Neuromonitoring

$P_{ti}O_2$

White paper

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Introduction

Multimodal monitoring has become increasingly common within intensive care and neurocritical units since, in 1866, the Dutchman Leyden outlined the technique of direct epidural measurement of intracranial pressure (ICP), followed by the underlining the importance of measuring intracranial temperature, and finally the arrival of technology capable of directly and accurately measuring in real time **brain tissue oxygen** ($P_{ti}O_2$), given that the brain is one of the organs of the body which is most sensitive to a potential reduction in oxygen..

Clinical studies have demonstrated that monitoring the oxygenation of brain tissue contributes to a better treatment of those patients identified as being at high risk of secondary brain ischemia by providing continuous information on the levels of tissue oxygenation.

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Disclaimer: the purpose of this White Paper is to be a technical guide for health professionals involved in the care of neurocritical patients. In any case, this document is not a substitute for, nor does it attempt to replace the clinical experience of a health team or the intervention protocols for the individual neurocritics in each hospital.

For more information about **NEUROVENT-PTO** catheter or **RAUMEDIC® MPR2 logO** monitor, please consult the usage instructions relating to each of the products.

1. What is $P_{ti}O_2$? Fundamental concepts

The role of $P_{ti}O_2$ in terms of the physiology of the supply/demand of oxygen in the brain continues to be the subject of debate. At a very basic level, one may say that it determines the amount of free oxygen, dissolved in brain tissue.

It is important to remember that the actual availability of O_2 in a tissue, in addition to depending on the partial pressure of O_2, depends on the haematic content of haemoglobin, on the affinity of haemoglobin to O_2, on the number of operational capillaries, on the ability to diffuse O_2 through cellular membranes, and on the characteristics of extra-cellular space[1].

The amount of brain oxygen depends on the oxygen content of arterial blood, the flow of blood in the brain, and the metabolic activity of brain tissue; these three components often change in patients with traumatic brain damage.

In order to achieve the multiparametric control of patients with brain damage that requires intracranial monitoring, the following fundamental concepts are important:

Saturation of Hb in the bulb of the internal jugular vein ($SjvO_2$)

Determine the balance between the provision of oxygen and the consumption of brain oxygen. $SjvO_2$ represents the percentage of oxygen combined with haemoglobin (oxygen saturation). The normal value is between 55 and 75%.

If $SjvO_2$ falls below 55-75%, this suggests that blood flow to the brain is not sufficiently meeting the oxygen requirements of the brain, causing the need for the brain to extract more oxygen from the blood.

An increase in $SjvO_2$ may also be important. If the brain damage becomes severe, the brain may not be able to extract oxygen, causing $SjvO_2$ to increase.

A limitation of monitoring $SjvO_2$ is that it only reflects the ability of one side of the brain to extract oxygen.

Oxygen extraction tension (Px)

This value refers to the extractable oxygen in arterial blood which may be transferred to tissues. It is influenced by the practical effects of pO_2, the concentration of effective Hb, and the affinity of Hb to O_2. It reflects the pO_2 at the end of the capillary assuming normal conditions. The extractable oxygen in arterial blood is considered to be insufficient when the Px is below 32 mmHg, potentially causing a hypoxia due to low extraction[2].

50% pressure saturation (p50)

The pO_2 at which oxygen saturates 50% of Hb defines the p50. The affinity of Hb to O_2 is considered high when the p50 is below 24 mmHg[2].

2. Why regulate $P_{ti}O_2$?

Different clinical studies have demonstrated the importance of multimodal monitoring which includes $P_{ti}O_2$ for when the control of this parameter would affect the patients' vital and functional prognosis:

Patients who have undergone multimodal monitoring, including ICP and $P_{ti}O_2$ have a greater likelihood of neurological recovery and a lower mortality.

- Patients monitored with PIC and $P_{ti}O_2$ were twice as likely to make a successful neurological recovery within 6 months, according to the Glasgow Outcome Scale scores. A 15% reduction in mortality also took place amongst these patients, compared with historical results[3].
- Patients whose multimodal monitoring included $P_{ti}O_2$, when compared with those patients monitored only through ICP control, were 70% more likely to experience neurological recovery within 3 months[4].
- Spiotta et al[5] compared a similar number of patients and discovered an almost threefold increase in the likelihood of improvement for multimodal-monitored patients, along with a significant improvement in mortality.
- Mortality rates in patients with conventional ICP monitoring and CPP control was 44%. Patients with brain tissue PO_2 monitoring ($P_{ti}O_2$) had a significantly reduced mortality rate of 25%[6].

Levels of $P_{ti}O_2$ below 15 mmHg and 10 mmHg are associated with increased mortality and poor prognostics.

- **$P_{ti}O_2$ < 10 mmHg** values for more than 30 minutes are linked to a mortality of 56% compared with a mortality of 9% present in those with higher values[7].
- The likelihood of death increases with the passing of time of tissue hypoxia with a **$P_{ti}O_2 \leq$ 15 mmHg** value[8], and with the occurrence of any PtiO2 period reading ≤ 6 mmHg[9].
- The risk of death or lasting damage increases fourfold after 6 months in patients with **$P_{ti}O_2$ <10 mmHg** at any point[10] during monitoring.
- Any period with a **$P_{ti}O_2$ < 10 mmHg** during the first 24 hours after head injury is a bad prognosis indicator[11, 12].

In the clinical field, multimodal monitoring applied to neurocritical patients has objectified $P_{ti}O_2$ as an extremely sensitive parameter whose information precedes that offered by other monitoring systems[8].

The following are the currently considered parameters:

15 mmHg threshold of light-moderate tissue hypoxia

10 mmHg threshold of serious tissue hypoxia

and **5 mmHg threshold of critical tissue hypoxia[2]**.

The therapeutic objective should be to **maintain $P_{ti}O_2$ levels above 20 mmHg**.

3. How does the NEUROVENT-PTO system work?

The configuration of the NEUROVENT-PTO catheter is shown below (**figure 1**). Taken from Huschak G. et al[13].

Figure 1

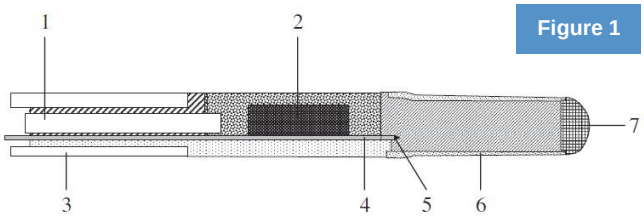


FIGURE 1. Diagram of the multiparameter neuromonitoring device Neurovent-PTO. 1: thermistor (T_{Br}); 2: pressure sensor (ICP); 3: polyurethane catheter; 4: glass fiber; 5: $p_{ti}O_2$—optical sensor spot (indicator immobilized in a solid matrix); 6: silicone tube; 7: silicone tip. ICP indicates intracranial pressure; $p_{ti}O_2$, partial pressure of brain tissue oxygen; T_{Br}, brain temperature.

NEUROVENT-PTO uses an optical method to measure $P_{ti}O_2$ (**figure 2**). The premise of measurement is based on the **effect of photodynamic extinction by the oxygen molecule.** It consists in a luminophore (L) enclosed in two separate compartments. These compartments are semipermeable to allow the diffusion of oxygen and thus enable its measurement whilst avoiding the direct contact between the luminophore and the brain tissue.

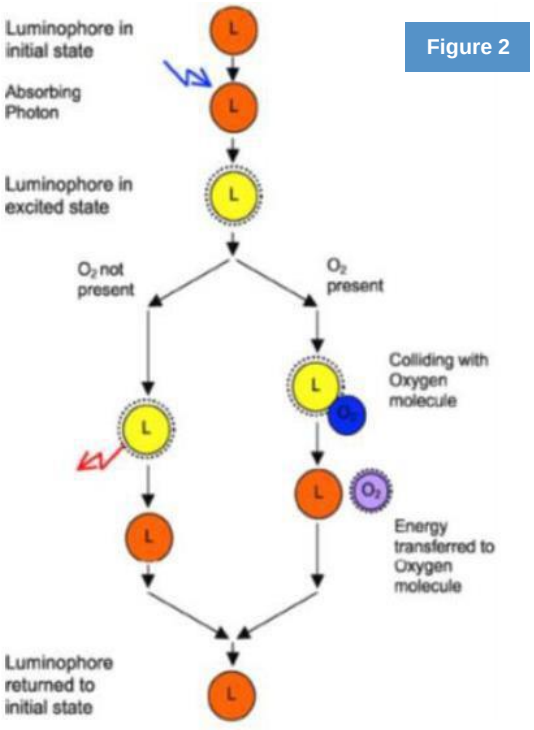
The luminophore (L) in the excited state, which contains Ruthenium, in conditions of lack of oxygen, emits a particular luminescence. In conditions with oxygen present, the collision of the luminophore (L) in an excited state and the extinguishing or reducing luminescence (oxygen) initiates a transfer of energy from the luminophore (L) to the oxygen in such a way that it removes luminescence from the former, differentiating the captured luminescence.

The relationship between the concentration of oxygen and the intensity of the luminescence according to the Stern-Volmer equation provides the concentration of tissue oxygen.

The **area of sensitivity** to oxygen in the NEUROVENT-PTO catheter is 22 mm^2. The length of the area which detects $P_{ti}O_2$ is 5.5 mm. The Licox system contains a Clarke-style element with an area of 13 mm^2 to detect oxygen (information provided by the retailer).

NEUROVENT-PTO does not require calibration before surgical insertion. The upper part of the microchip displays atmospheric or reference pressure, measured with a semi-conductor pressure sensor covered in a flexible silicon membrane.

Figure 2



This membrane is connected via a canal which links the sensor to the connector (it is not completely closed) and allows air to enter (atmospheric pressure). The pressure shapes the chip, allowing for calibration. There is, therefore, no risk of decalibration during the patient monitoring process.

The measurement of brain temperature is important given the calculation that $P_{ti}O_2$ should be corrected according to the brain temperature at the rate of 4.5% per degree centigrade[22]. It is not necessary with NEUROVENT-PTO to carry out these calibrations given that the joint $P_{ti}O_2$ and temperature measurement software makes the relevant adjustments in such a way that the results achieved are always real, considering the variations in brain temperature.

On the other hand, due to the technology used by NEUROVENT-PTO and its system of cranial positioning, with a PEEK screw, RAUMEDIC® catheters are resistant to electromagnetic changes. They are MR conditional at 1.5 T and 3.0 T.

Due to its technology and design NEUROVENT-PTO does not require cool storage and its shelf life is 2 years.

4. Indications and contraindications of use

Potential use indications[14]

According to published clinical studies on the measurement of $P_{ti}O_2$, the following potential indications exist:

- Severe brain damage
- Brain aneurysm surgery[15,16,17,18,19]
- Subarachnoid haemorrhage Hunt/Hess IV + V. Vasospasm[20,21,22,23,24]
- Arteriovenous malformation surgery[25,26,27]
- Removal of brain tumours (peritumoral area)[28,29]
- Malignant middle cerebral artery stroke[30]
- Paediatric stroke[31]
- Hepatic encephalopathy (with increased ICP)[32]

Contraindications of use

The insertion of RAUMEDIC® precision pressure catheters must be decided with particular care in cases of:

- Reye syndrome
- Bleeding disorders (coagulopathy) due to the increased risk of haemorrhages
- Use on breastfeeding children
- Sepsis, infection (particularly in the area where the catheter is inserted)
- Encephalitis
- Thrombolysis (risk of haemorrhages).

5. Where and how to place NEUROVENT-PTO?

Where to place NEUROVENT-PTO?

The location of the sensor is of vital importance for the interpretation of the measurement. There are basically two options:

A. Placement in the tissue at risk of hypoxia or in the penumbral area.

*In this case the $P_{ti}O_2$ information may be considered as a **regional indicator** but not as a global one of the human brain. Because of this, the information may be considered alongside $SjvO_2$ monitoring, which is a measure of general brain oxygenation.*

B. Placement in apparently normal areas or with diffuse injury

*In this case the $P_{ti}O_2$ information may be considered as a **global indicator of brain oxygenation** [14,33,34].*

How to place NEUROVENT-PTO?

Advice about placement to improve the prompt use of NEUROVENT-PTO:

- Use the dura opener to perforate the dura mater for 30 seconds.
- Wet the twist drill with saline to avoid blood entering the catheter during insertion.
- Wet the point of the catheter with physiological saline before insertion.
- Once introduced, rotate the catheter 15º on the longitudinal axis.

6. Types of brain tissue hypoxia

The types of **brain tissue hypoxia** (as classified by Siggaard-Andersen[35]) and adapted by Sahuquillo et al[36] and Poca et al[37] are shown in the following table (**figure 3**):

Types of brain tissue hypoxia **Figure 3**

Type of hypoxia	Cause		PtiO2 (mmHg)	P50 (mm Hg)	Px (mm Hg)
Hypoxia ischemia	↓ blood flow to brain	↓	≤ 15	24-29	N
Hypoxia through low extractability	Hypoxemia	↓	≤ 15	24-29	↓
	Anaemia	↓	≤ 15	24-29	↓
	High affinity of Hb to O2	↑	≤ 15	≤ 247	↓
Hypoxia through shunting	Arteriovenous shunts	N/↑	≤ 15	24-29	N
Hypoxia through malperfusion	Difficulties with the diffusion of O2 from Hb to the mitochondria				
		N/↑	≤ 15	24-29	N
Histotoxic hypoxia	Inhibition of mitochondrial cytochromes	N/↑	N	24-29	N
Hypoxia through uncoupling	Uncoupling between the reduction of =2 and the synthesis of ATP				
		N/↑	N	24-29	N
Hypermetabolic hypoxia	Increased metabolic needs	↓	≤ 15	24-29	N

Hb: haemoglobin. N: range of normality. P50: pressure of O2 at which Hb is 50% saturated. Px: O2 extraction pressure.

7. Advantages and limitations of $P_{ti}O_2$

The primary advantages and limitations of $P_{ti}O_2$ monitoring are as follows:

Advantages	Limitations
Easy use. **Precise measurements[38].** **Greater period of measurement with reliable results[39].** **Easy insertion and maintenance[40].** **Absence of significant complications[8,37].** **Ability to detect all types of brain tissue hypoxia (with theoretical exception of those caused by agents which block or uncouple the mitochondrial respiratory chain)[1,37].** **May increase the functional prognosis of neurocritical patients[6].**	Hyper or hypometabolism in the brain: in normal metabolic conditions, a decrease in $P_{ti}O_2$ below a certain umbral may be interpreted as cerebral hypoxia. However, under hyper or hypometabolic conditions it should be considered with care. The measurement of $P_{ti}O_2$ only monitors a small quantity of tissue. Does not detect tissue hypoxia caused by agents which block or uncouple the mitochondrial respiratory chain.

8. Intervention protocol[2]

Bearing in mind and referencing the protocol developed by the Virgen del Rocío Hospital in Seville (**figure 4**):

MARÍN CABALLOS AJ et al. MONITORING OF BRAIN TISSUE OXYGEN (PtiO2) IN CEREBRAL HYPOXIA: DIAGNOSTIC AND THERUAPEUTIC APPROACH

Figure 4

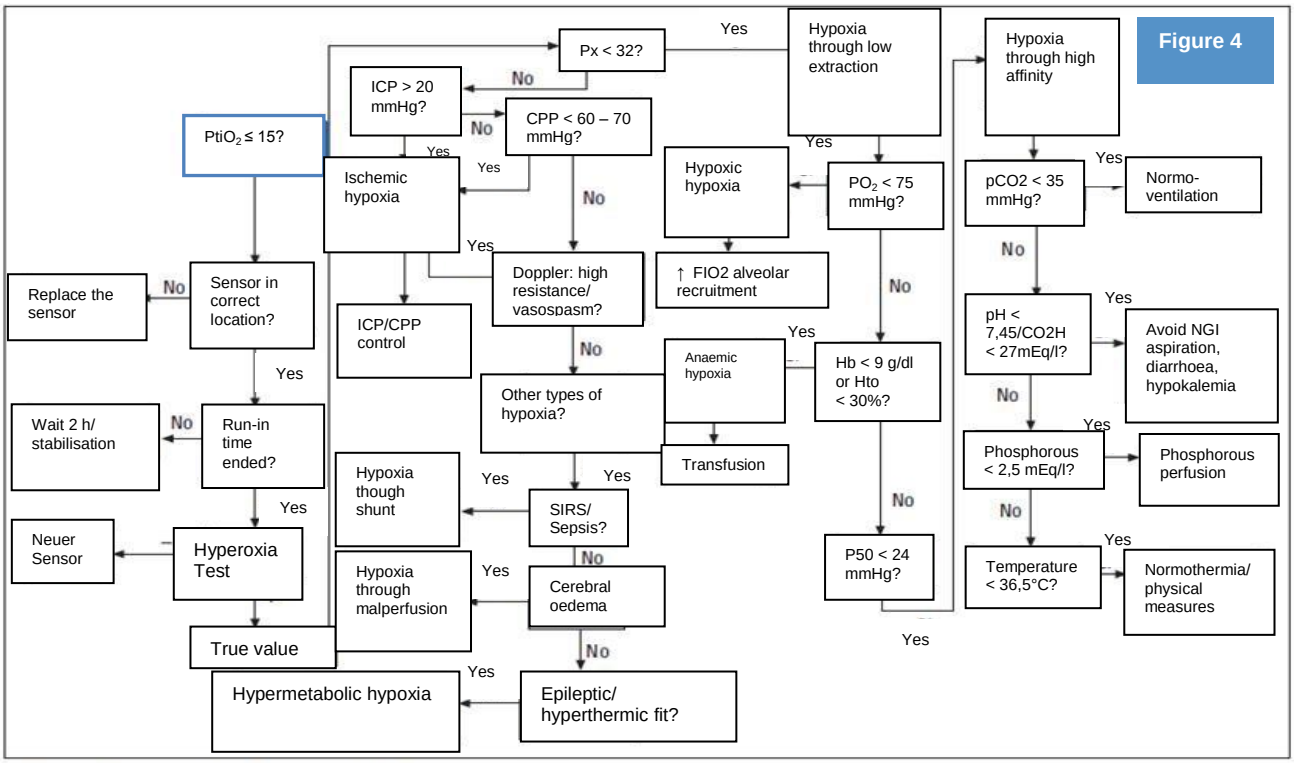


Fig. 4. Intervention protocol for cerebral hypoxia based on the monitoring of brain tissue oxygenation ($P_{ti}O_2$). Once the correct $P_{ti}O_2$ catheter size has been chosen, if tissue hypoxia is detected ($P_{ti}O_2$ < 15 mmHg), the next step is to identify its cause through measuring the oxygen extraction pressure (Px) and with other physiological variables. CO3H: bicarbonate; FiO2: fraction of inspired oxygen; Hb: concentration of haemoglobin; Hto: Haematocrit; pCO2: partial pressure of arterial carbon dioxide; pH: arterial acid-base levels; ICP: intracranial pressure; pO2: partial pressure of arterial oxygen; CPP: cerebral perfusion pressure; p50: 50% saturation pressure; SIRS: Systematic Inflammatory Response Syndrome; NGI: nasogastric intubation.

Following the placing of the intraparenchymal multimodal monitoring system and once the system has stabilised, offering true readings on the area being monitored, it is important to **maintain the $P_{ti}O_2$ above 20 mmHg**. When a **$P_{ti}O_2$ ≤ 15 mmHg** is detected (low $P_{ti}O_2$) we should consider:

1. True or artificial measurement

Discard the reading as false due to the incorrect placement of the $P_{ti}O_2$ catheter or the presence of a small haematoma around the $P_{ti}O_2$ catheter. The stabilisation time for measuring O_2 may range from between 2 and 48 hours. In any case, the hyperoxia test can be used in case of any doubt.

2. $P_{ti}O_2$ sensor malfunction

Once the system has stabilised and the misplacement of the $P_{ti}O_2$ catheter has been ruled out, for continued low $P_{ti}O_2$ levels a hyperoxia test may be carried out[37,41]. See the example (**figure 5**) from Poca M.A. et al[37]. Administering a 100% F_iO_2 with the ventilator should produce a prompt and significant increase in Pt_iO_2. If this does not take place, the sensor may be faulty, due to a breakage or the existence of a micro-haematoma where the sensor and tissue meet, undetected by the CT, affecting the measurement, which occurs in a small percentage of cases (<1%).

Figure 5

Neurocirugia
2005; 16: 385-410

Poca y col

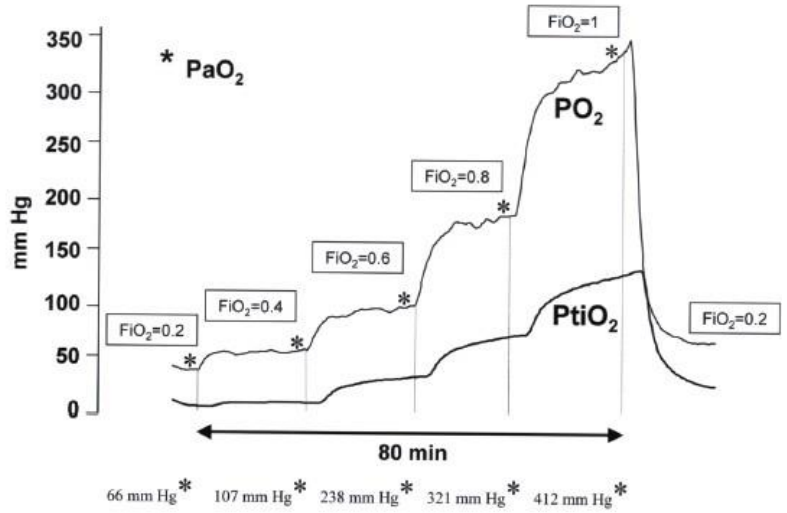


Fig. 11. Hyperoxia Test. The $P_{ti}O_2$ of the patient increases in parallel with the increase in FiO2. The changes in O_2 pressure may also be observed alongside through the simultaneous monitoring of transcutaneous gases (Radiometer). The asterisks show the periodic measurements of $Pa0_2$ obtained from conventional gasometric analysis.

3. Determine the Px (oxygenation of arterial blood)

A. Normal (> 32 mmHg)

When **arterial oxygenation is correct and ICP levels must be obtained:**

i. **ICP > 20 mmHg**: appears to be caused by **hypoexemic hypoxia** and therefore we must control ICP/CPP (intracranial pressure/cerebral perfusion pressure).

ii. **ICP < 20 mmHg**: check the CPP levels:

1. **If lower than 60-70 mmHg** it is recommended to increase CPP to raise $P_{ti}O_2$.
2. **If greater than 60-70 mmHg** (with no option to decrease CPP levels), it is recommended to discard the potential presence of vasospasm with Doppler:
    a. **If vasospasm is found with Doppler**, it is a result of hyopexemic hypoxia and it is recommended to control ICP/CPP.

a. **If vasospasm is not found with Doppler**, hypoexemic hypoxia and hypoxia through low extraction may be discarded, and other less-common causes of hypoxia should also be discarded:
    i. **Hypoxia through arteriovenous Shunt**: Systemic Inflammatory Response Syndrome (SIRS), sepsis…etc.
    ii. **Hypoxia by malperfusion**: avoid vasogenic and cytotoxic oedema.
    iii. **Hypermetabolic hypoxia**: caused for example by epileptic fit of fever.
    iv. **Histotoxic hypoxia**: cytochromes affected by toxins.
    v. **Decoupling hypoxia**: cytochromes affected by toxins.

B. Low (Px < 32 mmHg)

We should thus **normalise blood oxygenation.**

i. **Determine P_aO_2**: If < 75 mmHg, optimise oxygenation through ventilation methods (↑ F_iO_2, alveolar recruitment if possible, etc.).

ii. **Determine p50**: when the affinity of Hb to O_2 is excessive, p50 is lowered (p50 < 24 mmHg), and it is necessary to check the variables which shift the haemoglobin dissociation curve to the left:
    1. If due to **hypocapnia** (pCO_2 < 35 mmHg) or respiratory alkalosis: normalise mechanical ventilation parameters (normoventilation).
    2. If due to **metabolic alkalosis** (pH > 7.45): treat the underlying cause (intestinal loss, abuse of diuretics, dehydration, excess secondary bicarbonate due to increased reabsorption through hypocalcaemia or ingestion of alkalines) and increase volume with ClNa and ClK.
    3. If due to **hypophosphatemia** (phosphorous < 2.5 mEq/l): deliver a phosphate perfusion to avoid a deficit of 2-3 DPG.
    4. If due to **non-therapeutic hypothermia** (Temp. < 36.5ºC): physically induce normothermia.

iii. **Determine Hb**: in neurocritical patients with hypoxia and anaemia, red blood cell transfusion may increase for a prolonged period brain tissue oxygenation[42]. If Hb < 9-10 g/dl or heamatocrit < 30% perform a red blood cell transfusion.

9. Clinical References

1. Siggaard-Andersen M, Siggaard-Andersen O. Oxygen status algorithm, version 3, with some applications. Acta Anaesthesiol Scand Suppl 1995:107: 13-20.
2. Marin-Caballos A.J et al. Monitorización de la presión tisular de oxígeno ($P_{ti}O_2$) en la hipoxia cerebral: aproximación diagnóstica y terapéutica. Med. Intensiva [online]. 2008:vol.32, n.2 [citado 2016-02-24], pp. 81-90.
3. Narotam PK, Morrison JF, Nathoo N. Brain tissue oxygen monitoring in traumatic brain injury and major trauma: outcome analysis of a brain tissue oxygen-directed therapy. J Neurosurg. 2009;111(4): 672-682.
4. McCarthy MC, Moncrief H, Sands JM, Markert RJ, Hall LC, Wenker IC, et al. Neurologic outcomes with cerebral oxygen monitoring in traumatic brain injury. Surgery. 2009;146(4):585-590, discussion 590-591.
5. Spiotta AM, Stiefel MF, Gracias VH, Garuffe AM, Kofke WA, Maloney-Wilensky E, et al. Brain tissue oxygen-directed management and outcome in patients with severe traumatic brain injury. J Neurosurg 2010;113(3):571-580.
6. Stiefel MF, Spiotta A, Gracias VH, Garuffe AM, Guillamondegui O, Maloney-Wilensky E, Bloom S, Grady MS, LeRoux PD. Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring. J Neurosurg. 2005 Nov;103(5):805-11.
7. Bardt TF, Unterberg AW, Härtl R, Kiening KL, Schneider G-H, Lanksch WR. Monitoring of brain tissue pO_2 in traumatic brain injury: effect of cerebral hypoxia on outcome. Acta Neurochir. 1998;Suppl 71:153-6.
8. Van den Brink WA, van Santbrink H, Steyerberg EW, Avezaat CJ, Suazo JA, Hogesteeger et al. Brain oxygen tension in severe head injury. Neurosurgery. 2000:46:868-78.
9. Valadka AB, Gopinath SP, Contant ChF, Uzura M, Robertson CS.: Relationship of brain tissue pO2 to outcome after severe head injury. Crit Care Med. 1998;26:1576-81.
10. Maloney-Wilensky E, Gracias V, Itkin A, Hoffman K, Bloom S, Yang W, et al. Brain tissue oxygen and outcome after severe traumatic brain injury: a systematic review. Crit Care Med 2009;37(6): 2057-2063.
11. Van Santbrink H, Maas AIR, Avezaat CJ. Continuous monitoring of partial pressure of brain tissue oxygen in patients with severe head injury. Neurosurgery. 1996;38:21-31.
12. Dings J, Jäger A, Meixensberger J, Roosen K. Brain tissue pO_2 and outcome after severe head injury. Neurological Res. 1998;20:71-5.
13. Huschak G, Hoell T, Hohaus C, Kern C, Minkus Y, Meisel HJ. Clinical evaluation of a new multiparameter neuromonitoring device: measurement of brain tissue oxygen, brain temperature, and intracranial pressure. J Neurosurg Anesthesiol. 2009 Apr;21(2):155-60.
14. Nortje J, Gupta AK. The role of tissue oxygen monitoring in patients with acute brain injury. Br J Anaesth. 2006;97:95-106.
15. Arikan F, Vilalta J, Minoves T, Moncho D, Vilalta A, Moguer M, Ibarra B, Sahuquillo J. Detection of episodes of ischemic tissue hypoxia by means of the combined intraoperative neurophysiologic monitoring with the tissue oxygenation monitoring in aneurysm surgery. Neurocirugía (Astur). 2008 Apr;19(2):113-20.
16. Jödicke A, Hübner F, Böker DK. Monitoring of brain tissue oxygenation during aneurysm surgery: prediction of procedure-related ischemic events. J Neurosurg. 2003 Mar;98(3):515-23.
17. Szelényi A, Jung CS, Schön H, Seifert V. Brain tissue oxygenation monitoring supplementary to somatosensory evoked potential monitoring for aneurysm surgery. Initial clinical experience. Neurol Res. 2002 Sep;24(6):555-62.
18. Gelabert-Gonzalez M, Fernandez-Villa JM, Ginesta-Galan V. Intra-operative monitoring of brain tissue O_2 ($P_{ti}O_2$) during aneurysm surgery. Acta Neurochir (Wien). 2002:144:863-6, discussion 866-7.
19. Cerejo A, Silva PA, Dias C, Vaz R. Monitoring of brain tissue oxygenation in surgery of middle cerebral artery incidental aneurysms. Surg Neurol Int. 2011 Mar:23;2:37.
20. Cerejo A, Silva PA, Vilarinho A, Dias C, Vaz R. Intraoperative brain oxygenation monitoring and vasospasm in aneurysmal subarachnoid hemorrhage. Neurol Res. 2012 Mar;34(2):181-6.
21. Charbel FT, Du X, Hoffman WE, Ausman JI. Brain tissue PO_2, PCO_2, and pH during cerebral vasospasm. Surg Neurol. 2000:54: 432–7, discussion 438.

22. Kett-White R, Hutchinson PJ, Al-Rawi PG, Gupta AK, Pickard JD, Kirkpatrick PJ. Adverse cerebral events detected after subarachnoid hemorrhage using brain oxygen and microdialysis probes. Neurosurgery. 2002:50: 1213–21, discussion 1221–2.
23. Meixensberger J, Vath A, Jaeger M, Kunze E, Dings J, Roosen K. Monitoring of brain tissue oxygenation following severe subarachnoid hemorrhage. Neurol Res. 2003:25: 445–50.
24. Sandsnark DK, Kumar MA, Park S, Levine JN. Multimodal monitoring in subarachnoid hemorrhage. Stroke. 2012;43:1440-50.
25. Hoffman WE, Charbel FT, Edelman G, Ausman JI. Brain tissue oxygenation in patients with cerebral occlusive disease and arteriovenous malformations. Br J Anaesth. 1997:78: 169–71.
26. Hoffman WE, Charbel FT, Edelman G, Ausman JI. Brain tissue gases and pH during arteriovenous malformation resection. Neurosurgery. 1997:40: 294–300, discussion 300–1.
27. Arikan F, Vilalta J, Noguer M, Olive M, Vidal-Jorge M, Sahuquillo J. Intraoperative monitoring of brain tissue oxygenation during arteriovenous malformation resection. J Neurosurg Anesthesiol. 2014 Oct;26(4):328-41.
28. Tijero T, Ingelmo I, García-Trapero J, Puig A. Usefulness of monitoring brain tissue oxygen pressure during awake craniotomy for tumor resection: a case report. J Neurosurg Anesthesiol. 2002 Apr;14(2):149-52.
29. Pennings FA, Bouma GJ, Kedaria M, Jansen GF, Bosch DA. Intraoperative monitoring of brain tissue oxygen and carbon dioxide pressures reveals low oxygenation in peritumoral brain edema. J Neurosurg Anesthesiol. 2003:15: 1–5
30. Steiner T, Pilz J, Schellinger P, Wirtz R, Friederichs V, Aschoff A, Hacke W. Multimodal online monitoring in middle cerebral artery territory stroke. Stroke. 2001 Nov;32(11):2500-6.
31. Allen BB, Hoffman CE, Traube CS, Weinstein SL, Greenfield JP. Continuous brain tissue oxygenation monitoring in the management of pediatric stroke. Neurocrit Care. 2011 Dec;15(3):529-36.
32. Rajiv Jalan, MD. Intracranial hypertension in acute liver failure- Pathophysiological basis of rational management. Semin Liver Dis. 2003 Aug;23(3):271-82.
33. Rosea JC, Neill TA, Hemphill JC. Continuous monitoring of the microcirculation in neurocritical care: an update on brain tissue oxygenation. Curr Opin Crit Care. 2006;12:97-102.
34. Sarrafzadeh AS, Kiening KL, Unterberg AW. Neuromonitoring: brain oxygenation and microdialysis. Curr Neurol Neurosci Rep. 2003;3:517-23.
35. Siggaard-Andersen O, Ulrich A, Gothgen IH. Classes of tissue hypoxia. Acta Anaesthesiol Scand Suppl. 1995:107: 137-142.
36. Sahuquillo J, Amoros S, Poca MA, et al. Coexistence of regional cerebral hypoxia with normal or hyperemic brain detected by global monitoring methods. Analysis of apparently contradictory findings based on the Siggaard-Andersen model of tissue hypoxia. Acta Neurochir Suppl. 2002:81: 303-305.
37. Poca MA et al. Actualizaciones en los métodos de monitorización cerebral regional en los pacientes neurocríticos: presión tisular de oxígeno, microdiálisis cerebral y técnicas de espectroscopía por infrarrojos. Neurocirugía [online]. 2005:vol.16, n.5 [citado 2016-02-25], pp. 385-410.
38. Kiening KL, Unterberg AW, Bardt TF, Schneider GH, Lanksch WR. Monitoring of cerebral oxygenation in patients with severe head injuries: brain tissue pO_2 versus jugular vein oxygen saturation. J Neurosurg. 1996;85:751-7.
39. Sarrafzadeh AS, Unterberg AW, Kiening KL, Bardt TF, Schneider GH, Lanksch WR. Monitoring of cerebral oxygenation in traumatic brain injured patients. En: Bauer BL, Kuhn TJ, editors. Severe head injuries. Berlin: Springer Verlag. 1997:109-20.
40. Dings J, Meixensberger J, Roosen K. Brain tissue pO_2-monitoring: catheter stability and complications. J Neurological Res. 1997;19:241-5.
41. Dings J, Meixensberger J, Jäger A, Roosen K. Clinical experience with 118 brain tissue oxygen partial pressure catheter probes. Neurosurgery. 1998;43:1082-95.
42. Johnston AJ, Steiner LA, Chatfield DA, Coles JP, Hutchinson PJ, Al-Rawi PG, et al. Effect of cerebral perfusion pressure augmentation with dopamine and norepinephrine on global and focal brain oxygenation after traumatic brain injury. Intensive Care Med. 2004;30:791-7.