PROGNOSTIC VALUE OF THE SODIUM ALTERATIONS DURING THE FIRST SEVEN DAYS IN ADULTS PATIENTS WITH SEVERE BRAIN TRAUMA OF THE AUTONOMOUS INSTITUTE UNIVERSITY HOSPITAL OF LOS ANDES MERIDA BETWEEN JUNE 2017 - JUNE 2018

Luis Dulcey 1, Jonathan Pineda1, Hector Moreno1, Jose Sampayo1, Raimondo Caltagirone 2, Diana Marcela Villamizar Olartec 3
1 Residents in Internal Medicine ULA,
2 Specialist in Internal Medicine ULA Mérida,
3 Specialist in Physical Medicine and Rehabilitation
University Hospital of the Andes Mérida, Avenue. 16 of September Service of Internal Medicine Mezzanine Level. Telephone Number +573209671101. Electronic address:
luismedintcol@gmail.com

ABSTRACT
Objectives To establish the prognostic role of serum sodium alterations during the first seven days in patients diagnosed with severe brain trauma admitted to the adult emergency area of the autonomous university hospital of the Mérida Andes, from June 2017 to June 2018 Materials and Methods: Prospective, field and longitudinal sectional study. Patients older than 18 years with a diagnosis of head brain injury were selected, diabetes insipidus, inappropriate antidiuretic secretion and salt loser brain were evaluated in each patient of the sample. Results: 103 patients, 90.6% men and 9.4% women, the mean age was 25.8 years, the largest age group corresponded to those under 30 years, 79 (76.9%), accidents of Transients were the main cause of brain trauma 79 (76%), brain edema was the main tomographic finding, all tomographic findings showed statistical significance. The 3 types of neuroendocrine disorders related to sodium were presented, being diabetes insipidus the most frequent. total mortality was 22 (22.63%) patients of 103. Neurosurgical interventions were performed in 10 patients with a mortality of 8 (80%), (p <0.001). The Glasgow score in the live group was 9.7 compared to 6.3 points in the deceased subgroup (p <0.001). Conclusions: There is a higher mortality associated with sodium alterations, the greatest association corresponded to diabetes insipidus (p0.026), so it is vital to adequately manage these alterations.
Keywords: Craniocerebral Trauma, Diabetes Insipidus, Syndrome of Inadequate ADH Secretion, Mortality.

INTRODUCTION

Traumatic brain injury is a major public health problem in today's society in both developed and developing countries; traffic accidents and violent events continue to increase throughout the world, and despite the creation of new diagnostic means, the introduction of new neuro-protective drugs and the specialization in neuro-critical care, this type of trauma continues to have the highest mortality rate among all the types of trauma caused by the noxes that it generates\textsuperscript{1-2-3}. Acute brain injury triggers a damaging response characterized by local and systemic biocellular and molecular alterations, which create the conditions for further brain damage or determine secondary damaging processes that initiate or increase this response. Among them, changes in sodium, glycemia, and cellular and plasma osmolarity stand out. Alterations in sodium levels are among the most frequent complications presented by patients with traumatic brain injury of any nature, being greater in the case of severe\textsuperscript{4-5}. After trauma, edema at the cerebral level can stimulate an excessive release of antidiuretic hormone by the neuro axis pituitary and hypothalamus and renal tubules, which causes accumulation of water and dilutional hyponatremia, producing the syndrome of inappropriate secretion of antidiuretic hormone or its defect the presence of low secretion of this antidiuretic hormone may occur, resulting in diabetes insipidus\textsuperscript{3}. Although hyponatremia is often the consequence of brain damage, it becomes a new insult that worsens pre-existing damage, contributing to a worse outcome for patients with head trauma. It is of great importance the timely recognition and appropriate behavior before the neurocritical patient with sodium disorders, since these circumstances are the cause and other times in the patient with brain damage\textsuperscript{6-7-8-9-10-11}.

Multiple reviews have investigated the predictors of mortality from severe traumatic brain injury, concluding a statistically significant relationship between sodium disorders and increased plasma osmolarity, with these conditions increasing the mortality of the patients studied; Noting that despite the use of hyperosmolar substances for the management of cerebral edema, the guidelines for the treatment of head trauma are worth mentioning, it is important to periodically monitor serum osmolarity as well as sodium values and immediately correct any alteration outside the limits of desired values\textsuperscript{12-13-14-15-16-17-18}.

In this sense, it is for this reason that this study is proposed to evaluate the presence of Sodium disorders associated with the diagnosis of severe head trauma in view of the fact that its presence is related to a worse outcome, as well as being able to objectify the type of disorder through laboratory
tests for this purpose, in order to develop an effective medical practice in terms of the care of these patients, which are one of the main causes of morbidity and mortality in our city as well As in other regions of the country, it is appropriate to develop strategies for monitoring and early correction in order to improve the outcome of these patients, most of whom are young, and this affects the development of the nation due to the significant economic burden imposed by their care. as well as for the relatives for the serious consequences that could be triggered, therefore l The implications in all areas of the patient's environment become catastrophic.19-20-21-22-23.

Given that sodium alterations are associated with high morbidity and mortality, an observational cross-sectional study was carried out on the prevalence of these disorders, which is often underestimated in the adult emergency area of IAHULA Mérida during the June period. 2017 to June 2018 in order to know their frequency of presentation and subsequently know if our results are similar to the data presented in the literature in this regard in order to raise awareness about it and thus improve our comprehensive management approach to these patients.

One of the main difficulties is the limited literature available on the prevalence of sodium disorders in the context of head trauma, as well as publications on the specific topic of the use of therapeutic agents as part of a series of strategies that improve the prognosis of these patients.

Despite the current advances in the management of traumatic brain injury and the many strategies in this regard, although mortality rates have decreased significantly, doubts persist today regarding its management, as well as the need to investigate new strategies to optimize the prognosis. so complex of this picture.

The adequate evaluation and monitoring of sodium levels in these patients requires that the medical personnel involved in the management of these patients know the importance of these alterations in natremia and the implications regarding morbidity and mortality of these disorders, however, a large part of the Medical and nursing personnel do not pay attention to this variable due to ignorance on the subject, leading to a negative outcome and a worsening of the prognosis.

Given this fact, there is a need to know the pathophysiological mechanisms as well as the forms of presentation of these disorders and the measures to be taken before each of them in order to make them known to the medical and nursing staff who work at the Autonomous Institute Hospital Universitary de los Andes.
METHODOLOGICAL FRAMEWORK

OBJECTIVES OF THE STUDY

**General purpose**
To know the prognostic value of sodium alterations in patients admitted the first seven days with a diagnosis of severe traumatic brain injury to the emergency area of the Autonomous Institute Hospital Universitary de los Andes Mérida Venezuela in the period from June 2017 to June 2018.

**Specific objectives**
I. Describe the sociodemographic variables in the patients in the study.
II. Describe the mechanism of ECT in the patients in the study.
III. Describe the neurotomographic findings at admission, day 4 and 7 of admission of the patients included in the study.
IV. Describe the neuroendocrine abnormalities related to sodium on admission, day 4 and 7 of hospitalization in all the patients included in the study.
V. Describe the presence of sodium-related neuroendocrine disorders and survival in the first 7 days of the patients included in the study.
SAW. Correlate mortality in the first 7 days in patients with severe head trauma and associated factors in patients included in the study.

**Design of the investigation**
Prospective field study and longitudinal section

**Population and Sample**
214 patients entered the Adult Emergency Service of which only 103 could be taken that applied to the admission criteria, all had a diagnosis of severe head injury in the period from June 2017 to June 2018.

A. Inclusion criteria
to. Patient ≥18 years
b. Both genres
c. Trauma to the head of the brain according to the Glasgow classification.
d. Patient under Mechanical Ventilation
B. Exclusion criteria

to. Brain death
b. Patients requiring diuretic therapy
c. Acute kidney failure of any kind
d. Chronic Renal Failure in hemodialysis
and. Use of hypertonic solutions beyond 5 days.
F. Mechanical ventilation greater than 8 days.

Variable System
The following reference information will be evaluated in the patients included in the study:

I. Sociodemographic variables
to. Age
b. Sex
c. Origin
d. Occupation

II. Independent variables
to. Trauma Mechanism
b. Tomographic findings
c. Serum sodium value
d. Urinary density value
and. Type of sodium disorder

Bias control
Depending on the stage of the study in which they originate, the biases that interfere with the internal validity of a study have been classified into three main groups: a) selection biases, which refer to the errors that are introduced during the selection or monitoring of the study population; b) information biases, which are errors that are incurred during measurement processes in the study population, and c) confounding biases, which are caused by the impossibility of assigning exposure randomly in observational studies. and that basically originate from a non-comparability of the study groups. All non-experimental epidemiological design, to a greater or lesser extent, is susceptible to this type of
bias, so it is an imperative for researchers to adequately plan each stage of a study in order to avoid or minimize the possibility of making such mistakes.

Data processing and analysis
The information collected through the data collection tab in the Microsoft EXCEL 2011 program was tabulated. Later it will be processed in the SPSS program version 20.0 for Windows, applying measures of central tendency (mean, median and mode) and dispersion measures (range, variance and standard deviation). The T-Student test for dependent samples was applied when it was two measures and the Chi-Square test, in order to analyze and generate the discussion and conclusions of the study.

Ethical considerations
The carrying out of this work was in accordance with the recommendations for biomedical research of the Declaration of Helsinki of the World Medical Association at its 64th General Assembly, in Fortaleza, Brazil, in October 2013 and the provisions of the Code of Medical Deontology of the Venezuelan Medical Federation of March 20, 1985, in its Title V, Chapter 4, referring to research in human beings. Additionally, all patients who met the inclusion criteria and have the authorization of the family member to participate in the research, this will be informed the purpose of the research by the principal investigator verbally and once the family member or patient is adequately informed and agrees to be part of the study, will sign the informed consent specifically designed for this research (Annex 4).

RESULTS
Although 214 patients were found, 103 patients with clinical criteria for severe traumatic brain injury on the Glasgow scale who were admitted to the IAHULA adult emergency service in the city of Merida were included in the study. 90.6% (n: 94) corresponded to the male gender, the remaining 9.4% (n: 9) were female.

The distribution by age groups was carried out in three groups: those under 30 years of age, 31 - 44 years old, and 45 or over.

According to the clinical histories evaluated, the main mechanism of appearance of the TEC corresponded to vehicular accidents with 76%, followed by physical assaults with 12%, thirdly occupational accidents (8%) and lastly home accidents (4%).
A peak was observed in the month of December 2017, secondly in March 2018 and thirdly in February 2018.

It was noted that upon admission, cerebral edema was present in the entire sample, as well as subarachnoid hemorrhage in 61 (59.2%) patients, hemorrhagic contusions in 46 (45%) patients and parenchymal hematoma in 32 (31.06%) patients, all showing statistical significance (0.043). On day 4 it was observed for patients that cerebral edema decreased to 94 (91.26%), subarachnoid hemorrhage increased to 65 (63%) in the study members, hemorrhagic contusions increased to 54 (52.42%) patients and intraparenchymal hematoma was maintained in the same proportion compared to admission with one (p 0.031), the Greene mode was IIIA.

Finally on day 7 the number of patients with cerebral edema decreased to 86 (83.49%), subarachnoid hemorrhage increased to 68 (66.01%), likewise hemorrhagic contusions increased to 58 (56.31%) and in the case of intraparenchymal hematomas, there was no change since admission, all these correlations showed statistical significance (p 0.027) and the Greene mode was maintained compared to day 4.

The distribution was made based on the 3 sodium-related neuroendocrine abnormalities and head trauma. On admission, none of the patients presented sodium-related neuroendocrine disorder and traumatic brain injury. On day 4 of admission 10 (9.7%) patients presented Diabetes insipidus, and on day 7 it was seen in 7 (6.79%) patients, respectively. For inappropriate antidiuretic hormone secretion, this alteration was observed on day 4 in 8 (7.8%) and by day 7 it was seen in 4 (3.88%) patients. Finally, in the case of Salt Losing Brain, by day 4 this disorder was observed in 4 (3.88%) of the patients and on day 7 it was determined in 5 (4.85%) patients.

During the 7-day follow-up of the patients, it was observed that at admission no patient underwent neurosurgical intervention, on day 4 of the event 7 patients had undergone surgery. On day 7 of the event, 3 new patients were brought to the operating table for a total of 10. None of the initially operated patients required new reoperations of the neurosurgical type.

Diabetes insipidus, inappropriate antidiuretic secretion and salt-losing brain were defined as variables, as well as 7-day survival or not. It can be seen that the results of the independence tests for the variables in the case of each of the disorders presented there was a highly significant statistical correlation regarding their association with mortality in the first 7 days.

As it could be seen, 22 (22.66%) deaths occurred, the mean age of this group being higher compared to the group of living patients, this finding showed a quite significant statistical significance (<0.001). Regarding gender, the highest frequency of events occurred in the male group with percentages greater than 90% for both living and deceased (<0.001).
Regarding the association between days of mechanical ventilation and mortality, the mean was 6.8 days for the group of deceased and 4.6 days for the group of living patients with a statistical significance of (p 0.046).

Diabetes insipidus was found in 11 patients, with a higher frequency in 9 (81.8%) of the deceased in the study (p 0.026), for inappropriate antidiuretic secretion, this event appeared in 8 study members and was more frequent in the group of deceased 5 (62.5%) with said disorder (p 0.042).

For the salt-losing brain variable, this event was found more frequently in the group of deceased 4 (66.66%) compared to those living with a statistically significant value (p 0.031).

The neurosurgical intervention variable was performed in 10 patients, with a higher mortality observed in this group of patients 8 (80%), with a P value of <0.001. The Glasgow score in the living group was 9.7 compared to 6.3 points in the subgroup of deceased, the p value for this variable was <0.001.

**DISCUSSION**

Once the results of our study are presented, we can conclude and infer the following. Regarding the distribution by genders, the male group was much higher, the largest age group was made up of those under 30 years of age, this finding agrees with that found in other studies such as that of Chicote et al\(^{31}\) where the population is mainly young productive ages.

The main generating mechanism of the TEC corresponded to road events of any kind, which is consistent with studies carried out in other latitudes such as that of Stolwyk et al\(^{32}\), where it was found that the main producing mechanism of the TEC is secondary to automobile accidents.

Regarding the distribution by time of year, a higher frequency was observed during the month of December 2017, which is consistent with the festivities and the higher consumption of alcoholic beverages, as was observed in the study by Gerritsen et al\(^{33}\), where the association consumption was evidenced. of alcohol with this type of event and was also determined as a factor of worse prognosis.

The main finding observed in the skull scans of the patients in our study corresponded to cerebral edema resulting from ECT, followed by subarachnoid hemorrhage, later hemorrhagic contusions and finally intraparenchymal hematoma, additionally the mode of Greene's score to evaluate the tomography. It was II on admission and IIIA on days 4 and 7, the findings found in the tomography are consistent with what was found in the study by Mariños \(^{34}\), where the main findings are Greene II and IIIA.

Regarding neuroendocrine disorders, the main one observed was diabetes insipidus, secondly inappropriate secretion and lastly the salt-losing brain, our results are similar to those reflected in Dr.
Tan's review in which mention is made diabetes insipidus as the main disorder, in the second instance the inappropriate secretion of antidiuretics and lastly the brain that loses salt. For the variable need or not for neurosurgical intervention in the first 7 days, it was observed that only 10 of the 103 patients, of whom 7 were performed on the 4th day and 3 of them on day 7 of the event, no patient underwent surgery. day of admission, these findings are consistent with Dr. Morrison's review\textsuperscript{35} of 22,229 patients over a 10-year period in Pennsylvania where the proportion of patients operated on is close to 10% of admissions with severe ECT, results very similar to our study. When the 7-day survival was correlated or not in relation to the sodium disorders presented, a higher mortality was observed in those patients who developed any of the 3 disorders, but mainly Diabetes insipidus, which in itself was the most frequent of the 3, this This finding is in agreement with that observed by Hannon\textsuperscript{36} where diabetes insipidus linked to ECT significantly increased mortality and hence the recommendations for timely management of this complication or any of the remaining 2. Finally, it was observed that within the factors associated with mortality in the patients of our study, the mean age was 24.6 years for the group of the living and 38.9 years for that of the deceased, finding a statistical correlation of higher mortality in the longest-standing age groups as seen in the study by Murray\textsuperscript{37} et al. There was a higher mortality in the male gender related to the greater frequency of this type of events with motorcycle driving. A higher mortality was observed in the group subjected to a longer mechanical ventilation time of 5.9 days compared to that group that only stayed for 4.6 days, this finding agrees with that reported by Omar\textsuperscript{38} and collaborators where the longer the mechanical ventilation time, the greater were the complications for these patients. For the neurosurgical intervention variable, it was appreciated that only 2 of the patients who underwent this behavior survived and 8 of the patients who died died, this finding can be inferred that it is a consequence of the greater severity of the injuries and the prognosis of the group of patients operated on as has been validated in studies such as Owens\textsuperscript{39} conducted in Ireland where mortality was much less than just 12% compared to the 21.35% reported in the present study. Finally, it can be seen that the group of patients who survived had a Glasgow average of 10 compared to the group of the deceased, where the average was 6 with a value of p <0.001, this finding is correlated in the study by Rocchetti and collaborators\textsuperscript{40}, where the Glasgow score below 10 points, was correlated as a determinant of mortality.
CONCLUSIONS

Regarding the sociodemographic variables in the patients in the study, the majority were from the male gender and those under 30 years of age, all as a consequence of the use of vehicles in individuals of these age groups and gender.

The main mechanism of traumatic brain injury corresponded to traffic accidents, all of this conditioned by the lack of state policies aimed at reducing their frequency.

The neurotomographic findings during admission on day 4 and 7 were mainly cerebral edema and subarachnoid hemorrhage of traumatic origin, these findings in the brain tomography correspond to the magnitude of the trauma and the mechanism by which they occurred.

The neuroendocrine alterations of sodium related to head trauma in relation to the type and peak with which they appeared was very similar to that reported in the literature, so we should not underestimate their frequency and wait for them in those time periods.

The presence of neuroendocrine disturbances of sodium related to head trauma decreased the survival in the first 7 days, with the majority of deaths occurring in the first 5 days, so it is essential to monitor patients more vigorously during this period of time.

The main factors involved in the mortality of the first 7 days in the patients corresponded to the time of mechanical ventilation, age, gender, presence of neuroendocrine sodium disorder related to traumatic brain injury, and additionally, it was observed that the subgroup of patients who were taken A neurosurgical intervention showed a worse clinical outcome, therefore, close monitoring of these patients is essential.

RECOMENDATIONS

1. Expand the medium and long-term follow-up, to assess the role of sodium disturbances in patients with brain trauma.

2. Measure the effects of lack of treatment in patients with any of the neuroendocrine sodium disorders related to traumatic brain injury.

3. Expand the patient sample in order to improve the statistical power of this study and to be able to carry out a multicenter study, including highly complex hospital centers from other latitudes.

4. Sensitize adult emergency service personnel regarding the high mortality and prognostic implications of sodium disturbances in these patients.

5. Generate guidelines in the management of these patients to improve their prognosis and decrease morbidity and mortality in head trauma.
6. Implement traffic accident prevention programs and also explain to the population the potential risks of the association between driving some type of vehicle combined with alcoholic beverages.

7. Establish tools in the clinical practice of the Adult Emergency Service to assess the risk of these patients, establishing an adequate prognosis.

8. Continue with related research in the line of hydroelectrolytic alterations and mortality in head trauma.

9. Carry out neuroimaging studies at the most opportune moment for the patient, prioritizing their stabilization.

10. Coordinate actions with other services so that the multidisciplinary management of these patients improves the results in terms of morbidity and mortality.

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