results in animal models [32]. Among other possible combination therapies to find a synergistic therapeutic effect we can mention the use of the nanoparticle formulations to antagonize the glycine site on the NMDA receptor or glycine receptor antagonist along with TH.

Conclusions

During or after surgery the patient may loses heat, by the contribution of several factors: ambient temperature, cold fluid infusion, the position on the operating table, the methods of preoperative skin preparation, type of surgery and anesthesia. They add other factors related to patients: the elderly are more predisposed to heat loss; sex, women lose less heat; the existence of associated diseases, such as: peripheral vascular diseases, endocrine diseases, cachexia, physical constitution, pregnancy. Persistent hypothermia in surgical patient reflects failure of thermoregulatory mechanisms. Surgical interventions with the biggest losses of temperature are the ones at the peritoneum level, requiring more rapid closure of the peritoneal cavity. Heat loss during surgery may be accompanied by intra- or postoperative complications.

The mechanisms of action of TH are multiple and varied. Therapeutic hypothermia is one of the most important therapies for providing neuroprotection. The possible explanation for the benefits and the success of this therapy is probably the multiple mechanisms of action blocking the cascade of ischemia on many levels. Apoptosis programmed intracellular process which leads to cell death. The field of research of TH is very ample.

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