Imaging Evaluation of Physiological Effects during Normothermia, Hypothermia and Reheating

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Abstract - Cerebral blood flow (CBF) and PCO_2 are important and valuable physiological parameters during hypothermia. Radiographic imaging (Philips BV300) as an imaging technique can provide information about hypothermic effects. In this study, we acquired real-time radiographic images and PCO_2 values during normothermia, hypothermia and reheating in a rabbit model, in order to describe the cerebral blood flow and PCO_2 changes that occured due to temperature. Our radiographic images show that hypothermia was associated with general cerebral vasoconstriction, venoarterial shunts and PCO_2 decrease, resulting in a reduced cerebral circulation. During reheating, there was an increase in PCO_2. In conclusion, radiographic images are a valid technique to observe vascular changes in the cerebral circulation, associated with induced hypothermia.

Keywords: hypothermia, normothermia, reheating, imaging, vascular

I. Introduction

Researchers and clinicians are searching for an efficient brain protection technique in order to improve patients' outcome after surgery. In fact, several pharmacological agents in phase III trials for stroke, severe traumatic brain injury, and cardiac arrest have failed to fully protect the brain from vascular compromise. Therefore, there is a renewed interest in mild to moderate hypothermia for brain protection [1].

Hypothermia, defined as a core temperature <35°C has been used as a neuroprotective strategy treatment for several medical conditions, including, trauma, intracranial aneurysm surgery, stroke and neonatal hypoxic encephalopathy [2]. It can reduce cerebral metabolism by approximately 7% per 1°C, promotes cerebral vasoconstriction and vascular permeability and suppresses inflammatory mechanisms [2,3].

Although hypothermia protects the brain, the cerebral system is extremely vulnerable to ischemia, since it has high metabolic demands and limited energy stores. Moreover, carbon dioxide (CO_2) is considered to be one of the factors affecting cerebral blood flow during hypothermia [4].

Imaging of cerebral blood flow has also been shown to be useful, following different brain injuries, as it can help to define the cause and extent of injury, identify appropriate treatments and predict the outcome. Hence, radiographic imaging techniques, more specifically angiography, can be implemented easily in hospital centers, and are able to provide quantitative and qualitative perfusion data [5,6].

II. Methods

A. *Animals and Cooling Procedure*

Healthy New Zealand rabbits (n=10), weighing between 2,350 kg and 3,880 kg were anaesthetized with 40 mg/Kg sodium pentobarbital intravenously (i.v.) and allowed to breath spontaneously. A catheter was inserted in the right carotid artery in order to inject the contrast solution Ultravist-370 (Iopromida) at 50% (5cc) in three conditions: normothermia, hypothermia and reheating conditions.

In order to induce the state of hypothermia, the rabbits were cooled by immersion in iced water. A special bathtub with a support was designed (Institute of Physiology, Lisbon) in order to allow immersion and the adjustment of the water temperature. The animals were cooled until the rectal temperature reached 26°C (hypothermia conditions). They were then maintained at this temperature for a period of 3 h. After this period, the animals were reheated with hot water bags until the rectal temperature reached the initial value (38°C).

B. *Blood Pressure and Heart Rate measurements*

A Cournand catheter was introduced into the right femoral artery up to the thoracic aorta and connected to pressure transducers (Stahtam 5584-P23AA, Hato Rey, Puerto Rico) in order to monitor aortic blood pressure and heart rate (RM-150- Nihon Kodhen Polygraph, Tokyo, Japan) and to inject anesthetic and saline solutions.

C. *PCO_2 measurements*

For PCO_2 measurements we used ABL-2 (Acid-Base Laboratory) and three ABL controls (normal, acidic and alkaline) before the PCO_2 measurements.

D. Radiographic imaging

We used Philips BV 300 Plus C-Arm as an image intensification. We used the radiographic mode for the images acquisition during the contrast solution injection.

E. Statistical Analysis

Statistical analysis was performed with SPSS 19.0. The significance level was set at $p \leq 0.05$. The results are presented as mean ± SD.

III. RESULTS

A. Blood Pressure and Heart Rate measurements

In hypothermia conditions, there was a significant ($P< 0.01$) drop in mean aortic blood pressure from 122±3 to 51±18 mmHg. In addition, hypothermia induced bradycardia in all animals: the mean heart rate at normothermia was 139±41 beats per min and was reduced to 34±43 beats per min in hypothermic conditions ($p < 0.01$).

B. Cerebral vascular changes

Normothermic conditions. As expected, the contrast injection performed during normothermic conditions (38ºC) revealed that the perfusion territory of the right internal carotid artery was unchanged (Figure 1a).

Hypothermic conditions. In the hypothermic conditions (26ºC) there was carotid and arteriolar vasoconstriction, decreased venous return and the presence of venoarterial shunts (Figure 1b).

Reheating conditions. In reheating, it was observed the normalization of perfusion in carotid artery territory with the maintenance of peripheral vasoconstriction, decreased venous return and disappearance of venoarterial shunts (Figure 1c).

Fig.1. Cerebral angiographic images from a rabbit, during normothermic (a), hypothermic (b) and reheating conditions (c).

C. PCO_2 changes

In the left carotid artery, during hypothermia it was observed a significant increase in PCO2 values, from 45,7±6,8 (normothermia) to 76,7±21,6 (hypothermia) (68% increase, $p<0.001$). During reheating, the PCO_2 values decreased to 59,2±39,1 ($p<0.05$).

In the jugular vein, with the catheter inserted in cephalic direction, it was observed a significant increase in PCO_2 values from 53,3±8,2 (normothermia) to 64,3±17,1 (hypothermia) (21% increase, $p<0.05$) (Figure 2). In the jugular vein with the catheter inserted in the caudal direction, it was observed a significant increase in PCO_2 values from 53,3±19,4 (normothermia) to 74,2±22,4 (hypothermia) (39% increase, $p<0.001$).

III. DISCUSSION/CONCLUSION

A decrease in cerebral blood flow is a well established consequence during surgical procedures, such as cardiopulmonary bypass with extracorporeal circulation during hypothermia [7].

Using angiography as an image technique, we were able to observe changes in cerebral circulation due to hypothermia, which may be beneficial in patients with stroke or during vascular surgical procedures. Indeed, the angiographic images showed that hypothermia was associated with general cerebral vasoconstriction and venoarterial shunts appearance resulting in a diminished cerebral circulation and metabolism [8]. In addition, according to previous studies, during hypothermia all animals had hypotension and bradycardia which was reversible after reheating [9].

Furthermore, several studies showed that hypothermia affects blood gas parameters such as pH and PCO_2. This is relevant, because PCO_2 is known to affect vascular tone, therefore, cerebral perfusion [10]. During hypothermia the present results found a significant increase in PCO_2, suggesting that CO_2 production occurred due to a markedly decrease in temperature (26ºC, which increases the risk of insufficient blood flow during hypocapnia), thus protecting the central nervous system.

In conclusion, the main finding of the present study is that vascular changes in cerebral circulation, as a result of hypothermia, may be quickly and efficiently assessed by radiographic imaging.

REFERENCES

[1] Ramani, R.(2006). Hypothermia for brain protection and resuscitation. Current Op in Anesthesiology,19(5),487-491.

[2] Luscombe, M., & Andrzejowski, J. C. (2006). Clinical applications of induced hypothermia. Continuing Education in Anaesthesia, Critical Care & Pain, 6(1), 23-27.

[3] Escalda, A., Alves, N., Escalda, M., et al. (1988). Effect of induced hypothermia on the systemic circulation. *Comptes* rendus des séances de la Société de biologie et de ses filiales, 182(5), 513.

[4] Parissis, H., Hamid, U., Soo, A., & Al-Alao, B. (2011). Brief review on systematic hypothermia for the protection of central nervous system during aortic arch surgery: a double-sword tool?. Journal of cardiothoracic surgery, 6(1), 1.

[5] Soma, Y., Hirotani, T., Yozu, R., Onoguchi, K., Misumi, T., Kawada, K., & Inoue, T. (1989). A clinical study of cerebral circulation during extracorporeal circulation. The Journal of thoracic and cardiovascular surgery,97(2),187-193.

[6] Lawton, M. T., Raudzens, P. A., Zabramski, J. M., & Spetzler, R. F. (1998). Hypothermic circulatory arrest in neurovascular surgery: evolving indications and predictors of patient outcome. Neurosurgery, 43(1), 10-20.

[7] Hillier,S.C., Burrows,F.A., Bissonnette,B., & Taylor,R.H. (1991). Cerebral hemodynamics in neonates and infants undergoing cardiopulmonary bypass and profound hypothermic circulatory arrest: assessment by transcranial Doppler sonography. Anesthesia & Analgesia,72(6),723-728.

[8] Bisschops, L. L., Hoedemaekers, C. W., Simons, K. S., & van der Hoeven, J. G. (2010). Preserved metabolic coupling and cerebrovascular reactivity during mild hypothermia after cardiac arrest. Critical care medicine, 38(7), 1542-1547.

[9] Knafelj R, Radsel P, Ploj T, Noc M (2007) Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. Resuscitation 74:227–234.

[10] Groenendaal, F., De Vooght, K. M., & van Bel, F. (2009). Blood gas values during hypothermia in asphyxiated term neonates. Pediatrics, 123(1), 170-172.