PEDIATRIC NEUROMONITORING IN SEVERE HEAD TRAUMA

Authors:

Daysi Abreu Pérez MD PhD[1]. https://orcid.org/0000-0001-8414-0542

Angel J. Lacerda Gallardo MD PhD[2]. https://orcid.org/0000-0001-9171-2000

Jose Antonio Gálvez MD[3]. https://orcid.org/0000-0003-2986-362X

1- Department of Pediatric Intensive Care Unit. "Roberto Rodríguez Fernández" General Teaching Hospital of Morón, Ciego de Ávila, Cuba.

2- Department of Neurosurgery. "Roberto Rodríguez Fernández" General Teaching Hospital of Morón, Ciego de Ávila, Cuba.

3- Department of Neurosurgery. General Teaching Hospital of Morón, Ciego de Ávila, Cuba.

Short running title: Neuromonitoring in pediatric trauma.

Daysi Abreu Pérez MD PhD. dabreup2016@gmail.com

Corresponding author: Angel J. Lacerda Gallardo MD PhD.

lacerdagallardoangeljesus@gmail.com

Jose Antonio Gálvez MD. galvezjosea1988@gmail.com

KEYWORDS: Severe head trauma, Neuromonitoring, Treatment of severe head trauma.

Summary:

Introduction: Among all types of trauma in children, traumatic brain injury has the greatest potential for the development of devastating consequences, with nearly three million affected individuals each year worldwide. **Method:** A quasi-experimental study was conducted in pediatric patients with severe traumatic brain injury, whose objective was to evaluate the use of continuous multimodal neuromonitoring of intracranial parameters as a guide in the treatment of children of different age groups. The patients were divided into two groups according to the treatment received; clinical and imaging monitoring was performed in both. Group I included those whose treatment was guided by multimodal neuromonitoring of intracranial parameters such as intracranial pressure, cerebral perfusion pressure and intracranial compliance, and group II included those who had only clinical and imaging monitoring. **Results:** 80 patients were studied, 41 in group I and 39 in group II. There were no significant differences between the groups with respect to the sociodemographic variables and the results; as a consequence both forms of treatment were outlined, for patients with multimodal neuromonitoring and for those who only have clinical and imaging monitoring. **Conclusions:** It is concluded that both treatment schemes can be used depending on technological availability, although the scheme with multimodal neuromonitoring is optimal.

KEYWORDS: Severe head trauma, Neuromonitoring, Treatment of severe head trauma.

Introduction:

The greatest challenge for medical personnel caring for paediatric patients affected by severe traumatic brain injury (sTBI) is to avoid or minimize secondary brain damage [1,2]. These are dynamic and complex changes that occur in brain physiology and biochemistry, produced by hypoxia and hypotension, which trigger the development of oedema, as the beginning of a cascade that generates intracranial hypertension (ICHT), reduction in cerebral blood flow (CBF), limited oxygenation and, as a consequence, poor results [1,2].

Among all types of trauma in children, traumatic brain injury (TBI) has the greatest potential for the development of devastating consequences, with nearly three million affected individuals each year worldwide [3]. It is also the main cause of disability and death worldwide at these ages, regardless of the cause. Traffic accidents are the most common cause of TBI in all ages and are estimated to be the seventh cause of death by 2030 [3].

The frequency of sTBI in paediatrics is highly variable, the numbers are usually lower in developed countries compared to underdeveloped or developing countries, with a global annual incidence of emergency department visits of 691/100,000, hospitalizations amounting to 74/100,000 and deaths at 9/100,000 [4].

In Cuba, sTBI are closely related to accidents and constitute the fifth cause of death in adults and the first in those under 45 years of age [5], but there are no national rates on the incidence and prevalence in the paediatric population. In

previous experiences published by our group, it was found that only 2.39% of all head injuries in children were serious, with mortality for this subgroup of 31.25% [6].

ICHT is a complication frequently associated with these cases and the time of exposure of brain tissue to high levels of intracranial pressure (ICP) is directly related to unfavourable results [7], so its monitoring and control are essential.

Advances in multimodal neuromonitoring (MMN) of intracranial physiology and, correspondingly, neurointensive treatment, have facilitated the understanding and identification of optimal therapeutic targets after the traumatic event has occurred in the adult patient; however, these strategies should not be applied to the paediatric population, consequently its benefits are still debated in the world scientific community [8].

For some decades now, there has been sufficient evidence that the ICP doesn´t reflects all the clinical picture, especially if the patient is in a state of sedation or neuromuscular blockade and artificial mechanical ventilation (AMV) [9,10] so, the MMN is presented as an essential source of information for the neurointensivist, such as cardiovascular or respiratory monitoring for other sub-specializations within intensive care; however, this is an aspect that is currently controversial, despite the fact that it is known that ICHT events without clinical translation represent a serious risk factor for mortality.

The lack of consensus in the international scientific community on the benefit of MMN as a guide for the treatment of paediatric patients suffering from sTBI and the lack of knowledge of the optimal thresholds of ICP and cerebral perfusion

pressure (CPP) in children of different ages, demands the design and execution of clinical studies that allow obtaining the necessary evidence on the subject and facilitate the use of appropriate therapeutic measures, to guarantee the necessary balance between the structures contained in the intracranial compartment.

The child is not a small adult, there are anatomical and physiological differences between paediatric age groups and between children and adults, which must be considered to guarantee optimal treatment adjusted to each age group [11].

The publication of the treatment guidelines for sTBI in infants, children and adolescents, sponsored by the American Brain Trauma Foundation and its updates [10], have not provided sufficient scientific evidence on the optimal ICP and CPP thresholds to initiate the treatment of ICHT in childhood, which is extremely controversial.

In Cuba, the information available on the subject is scarce, the experience of the working group of the "Roberto Rodríguez Fernández" General Teaching Hospital of Moron, in Ciego de Avila, stands out [12-14].

Based on the above, the following research problem arises: Will the contribution of MMN be superior to clinical and imaging monitoring as a guide for the optimal treatment of paediatric patients with sTBI? With the hypothesis that continuous neuromonitoring of ICP, CPP and intracranial compliance will contribute to obtaining better results at discharge in paediatric patients with sTBI, we proposed the following objective: to evaluate the use of continuous MMN of

intracranial parameters as a guide, in the treatment of children of different age groups who suffer from a TBI.

Method:

A quasi-experimental study was carried out with all patients admitted to the paediatric intensive care unit of the "Roberto Rodríguez Fernández" General Teaching Hospital of Morón, in the province of Ciego de Ávila, Cuba, with a diagnosis of sTBI, in the period between 2000 and 2020.

There were two groups. In group I, 41 patients were included, to whom a diagnosis and treatment algorithm based on clinical and imaging neuromonitoring was applied, to which MMN was added. In group II with 39 cases, a diagnosis and treatment algorithm guided only by clinical and imaging monitoring was applied. For this process, the medical records of the patients were reviewed and the information was extracted, according to the algorithm proposal arising from the "Buenos Aires Consensus" on the treatment of sTBI in patients without invasive neuromonitoring, held in 2015, which was attended by one of the authors of this study (AJLG) and which was published in 2020[18]. The data of the patients included in this group and who were treated before 2015 were adjusted to the requirements of CREVICE modified by the authors. The constitution of the groups was not randomized.

All cases were evaluated and studied in a medical emergency and were then admitted to the paediatric intensive care service.

Evaluation of the algorithms before the quasi-experiment

In the first phase of the study, the work algorithms were designed or modified for both groups of patients; those of group II were adjusted to the characteristics of the paediatric patients, taking as references those proposed by CREVICE [15], which were presented to the neurosurgery and paediatric intensive care groups, to submit them to expert judgment, according to the qualitative technique of the nominal group [16].

Nominal group structure

The nominal group was made up of 12 specialists with sufficient experience in the treatment of paediatric sTBI, who work in the neurosurgery and paediatric intensive care services of the "Roberto Rodríguez Fernández" General Teaching Hospital in Morón, Ciego de Ávila.

At the end of the debate, 100% of the members of the nominal group considered that the algorithms were adequate.

Inclusion criteria:

The age from one month to 17 years old, 11 months and 29 days. TBI with GCS of four to eight points and Patients whose parents or guardians offered their consent to participate in the research and signed the document, after having received information about the characteristics of the study.

Exclusion criteria:

Transfer of the paediatric patient to another hospital due to associated injuries. Non-acceptance of parents or guardians of the patient to participate in the study. GCS of three points

Criteria for MMN

Abnormal CT on admission, patient with normal CT and presence of unilateral or bilateral motor postural alterations, and systolic blood pressure below the 5th percentile for each age group.

Clinical monitoring

Continuous clinical monitoring was carried out in both groups by the group of paediatric intensivists and neurosurgeons, 24 hours a day, which was characterized by cardiorespiratory, hemodynamic, hydromineral and acid-base balance, and hemogasometric monitoring. The clinical examination included the neurological profile of the patients at least every four hours, with which the level of consciousness was observed in cases that allowed it, the pupillometry and pupillary reactivity, the respiratory and hemodynamic pattern, the motor pattern and the level of cephalocaudal degradation of the patient as an integrator of the neurological state.

Imaging monitoring

This was carried out in both groups. CT studies were performed on admission and sequentially after 12 hours of evolution if the first CT was obtained in the first four hours of evolution of the trauma. New studies were indicated after 24 hours and 48 hours of evolution. They were also urgently indicated in the event of any neurological deterioration or sustained elevations in ICP above the values considered for each age group for 15 minutes, despite the use of measures to control ICP.

Evaluation of CT images on admission was performed according to the classification of Marshall et al [17]. The volume of the focal lesions was calculated according to the ellipsoid law [18].

The diameter of the optic nerve sheath (ONSD) was also measured in the initial and sequential CT scans. This measurement was also performed with orbital ultrasound in the paediatric intensive care unit, at the patient's bedside. The measurement was made three mm behind the eyeball transverse to the optic nerve.

Simple chest Simple x-rays of long bones, rib cage and bony pelvis were indicated for patients with injuries at these levels.

Abdominal ultrasounds and transcraniectomy were indicated at medical discretion in selected patients.

Description of the algorithms

The diagnosis and treatment algorithm for patients with MMN begins from the trauma site or previous phase to the neurotrauma centre (Figure 1).

The measures to control ICP were organized into three levels (Table 1), so that they were introduced in an additive and staggered manner although, depending on the therapeutic needs and technological availability, they may not follow the order in which they are described within the same level and even between different levels. The downscaling or withdrawal of the measures was carried out in the same order in which they were introduced, depending on the clinical

symptoms, the neuroimaging and the information on the different MMN variables.

The diagnosis and treatment algorithm for patients without MMN was based on the CREVICE clinical and imaging monitoring protocol, which has its origins in the Buenos Aires consensus, carried out in 2015 and published in 2020 [15]. (Figure 2), to which modifications were made to adjust it to the objectives of the present study with paediatric patients.
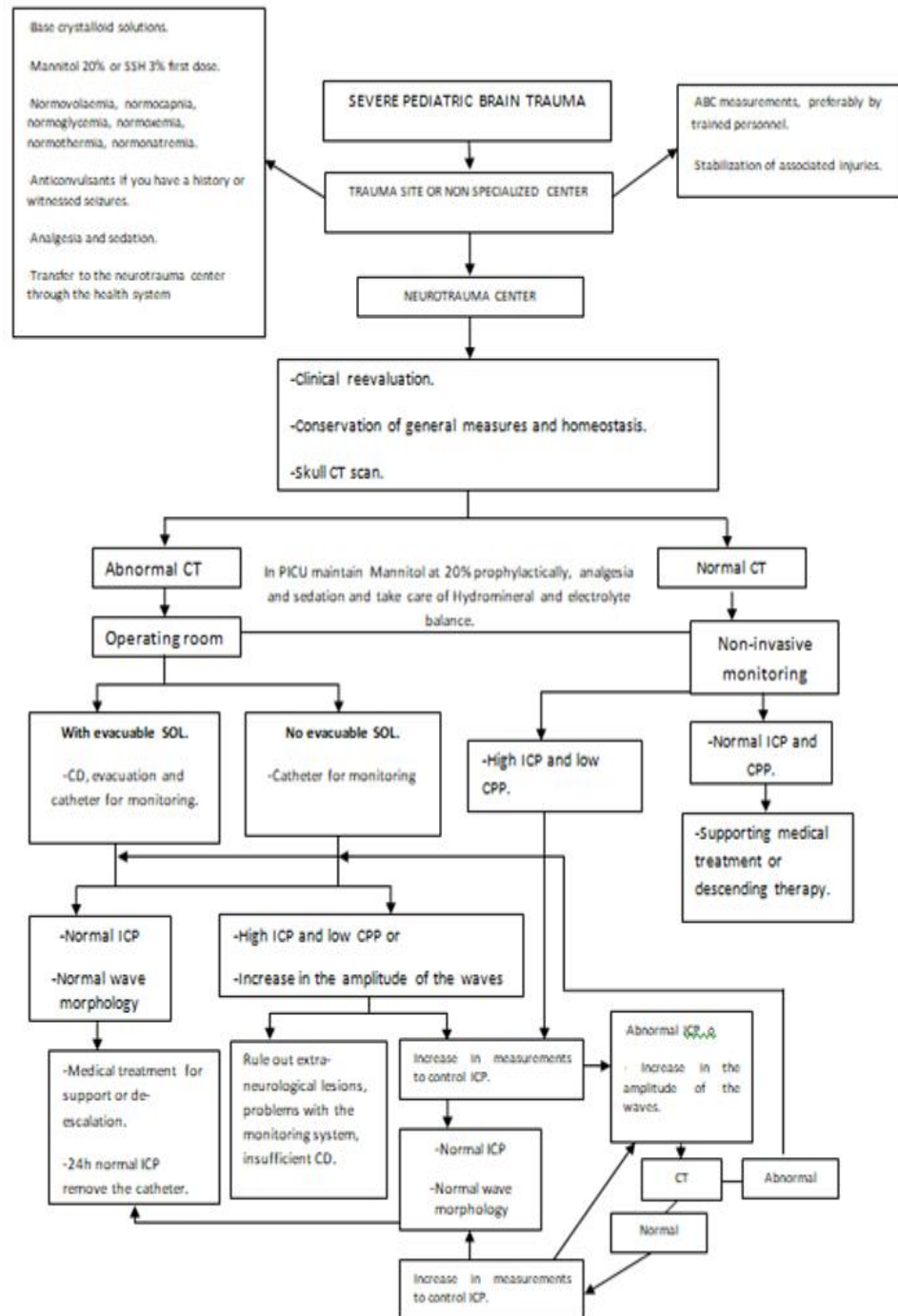
Base crystalloid solutions.

Mannitol 20% or SSH 3% first dose.

Normovolaemia, normocapnia, normoglycemia, normoxemia, normothermia, normonatremia.

Anticonvulsants if you have a history or witnessed seizures.

Analgesia and sedation.

Transfer to the neurotrauma center through the health system

SEVERE PEDIATRIC BRAIN TRAUMA

ABC measurements, preferably by trained personnel.

Stabilization of associated injuries.

TRAUMA SITE OR NON SPECIALIZED CENTER

NEUROTRAUMA CENTER

-Clinical reevaluation.

-Conservation of general measures and homeostasis.

-Skull CT scan.

Abnormal CT

In PICU maintain Mannitol at 20% prophylactically, analgesia and sedation and take care of Hydromineral and electrolyte balance.

Normal CT

Operating room

Non-invasive monitoring

With evacuable SOL.

-CD, evacuation and catheter for monitoring.

No evacuable SOL.

-Catheter for monitoring

-High ICP and low CPP.

-Normal ICP and CPP.

-Supporting medical treatment or descending therapy.

-Normal ICP

-Normal wave morphology

-High ICP and low CPP or

-Increase in the amplitude of the waves

Abnormal ICP/A

- Increase in the amplitude of the waves.

-Medical treatment for support or de-escalation.

-24h normal ICP remove the catheter.

Rule out extra-neurological lesions, problems with the monitoring system, insufficient CD.

Increase in measurements to control ICP.

-Normal ICP

-Normal wave morphology

CT

Abnormal

Normal

Increase in measurements to control ICP.

Figure1. Work algorithm for pediatric patients with MMN.

ICHT was clinically suspected and treatment was initiated in the presence of one major criterion or two minor criteria [15].

Major criteria: 1- Compressed cisterns (Marshall Classification III) on CT, 2- Midline dislocation ≥ 5 mm (Marshall Classification IV) on CT, 3- Lesion with mass effect not evacuated on CT.

Minor criteria: 1- Glasgow motor scale ≤ 4, 2- Pupillary asymmetry, 3- Abnormal pupillary reactivity, 4- Marshall Grade II diffuse axonal injury (Cisterns present with 0-5 mm dislocation or focal lesions of high density or mixed less than or equal to 25 cm^3).
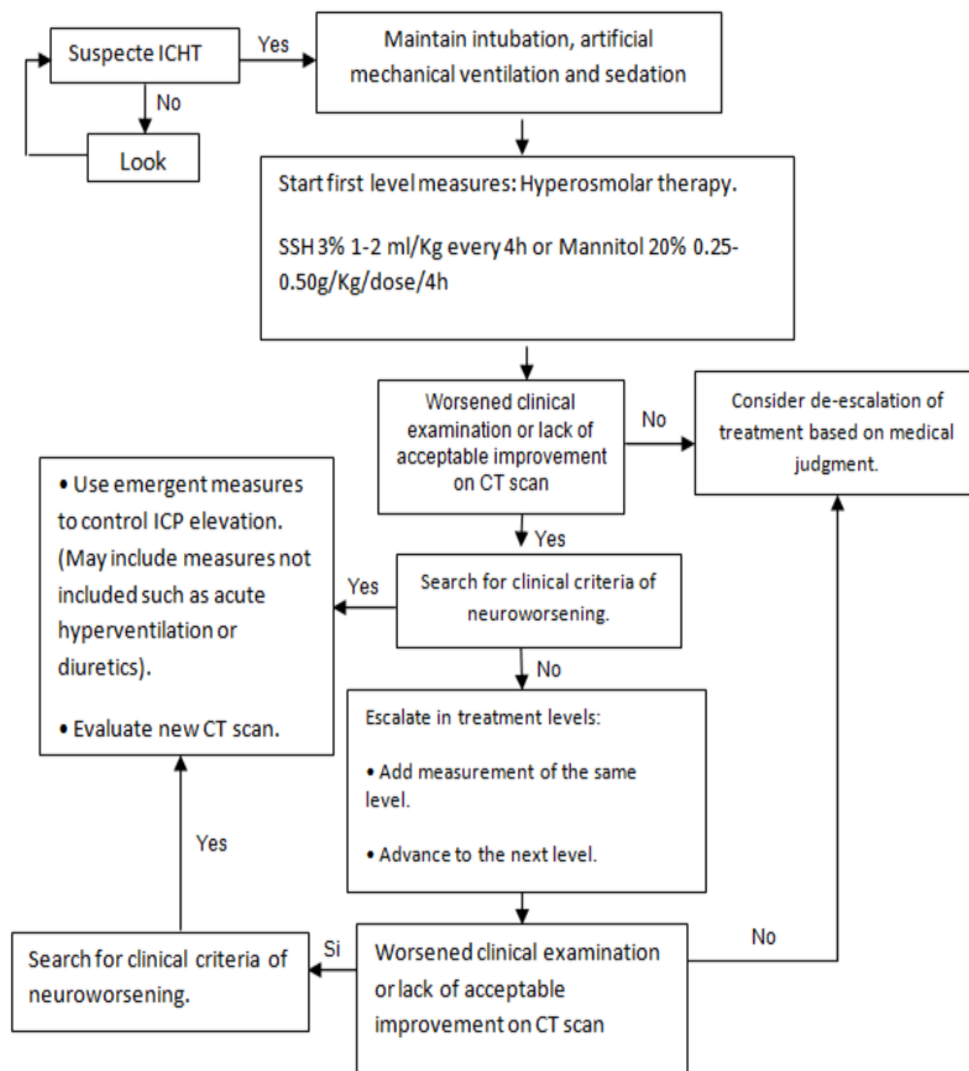
Figura 2. Work algorithm for pediatric patients with clinical and imagenological monitoring.

If there is suspicion of ICHT, the patient is kept intubated, with artificial mechanical ventilation, baseline sedation, and first-level treatment measures are initiated (Table 1). An essential objective was to achieve and maintain a MAP ≥ 5th percentile for each age group.

Level 1	• CSF drainage. Five milliliters up to four times in an hour.
	• 20% mannitol regimen in boluses at 0.25-0.50g/kg/4h.
	• 3% Hypertonic Saline Solution Scheme in boluses at 1-

	2ml/Kg/4h. • Maintain normothermia with a threshold of 37.5ºC. • Primary decompressive craniectomy.
Level 2	• Deepen sedation. • Moderate hyperventilation PaCO2 ≥ 30-35 mmHg. • 3% Hypertonic Saline Solution in continuous infusion. • Neuromuscular blockers.
Level 3	• Delayed or secondary decompressive craniectomy. • Barbiturate coma. • Lumbar CSF drainage. • Surface hypothermia with threshold < 37ºC.

Table 1. Treatment levels for ICHT.

If the clinical examination or CT scan is stable or shows signs of acceptable improvement, therapeutic de-escalation is considered according to the specialist's criteria. In this scheme, frequent neurological examinations by the medical team are required.

Neuroworsening was considered when any of the following findings appeared during the physical examination: 1- Decrease of more than one point on the Glasgow motor scale, 2- New loss of pupillary reactivity, 3- Appearance at intervals of pupillary asymmetries of more than two millimetres of difference or bilateral mydriasis, 4- Appearance of a new motor focus and 5- Presence of a brain herniation syndrome (Example: Cushing's triad) [15].

Variables such as age, sex, origin, transportation used for transfer, time between the trauma and arrival at the neurotrauma centre, treatment in the phase prior to the neurotrauma centre, clinical and imaging diagnoses upon admission were studied, the presence of neuroworsening, the characteristics of the sequenced CT scans, the GCS at admission and its relationship with the GOS, the quantitative values of the ICP and its relationship with the qualitative

characteristics of the pulse waves. We also evaluated CPP in group I and intracranial compliance as well as the treatments used in the PICU, complications and results.

To personalize the treatment according to the different age groups, the anatomical and physiological characteristics that distinguish children in different age groups and with adults were considered.

Systemic blood pressure.

Those who had figures lower than the fifth percentile for all ages were considered hypotensive (SBP: <65 mmHg for infants, <78 mmHg for one-year-old children, <84 mmHg at five years, <88 mmHg at 10 years, and < 98 mmHg over 14 years of age) (Diastolic Blood Pressure (DBP): <40 mmHg in infants and children aged one year, <44 mmHg at five years, <52 mmHg at 10 years and <60 mmHg over 14 years years).

The normotensives were those who showed figures between the 25th and 75th percentile (SBP: 84-100 mmHg in infants and at one year, between 92-104 mmHg at five years, between 100-116 mmHg at 10 years and 110-124 mmHg in those over 14 years old) (DBP: between 50-62 mmHg in the infant and at one year, between 55-62 mmHg at five years, between 66-74 mmHg at 10 years and between 70-80 mmHg in the older 14 years).

Hypertensive patients presented values higher than the 90th percentile (SBP: 100 mmHg in infants and at one year, >108 mmHg at five years, >120 mmHg at 10 years and >132 mmHg in children over 14 years of age) (DBP: >67 mmHg in

infants and one-year-old children, >68 mmHg at five years, >80 mmHg at 10 years and >70 mmHg in those over 14 years of age). From these values, the mean arterial pressure (MAP) is calculated through the formula two times the diastolic pressure plus the systolic pressure over three.

Particularization of the ICP

Patients were divided according to normal ICP values in each age group, taking the maximum value for evaluation. Infants: normal values between 3-6 mmHg, divided into a) less than six millimetres of mercury and b) six or more millimetres of mercury [19, 20].

Children over 1 year of age: normal values 7-15 mmHg, as the pressure range is so wide, as well as the age range, we divided this group into two subgroups (the existence of buffer mechanisms was considered up to approximately four years of age). In children 1-4 years old the normal value is 10 mmHg, it is divided into: a) less than 10 mmHg and b) 10 or more mmHg. For children between five and 17 years, 11 months and 29 days, the normal value is 15 mmHg, and they were divided into a) less than 15 mmHg and b) 15 or more millimetres of mercury [19, 20].

ICHT was treated when the values were higher than the upper normal value for each age group, with the exception of those who presented lesions occupying intracerebral space, located in the uncus of the temporal lobe or in the basal frontal region, in which the therapeutic behaviours were evaluated individually.

Specification of the CPP:

CPP was calculated according to the conventional formula CPP = MAP–ICP, where MAP is the mean arterial pressure obtained in turn by the formula two perform the calculation.

As MAP values vary according to age groups and its normal range fluctuates between the fifth and 90th percentile and, furthermore, ICP values also vary according to age, to calculate this variable the following values were used: minimum MAP and maximum ICP values for each age group. Optimal values were considered [20].

• For infants and children between one and four years old, 47 mmHg, so the results were divided into a) less than 47 mmHg and b) 47 or more mmHg.

• For children between five and 17 years, 11 months and 29 days, the normal figure is 50 mmHg, so they were also divided into a) less than 50 mmHg and b) 50 or more mmHg.

For patients with normal first CT, non-invasive monitoring with carotid Doppler, transcranial Doppler, head CT, transcraniectomy ultrasound, and ONSD by transorbital ultrasound or CT is indicated. To estimate ICP and CPP, data obtained from transcranial Doppler are used with the application of the formula: ICP=MAP-CPPe, where CPPe=MAPxVd/Vm-1+14. The flow chart is inserted in the variants described above according to the quantitative values and qualitative characteristics of the ICP and CPP waves.

Particularization of intracranial compliance

This variable was determined in the group with invasive ICP monitoring, using the pressure volume index (PVI), which was calculated by adding CSF volume or subtracting it. The applied technique was selected depending on the ICP at the time of the calculation, if the ICP was normal or below the normal value it was performed by addition, if the ICP was elevated it was performed by subtraction to avoid unwanted elevations and the generation of possible pressure cones.

To calculate the normal ranges of PVI by adding one millilitre (ml) of solution, it is necessary to know the normal permissive upper ICP value by age group and to this value add and subtract four, which is the normal permissive value of elevated ICP in mmHg before the injection of one ml of solution into the intracranial cavity.

The distribution of the normal ranges of PVI by age would be: For those under one year of age with permissive upper normal ICP at six millimetres of mercury (6±4 mmHg), the normal IPV would be in the range between 0.33 ml-0.60 ml.

For children older than one year in which the normal ICP is between seven to 15 mmHg, it would be 7±4 and 15±4 mmHg, the normal IPV is between 0.63 ml and 0.79 ml. For the subgroup of children between one and four years of age in whom the normal permissive upper ICP value is 10 mmHg (10±4 mmHg), the normal IPV would be in the range between 0.60 ml-0.71 ml.

For the age subgroup between five and 17 years in which the upper normal ICP value is 15 mmHg, then it would be 15 ±4 mmHg, the normal PVI is between 0.74 ml and 0.79 ml.

The data was obtained from the medical records and was entered into a database built with the SPSS version 21.0 system for Windows. The non-parametric Mann-Whitney U tests were applied to compare two sample means and the Kruskal-Wallis to compare medians. We also used Fisher's Exact Test to relate two quantitative variables.

Results:

Table 2 shows the general characteristics of both groups, which shows that there was a predominance in both cases between 5-17 years of age, the transportation used mostly was healthcare and the time period between the moment of the accident and arrival at the neurotrauma centre was predominantly between 0-3 hours.

General variables	Category	Group I			Group II		
		No.	%	*p	No.	%	*p
Age	Less than 1 year	2	4,9	0,000			0,000
	1-4 years	4	9,8		3	7,7	
	5-17 years	35	85,3		36	92,3	
Sex	M/F	28/13	65,1/30,2	0,019	28/11	71,8/28,2	0,021
Area of origin	South	23	56,1	0,435	27	69,2	0,398
	North	18	43,9		12	30,8	
Transport used	Sanitary	37	90,2	0,000	36	92,3	0,000
	No Sanitary	4	9,76		3	7,7	
Time to arrival at the	0-3 hours	29	70,7	0,000	31	79,5	0,000
	4-6 hours	9	22		8	20,5	

neurotrauma center	7-12 hours		7,3				
		3					
* Pearson chi square.							

Table 2. General characteristics.

In the phase prior to the neurotrauma centre, most of the children had received a dose of brain dehydrators and had been resuscitated with crystalloid-type fluids (0.9% physiological saline solution).

In the clinical diagnoses upon admission, there was a predominance of moderate diffuse axonal damage, 20 patients (48.8%) in group I and 13 cases (33.3%) in group II.

The GCS upon admission and its relationship with the GOS, showed that in both groups patients with GCS upon admission predominated in eight points, 21 cases (51.2%) in the group I, of which 18 (85.7%) were left with mild or no sequelae and 22 (56.4%) in group II, of which 17 (77.3%) were left with light or no sequelae. In both groups, all the cases admitted with GCS at three points died.

The use of CT upon admission was a decisive element in the application of the algorithms. In group I, grade IV diffuse axonal lesions (displacement) predominated, with 18 cases (43.9%) and grade III (swelling) with 12 patients (29.3%). In group II, 17 cases (43.6%) showed Marshall type IV and 14 (35.9%) showed grade III.

When comparing the status of the structures in the midline in the CT at admission between the groups, it is evident that in both there was a relationship between dislocations of 0-10 mm with those discharged alive, while patients with dislocations greater than 10 mm, They were related to the deceased. When applying the Mann Whitney U test, a correlation was found between these two variables with a significance level of p≤0.03 in group I and p≤0.04 for group II. Furthermore, in group I, compressed cisterns were more frequent with 20 cases (48.8%) of which 18 (90%) were discharged alive and absent cisterns in 18 patients (43.9%) of which 10 (55, 6%) died. In group II, 25 cases (64.1%) had absent cisterns, of which 14 (56%) died and 14 patients showed compressed cisterns (35.9%), all of whom survived.

Optic nerve sheath diameters (ONSD) measured on CT at admission were homogeneous in both groups, with a greater frequency of those with 3.5 mm or less, 21 (51.2%) in group I and 18 (46.2%) in group II. When relating the ONSD with the average ICP values in group I, it was striking how 24 (85.7%) of 28 cases in the range between less than 3.5 mm and 5.5 mm had normal ICP values and 12 (92.3%) of 13 children with diameters greater than 5.5 mm had high ICP values for their age. When applying the Mann Whitney U test, we found a correlation between ONSD and ICP for a significance level of (p≤0.000).

Continuous monitoring of ICP in group I showed that in the first 24 hours of starting treatment, 25 patients (61%) had normal values for their age, while the number of patients with normal ICP increased between the second and on the

fifth day of evolution to 33 cases (80.5%). In group II, since there was no MMN, the clinical and imaging estimation of the existence of ICHT was used, which is less reliable, so all patients in group II had suspicion of ICHT in the first 24 hours, while in the following 25-120 hours of evolution, only 16 patients (41%) showed normal ICP criteria, with a difference between the groups of 39.5%.

CPP was the second most important variable considered in group I. In the study, a predominance of normal CPP values was observed in 27 cases (65.9%), which correspond to the predominance of normal CPP values and ICP from the first 24 hours after starting treatment. When relating CPP to the status at discharge, we found that 11 (91.7%) of the 12 deceased patients had decreased CPP and 26 (89.7%) of the living discharged patients had normal CPP. By applying Fisher's exact statistic, a significant result is obtained (p≤0.000), which indicates that exposure to a decreased CPP is associated with deceased discharge and that decreased CPP behaves as a risk factor that increases 21. 2 times the risk of dying in those exposed to this characteristic, compared to patients with normal CPP.

Regarding intracranial compliance, a discrete predominance of patients with "loose" compliance and its significant correlation with normal ICP was observed. "Compromised" compliances were second in frequency and were related to increased ICP. Normal compliances were the least frequent and in which there was 50% shared representation between elevated and normal ICPs. If we combine the "normal" ones with the "loose" ones, we would reach 24 (58.5%), a little more than half of the patients. By correlating intracranial compliance with

the characteristics of the ICP pulse waves, we observed that 76% of the patients with normal ICP had normal pulse wave morphologies while 62.5% of the cases with elevated ICP had altered pulse waves morphologies.

In the clinical evolution we observed that in group I nine patients (22%) presented criteria for neuro-deterioration, 3 of them (33.33%) had a decrease in the Glasgow motor scale, 3 (33.33%) %) a new loss of pupillary reactivity, 2 (22.23%) presented pupillary asymmetries at intervals and 1 (11.11%) had a new motor focus. In group II, 18 cases (46.1%) showed neuro-deterioration, with a difference of 24.1% in favour of group II. Six (33.33%) had a decrease in the Glasgow motor scale, 3 (16.67%) a new loss of pupillary reactivity, 4 (22.22%) pupillary asymmetries at intervals, 2 (11.11%) and 3 (16.67%) showed brain herniation.

Figure 3 shows the treatment used in the neurotrauma centre. It is striking how analgesia and sedation and 20% mannitol were used in 100% of the cases in both groups and primary decompressive craniectomy was used in 30 patients (73.17%) in group I and in 16 patients (41 .02%) of group II.
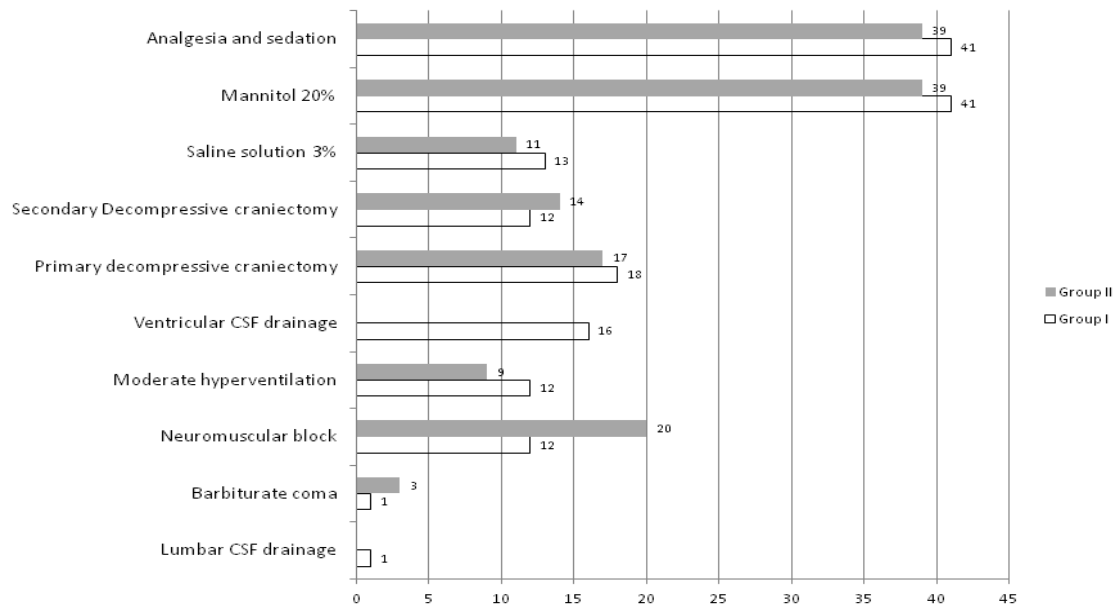
Figure 3. Treatment used.

The sequenced CT images, with respect to the images obtained at admission, showed that in group I, there was a predominance of "improved" CT scans 29 (70.7%) (p≤0.000) while, in group II only 16 (41%) showed this characteristic, with a difference between the groups of 29.7%.

When analysing the "unchanged" CT scans, we found a higher frequency in group II, with a percentage difference between the groups of 21.4%. Regarding the "worse" CTs, there was also a higher frequency in group II, but with a lower percentage difference of 8.3%. When applying the Mann-Whitney U test we found that there was a significant difference between the groups.

Regarding complications, we found that there was a greater frequency of extra-neurological complications in both groups, among which healthcare-related infections (HAIs) predominated, with 17 cases (41.5%) in group I and 30

patients (76.9%) (p≤0.000) in group II, with a percentage difference between the groups of 35.4%. This difference in favour of group II was probably related to the longer length of stay of these patients and the longer time of AMV.

Among the neurological complications, ICHT predominated in both groups, with 17 patients (41.5%) in group I and 25 patients (64.1%) (p≤0.005) in group II, with percentage difference between the groups of 22.6%. This was also the complication most related to deaths in both groups. When applying the Mann-Whitney U test, we found significant differences between the groups in high airway infections (p≤0.005) and to a lesser extent with ICHT (p≤0.07), in both cases with predominance for group II.

Figure 4 shows the results and shows how in group I, more than half of the patients, 24 (58.5%), were left with mild or no sequelae, with a mortality of 29.3%. In group II, 18 cases (46.1%) were left with mild or no sequelae, with a negative percentage difference of 12.4% compared to group I. In group II, 14 patients died (35.9%), for a percentage difference of 6.7% higher compared to group I. When applying the Pearson chi-square test for the status at discharge, with the categories discharged alive or deceased, there were no differences between the groups (p≤0.694).
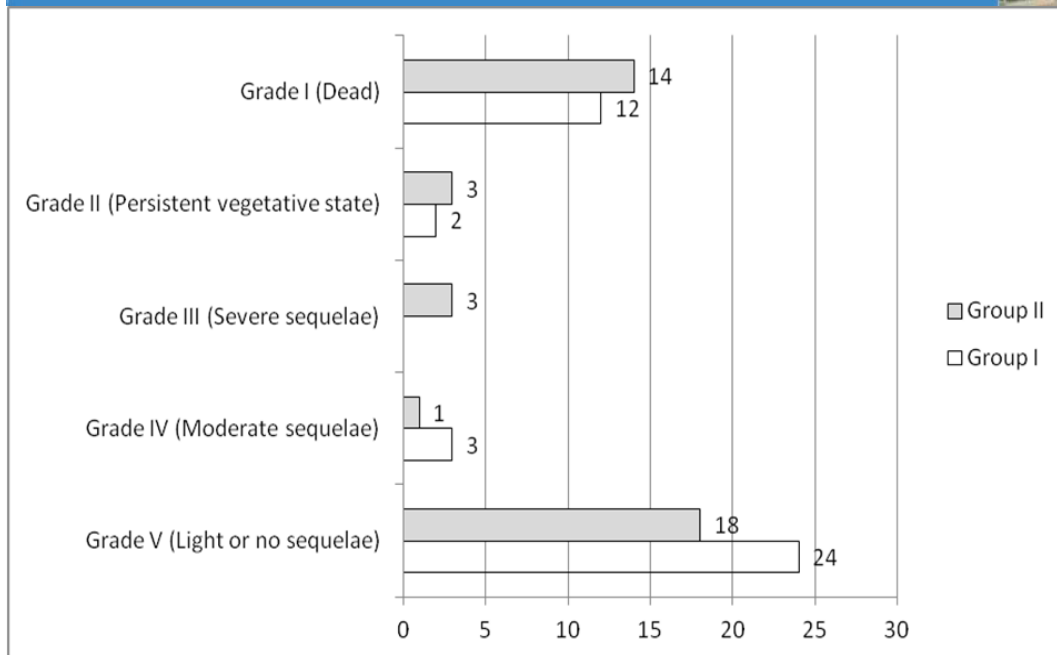
Figure4. Result.

When we analysed the results stratified into satisfactory (GOS between Grades III-V) and unsatisfactory (Grades I and II), we found that in group I 27 (65.9%) had satisfactory results and 14 (34.1%) unsatisfactory, with a difference of 31.8% towards the predominance of satisfactory results. In group II, 17 patients (43.6%) had unsatisfactory results and 22 (56.4%) had satisfactory results, with a percentage difference in favour of satisfactory results of only 12.8%. The percentage difference in satisfactory results between the groups was 19% in favour of group I.

Discussion:

The real contribution of the different neuromonitoring variants in paediatric patients with sTBI is still controversial. Undoubtedly, ignoring the information

offered by these methods would be similar to asking a cardiologist to treat a myocardial infarction without electrocardiographic monitoring, because patients undergoing MMN receive a personalized treatment modality, which allows early diagnosis of the state of different intracranial variables, to optimize the treatment and diagnosis of complications, which facilitates their rapid solution, so its use is recommended in centres that have the required technology, which agrees with what has been reported by other authors. [21, 22]. The publication of some studies such as BEST-TRIP and others [21, 23], which have not been able to prove the benefit of using these techniques, adds controversy to the topic.

ICP was the main variable to be considered in this study. In group I, by having continuous monitoring, it was possible to quickly diagnose the control of this parameter and identify those in which high values persisted and trigger therapeutic escalation quickly. For the application of the algorithm without MMN in group II, the clinical and imaging criteria for the suspicion of ICHT were very important, but without the specificity provided by continuous ICP monitoring, so it can be seen that all patients had criteria of elevated ICP in the first 24 hours of admission and the diagnosis of its control was delayed, which shows the advantage of having MMN in terms of speed in obtaining diagnoses and quickly escalating to the therapeutic level, however these findings did not show significant differences regarding the results.

In most of the studies reviewed, the threshold for the treatment of elevated ICP for all paediatric patients is recommended at 20 mmHg [10], a very controversial

criterion, as neurophysiological variables that change with paediatric age are accepted nationally and internationally and which suggest that thresholds should be personalized for each age group [19]. Few attempts have been made to guide treatment in these patients with different thresholds for each age group, as in the present study, the information available on this aspect is that no significant differences have been found in relation to the dichotomized results of the GOS six months after the trauma [21]. No differences were found between the groups in this study either.

Currently there is a tendency to consider that the quantitative value of ICP alone is not sufficient to initiate treatment in the event of intracranial hypertension [24], it is necessary to consider the qualitative element, the morphology of the pulse waves that they express the state of intracranial compliance. In the present study, this determination was made in Group I, but not in Group II, and when the results were compared, there were no significant differences with regard to mortality. This information reinforces the already established criterion that by controlling ICP, the pressures in the different intracranial compartments are balanced and in this way compliance improves. In those cases in which this objective is not achieved, it is necessary to find a therapeutic alternative, which in this study it was decompressive craniectomy, which converts the cranial cavity from a "closed home" to an "open home" and opens a therapeutic window first for evacuation of space-occupying lesions and rearrangement of structures and then diagnostic by serving to monitor intracranial structures through the use of transcraniectomy cranial ultrasound.

CPP was another important variable in the treatment of neuro-traumatized paediatric patients. This was only calculated in group I, the work system planned for this study was based on the personalization of the treatment according to different age groups [20], finally the work team could not make comparisons between groups because the majority of the patients were between 5-17 years of age, however, data obtained in studies with a low level of evidence suggest maintaining values between 40-50 mmHg (level of evidence class III). They also state that there may be specific thresholds for different age groups, with values that could be below those recommended in younger children or higher than the range stated for older children [10], which is consistent with the concept of treatment for these patients that the authors defend in the present study [19, 20], although this idea must be verified in subsequent studies.

In the neuromonitoring imaging of both groups, in addition to the elements usually considered in the admission CT, the measurement of the optic nerve sheath diameter (ONSD) was very important, especially in group II, in which we found a greater frequently those with 3.5 mm or less, 21 (51.2%) in group I and 18 (46.2%) in group II. When relating the ONSD with the average ICP values in group I, it was striking how 24 (85.7%) ($p \leq 0.000$) of 28 cases in the range between less than 3.5 mm and 5.5 mm, had values normal ICP and 12 (92.3%) ($p \leq 0.000$) of 13 children with diameters greater than 5.5 mm had high ICP values for their age. This finding could be a suggestion to start the treatment of ICHT when the ONSD is above 3.5 mm. Kayadibi et al. [25], demonstrated the effectiveness of measuring the ONSD in children to estimate ICP by correlating

it with CT findings through the Rotterdam scale. Other authors agree on the correlation between ONSD and ICP in adults [27, 28], so it is necessary to pay more attention to this variable in subsequent studies.

Neuro-deterioration occurred in nine patients (22%) in Group I, while in Group II 18 cases (46.1%), with a difference of 24.1% in favour of Group II. This result differs from what was reported in the BEST TRIP study [23], where there were no significant differences between the groups.

The inclusion of these criteria in the algorithms was decisive for the indication of sequential imaging studies, to investigate the appearance of new focal lesions or the worsening of existing ones and advance therapeutic escalation. In group I, since there was continuous monitoring of ICP and CPP, the appearance of these clinical signs could be suspected and prevented in some patients, which was not possible in group II.

The measures to control ICHT were organized depending on the needs to be treated and these did not always follow the planned order. Analgesia and sedation were used in all cases studied in both groups (100%), with the dual objective of guaranteeing patient-artificial ventilation machine synchrony and thus avoiding ICHT events. This was not considered in any of the algorithms as a direct measure to control ICP elevations, but rather as a basic treatment.

In both study groups, the level of intense intensive therapy predominated, probably directly related to the number of patients who underwent primary DC; there were no significant differences between the groups. Generally, patients who have been subjected to an intense level of therapy show worse results [30],

however, although in this study all the deceased had this level of therapy, 11 cases (47.8%) in group I and 17 (43.6%) in group II survived.

There was a higher frequency of extra-neurological complications in both groups, among which healthcare-related infections (HAIs) predominated, with 17 cases (41.5%) in group I and 30 patients (76.9%) ($p \leq 0.000$) in group II, with a percentage difference between the groups of 35.4%. This difference in favour of group II was probably related to the longer length of stay of these patients. Among the neurological complications, ICHT predominated in both groups, with 17 patients (41.5%) in group I and 25 patients (64.1%) ($p \leq 0.005$) in group II, with a percentage difference between the groups of 22.6%. This was also the complication most related to deaths in both groups.

The results in this study did not show significant differences between the groups. This finding does not reject the importance of MMN, it is simply an argument that justifies the use of any of the two treatment variants and to a certain extent resolves an existing scientific and therapeutic contradiction for several years now [23,29], although undoubtedly patients whose treatment is established under the guidance of the MMN, receive a personalized treatment modality, which allows an early diagnosis of the state of different intracranial variables, which optimizes the treatment and the diagnosis of complications, which facilitates their rapid solution, so its use is recommended in centres that have the required technology, which agrees with what was reported by other authors [21, 30].

The BEST-TRIP [23], a trial carried out in Latin America (Bolivia and Ecuador) in patients over 13 years of age, had two study arms, one with invasive ICP monitoring and the other with clinical and imaging monitoring. The report was carried out in 2012 and its authors concluded that, although there was a trend towards lower mortality and better care in patients with ICP monitoring, in terms of results there were no differences between treatment modalities, which coincides with what was found in the present work. This study was highly criticized for its methodological limitations.

There are several elements to consider in this topic that should not be ignored. MMN does not impact mortality by itself; it is the therapeutic measures generated with the information obtained that can modify the natural evolution of the disease and influence this variable [29], and every patient with sTBI may or may not have MMN, must be subjected to treatment to control general and intracranial parameters such as the rise in ICP and the fall in CPP, phenomena that frequently occur in this type of patient.

It is necessary to individualize treatments in sTBI because results differ between different GCS scores regardless of the use or not of MMN. In the treatment systems for these cases, novel elements must be considered from the anatomical, physiological and interpretation points of view of the information offered by the type of neuromonitoring available, which may have an impact on the results [24].

In conclusion, we can report that clinical and imaging monitoring was sufficient to guide treatment in the group without MMN, although the authors consider that

MMN represents the ideal method to guide treatment in paediatric patients with sTBI.

There were no significant statistical differences between the groups regarding the results, but MMN showed advantages over clinical and imaging monitoring: The information provided facilitated the earlier identification of elevations in ICP and falls in CPP. It allowed combining the quantitative analysis with the qualitative analysis of the ICP. It guaranteed personalized treatment of patients according to their age groups. Overall mortality was 6% lower in this group. The number of patients with mild or no sequelae was higher. The time of artificial mechanical ventilation was shorter. The stay in the PICU was shorter.

Reference:

1. Godoy DA, Murillo-Cabezas F. Evolutionary conceptualization of the injury mechanisms in traumatic brain injury. Med Intensiva. [Internet]. 2022 Feb [citado 2022 feb 28]; 46(2):90-3; https://pubmed.ncbi.nlm.nih.gob/32192779

2. Appavu B, Burrows BT, Foldes S, Adelson PD. Approaches to multimodality monitoring in pediatric traumatic brain injury. Front Neurol. [Internet]. 2019 nov [citado 2020 feb 28];10:1261. Disponible en: https://doi.org/10.3389/fneur.2019.01261

3. Hankinson TC, Beauchamp K. Pediatric Traumatic Brain Injury: The Global View. World Neurosurg. [Internet]. 2016 ago [citado 2020 ene 12];92:540-1; https://pubmed.ncbi.nlm.nih.gob/27302559

4. Pedersen SH, Lilja-Cyron A, Astrand R, Juhler M. Monitoring and Measurement of Intracranial Pressure in Pediatric Head Trauma. Front Neurol. [Internet]. 2020 ene [citado 2020 feb 12];10:1376. Disponible en: https://doi.org/10.3389/fneur.2019.01376

5. Cuba. Ministerio de Salud Pública. Dirección Nacional de Registros Médicos y Estadísticas de Salud. Anuario estadístico de salud 2021. La Habana: MINSAP; 2021. Available from: Anuario-Estadistico-de-Salud-2021.-Ed-2022.pdf (sld.cu) [Last accessed: 12/23/2023].

6. Lacerda-Gallardo AJ, Abreu-Pérez D. Traumatic brain injury in paediatrics. Our results. Rev Neurol. [Internet]. 2003 ene [citado 2019 mar 6];36(2):108-12; https://neurologia.com/articulo/2002213

7. Young AM, Donnelly J, Czosnyka M, Jalloh I, Liu X, Aries MJ, et al. Continuous multimodality monitoring in children after traumatic brain injury-preliminary experience. PLoS One. [Internet]. 2016 mar [citado 2020 ene 9];11(3):e0148817. Disponible en: https://doi.org/10.1371/journal.pone.0148817

8. Dewan MC, Mummareddy N, Wellons JC 3rd, Bonfield CM. Epidemiology of Global Pediatric Traumatic Brain Injury: Qualitative Review. World Neurosurg. [Internet]. 2016 jul [citado 2020 enero 8]; 91:497-509.e1. Disponible en: https://doi.org/10.1016/j.wneu.2016.03.045

9. Piriz Assa AR, Abdo-Cuza A, De la Cruz De la Cruz HR. Ecografía Doppler transcraneal para estimar la presión intracraneal y presión de perfusión cerebral en pacientes pediátricos neurocríticos. Rev Cuban Pediatr. [Internet]. 2022 mar [citado 2022 abr 19];94(2):e1597; http://www.revpediatria.sld.cu/index.php/ped/article/view/1597

10. Kochanek PM, Tasker NC, Carney N, Totten AN, Adelson PD, Seden NR, et al. Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines. Pediatr Crit Care Med. [Internet]. 2019 mar [citado 2019 may 3];20(3S):S1-S82. [PubMed: 22217782]. Disponible en: http://doi.org/10.1093/neuros/nyz051

11. Nacoti M, Fazzi F, Biroli F and the Collaborative Pediatric TBI Working Group. Addressing Key Clinical Care and Clinical Research Needs in Severe Pediatric Traumatic Brain Injury: Perspectives From a Focused

International Conference. Front. Pediatr. [Internet]. 2021 ene [citado 2021 feb 6]; 8:594425; http://doi.org/10.3389/fped.2020.594425

12. Abreu-Pérez D, Lacerda-Gallardo AJ, Montero-Álvarez L, Martín-Pérez JC. Neuromonitorización y manejo del traumatismo craneoencefálico grave en pediatría. Rev Cub Med Int Emerg. 2010;9 (3):1830-41.

13. Abreu-Pérez D, Lacerda-Gallardo AJ, Díaz-Agramonte JA, Martín-Chaviano D. Neuromonitorización en el trauma craneoencefálico grave en pediatría. Neurocirugía. [Internet]. 2016 jul-ago [citado 2019 dic 9];27(4):176-85. Disponible en: http://doi.org/10.1016/j.neucir.2015.11.004

14. Gallardo AJL, Pérez DA, Pazos MM, Caraguay GPV, Criales GMO, Songoro PE. Decompressive Craniectomy in Pediatric Severe Head Trauma. Int J Pediatr Res. [Internet]. 2018 jun [citado 2019 ene 9];4(1):033. Disponible en: http://doi.org/10.23937/2469-5769/1510033

15. Chesnut RM, Temkin N, Videtta W, Petroni G, Lujan S, Pridgeon J, et al. Consensus-based management protocol (CREVICE Protocol) for the treatment of severe traumatic brain injury based on imaging and clinical examination for use when intracranial pressure monitoring is not employed. J Neurotrauma. [Internet]. 2020 jun [citado 2021 ene 7];37(11):1291-99. Disponible en: http://doi.org/10.1089/neu.2017.5599 Epub 2020 mar 4.

16. Caballero-Martínez F. Mejora de un método de consenso experto para reducir la variabilidad de la práctica clínica [tesis]. Madrid (España): Universidad Autónoma de Madrid; 2014; Available from:

https://repositorio.uam.es/handle/10486/662738 [Last accessed: 12/23/2023].

17. Marshall LF, Marshall SB, Klauber MR, Van Berkum, Clark M, Eisenberg HM, et al. A new classification of head injury based on computarized tomography. J Neurosurg. [Internet]. 1991 nov [citado 2019 may 24];75(Suppl):S14-20. Disponible en: http://doi.org/10.3171/sup.1991.75.1s.0s14

18. Won SY, Zagorcic A, Dubinski D, Quick-Weller J, Herrmann E, Seifert V, et al. Excellent accuracy of ABC/2 volume formula compared to computer-assisted volumetric analysis of subdural hematomas. PLoS One. 2018 Jun 26;13(6):e0199809. Disponible en: https://pubmed.ncbi.nlm.nih.gov/29944717/

19. Abreu-Pérez D, Lacerda-Gallardo AJ. Características anatómicas y fisiológicas que influyen en la presión intracraneal y la presión de perfusión cerebral en el paciente pediátrico con traumatismo craneoencefálico grave. Medicina Clínica y Social. [Internet]. 2021 ene-abr [citado 2021 may 16] ; 5(1):44-9; https://scielo.iics.una.py/scielo.php?script=sci_arttext&pid=S2521-22812021000100044

20. Abreu-Pérez D, Lacerda-Gallardo AJ. Presión de perfusión cerebral en pacientes pediátricos con traumatismo craneoencefálico grave. Med. clín. soc. [Internet]. 2021 [citado 2023 dic 17]; 5(2):65-71; https://doi.org/10.52379/mcs.v5i2.195

21. Appavu B, Burrows BT, Nickoles T, Boerwinkle V, Willyerd A, Gunnala V, et al. Implementation of multimodality neurologic monitoring reporting in pediatric traumatic brain injury management. Neurocrit Care. [Internet]. 2021 mar [citado 2022 nov 8]; 35:3-15 Disponible: https://doi.org/10.1007/s12028-021-01190-8

22. Laws JC, Jordan LC, Pagano LM, Wellons III JC, Wolf MS. Multimodal neurologic monitoring in children with acute brain injury. Pediatric Neurology. [Internet]. 2022 feb [citado 2022 nov 12]; 129:62-71. Disponible en:

https://doi.org/10.1016/j.pediatrneurol.2022.01.006

23. Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, et al, for the Global Neurotrauma Research Group. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med. [Internet]. 2012 dic [citado 2017 mar 10];367:2471-81. Disponible en: https://doi.org/10.1056/NEJMoa1207363

24. Godoy DA, Badenes R, Murillo-Cabezas F. Diez mandamientos fisiológicos a lograr durante el traumatismo craneoencefálico grave. Rev Esp Anestesiol Reanim [Internet]. 2021 May [citada 2021 jun 30]; 68(5):280-92; http://doi.org/10.1016/j.redar.2020.09.005

25. Kayadibi Y, Tekerek NU, Yeşilbaş O, Tekerek S, Üre E, Kayadibi T, et al. Correlation between optic nerve sheath diameter and Rotterdam computer tomography scoring in pediatric brain injury. Ulus Travma Acil Cerrahi Derg. [Internet]. 2020 mar [citada 2020 may 2];26(2):212-21. Disponible en: https://pubmed.ncbi.nlm.nhi.gov/32185780/

26. Lee SH, Kim HS, Yun SJ. Optic nerve sheath diameter measurement for predicting raised intracranial pressure in adult patients with severe traumatic brain injury: A meta-analysis. J Crit Care. [Internet]. 2020 abr [citada 2020 may 2]; 56:182-87;

https://pubmed.ncbi.nlm.nhi.gov/31945584/

27. Liu M, Yang ZK, Yan YF, Shen X, Yao HB, Fei L, et al. Optic nerve sheath measurements by computed tomography to predict intracranial pressure and guide surgery in patients with traumatic brain injury. World Neurosurg. [Internet]. 2020 feb [citada 2021 ene 12];134:e317-e324. Disponible en: https://pubmed.ncbi.nlm.nhi.gov/31629929/.

28. Huijben JA , Dixit A, Stocchetti N, Maas AIR, Lingsma HF, van der Jagt M, et al. Use and impact of high intensity treatments in patients with traumatic brain injury across Europe: a CENTER-TBI analysis. Crit Care. [Internet]. 2021 feb [citado 2021 may 14]; 25:78. Disponible en: https://doi.org/10.1186/s13054-020-03370-y

29. Delaplain PT, Grigorian A, Lekawa M, Mallicote M, Joe V, Schubl SD, et al. Intracranial pressure monitoring associated with increased mortality in pediatric brain injuries. Pediatric Surg Int. [Internet]. 2020 ene [citado 2021 oct 1];36:391-98. Disponible en: http://doi.org/10.1007/s00383-020-04618-y

30. Laws JC, Jordan LC, Pagano LM, Wellons III JC, Wolf MS. Multimodal neurologic monitoring in children with acute brain injury. Pediatric Neurology. [Internet]. 2022 feb [citado 2022 nov 12]; 129:62-71. Disponible en:

https://doi.org/10.1016/j.pediatrneurol.2022.01.006