Fluid therapy of brain edema and intracranial hypertension in children

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Background

Brain edema (BE) and intracranial hypertension (ICH) are the common severe syndromes in the Dept of Pediatrics and Neurology. There is a great change of the research of the pathophysiology and treatment of these syndromes in the last 30 years.

Stage of limitation of both fluid and salt intake

Time earlier than 1975, the fluid intake of the BE and ICH in children were limited <1,000-1,200 mL/m²·d or <30-60 mL/kg·d (1-3). Both intake of fluid and sodium salt (NaCl) were limited in order to reduce the edema of brain. Mannitol and diuretics were already used in that time, some patient after treatment passing a lot of urine and became dehydrated but the intake of fluid and salt were still limited. The fault of the treatment caused dehydration, and even shock etc., the mortality of BE and ICH in children was very high even >60% (4) in that period.

Stage of no limitation of both fluid and salt

There were quite a number of reports discovered that the fault of treatment of BE and ICH in children with the strict limitation of both fluid and salt and the change of this principle of treatment in 1979-2002 (4). For example Gellis SS et al. (ed) Current Pediatric Therapy 1971 (5th ed) limited the fluid intake of BE in children to 1,000-1,200 mL/m²·d and limited the salt intake too (1). The 13th ed (1990) of that book no limitation of fluid and salt intake and maintained the normal fluid and electrolytes balance was its principle of treatment (5). Youman JR Neurological Surgery 4th ed (1996) made clear the principle of treatment for the ICH of traumatic brain injury (TBI) should maintain the balance of body fluid and electrolytes (6). Since then the majority textbooks with no more limitation of fluid and salt intake treatment for both BE and ICH in children. However, only a few textbooks still persisted the limitation of fluid principle of treatment (7).

Stage to maintain proper cerebral perfusion pressure (CPP)

There are quite a number of research discovered that to maintain the proper CPP is very important in the treatment of TBI. It is very important of maintaining CPP to 70-100 mmHg in order to avoid the secondary injury of anoxemia of brain after TBI, which is said to be the most important factor to influence the prognosis.

The mechanism of lowering of CPP after TBI

CPP=BP-ICP. CPP’s normal range is about 70-100 mmHg (8). The cerebral blood flow is direct proportion to CPP and inverse proportion to cerebral vascular resistance (CBF = CPP / CVR). Youman’s Neurosurgery (2004) presented the normal cerebral automatic vascular regulation maintained the CPP about 50-150 mmHg and maintained the CBF in normal range. In severe TBI, the ICP raised up and/or BP lowered down, cerebral vascular resistance increased etc., all these factors lowered down the CBF. The treatments of severe TBI at time of lowering down the CPP, was to rise up the BP or to lower down the ICP (9).

Juul (2000) discovered that to rise up the BP of the TBI patient by iv hypertonic saline or dopamine etc. seems easier
to rise up the CPP. He used these treatments to rise up the BP 30 mmHg with no significant change of the patient’s ICP (10).

Tan (2005) animal experiment of TBI and BE in rabbits: the result discovered that the group which CPP maintained 60-80mmHg, the average BE was mild than the groups CPP <50 mmHg or >90 mmHg (11).

The joint venture of the brain trauma foundation etc. (2003)
Considered that the treatment of patient of severe TBI of adult with ICH, the CPP should be maintained >60-70 mmHg (12). Both text books of Nelson’s Pediatrics of 2004 and 2007 pointed out that the CPP of BE in children should be maintained: Infant and young children >40 mmHg, children >50 mmHg, young adult >60-70 mmHg (13,14).

The current clinical treatment of BE and ICH in patients by the use of hypertonic saline solution (HTS)

Mechanism of treatment of HTS
After iv injection of HTS it raised up the serum Na+ concentration and the osmotic pressure. Then the tissue fluid is absorbed into the intravascular space resulting to reduce edema of brain tissue. As compared with mannitol, HTS is less easier to pass the blood brain barrier (BBB) and formed a blood brain gradient between the intra and extra vascular spaces, thus both the BE and ICH are reduced.

The clinical research of HTS treatments
Rockswold (2009) treated 25 cases of TBI with ICH. The average GCS was 5.7, one dose of 23.4% of NaCl 30 mL/15 min, iv. The average reduction of ICP was 8.3 mmHg (P<0.0001) and the Pbt O2 improved 3.1 mmHg (P<0.01). The CPP before treatment <70 mmHg and the average increasing of CPP after treatment was 6 mmHg (P<0.0001). No significant complication of the treatment was seen in this group. Follow up 6 months: mortality 28%, prognosis of dichotomy of GCS fairly well. The conclusion: one dose of 23.4% NaCl iv improved both the CPP and brain tissue oxygen tension (PbtO2) of the patients (15).

Yildizdas (2005) treated 67 similar cases of BE patients of Dept of Pediatrics. They were divided into 3 groups. (I) Mannitol group 22 cases with 0.25-0.5 g/kg iv and the average time of coma was 123.0±48.2 days, mortality 50%. (II) HTS group 25 cases 3% of HTS maintained of the serum Na+ 155-165 mmol/L, and the average time of coma 88.6±4.25 days, mortality 25%. (III) Use HTS and mannitol alternatively for 20 cases, average time of coma was 87.52±26.1 days, mortality 20%. The mortality of group (I) in compared separately with group (II) or (III), with significant difference (P<0.05).There were 4 (8.9%) cases of the 45 HTS treated cases discovered to have high choric acidosis. The conclusion was HTS or alternate with mannitol treatment for BE in children was better than mannitol treatment alone (16).

To reduce the mortality of TBI complicated with shock: These cases of severe TBI frequently accompanied with hemorrhagic shock while the tissue perfusion was impaired and the mortality may increase of double times (17). HTS iv treatment quickly increased the osmolarity and volume of blood and improved the tissue perfusion. There was report of the use of HTS treatment for TBI complicated with shock, and increased its survival rate double times (18).

Side effects of HTS treatments
HTS iv may induce high osmolarity of serum and renal failure. Khanna (2000) iv HTS to treat the severe cases of TBI in children complicated with ICH for 10 cases (while the other treatments all failed). 3% HTS iv was given continuously to maintain the serum Na+ 157-187 mmol/L (normal <150 mmol/L) and blood osmolarity 330-431 mOsm/L (normal <320 mOsm/L) for 48-72 hrs. At time of these treatments the ICP lowered and CPP rose significantly. Two of the 10 cases developed renal failure that were cured after treatment of hemodialysis (19).

Yildizdas use 3% HTS iv to treat BE in children for 45 cases, 4 (8.9%) of them discovered to have high choric acidosis (16).

The conclusion: (I) HTS induced high serum Na+ and blood osmolarity which were very effective to increase of CPP and lowering of ICP; (II) These important side effects of HTS were high choric acidosis or occasional renal failure.

The use of hypertonic NaHCO3

The use of hypertonic NaHCO3 for the treatment of BE and ICH in children

According 3581 cases of BE and ICH of children in the BE of Children Association Research Group of 16 Hospitals in China, more than 80% of these cases who were complicated with acidosis (20). Acidosis increases the
permeability of the blood brain barrier (BBB) and the BE aggravated. Therefore the correction of acidosis in cases of BE was very important. The first step of treatment in these groups was given iv hypertonic NaHCO$_3$ of 4% (or 2% for infant) 6 mL/kg/dose iv (or by drip) for one dose. Several doses were continued to correct the metabolic acidosis and rising up the CO$_2$ combining power to 40 vol% (normal range, 40-60 vol%).

The use of hypertonic NaHCO$_3$ in these groups was in large doses and with few side effects. The mortality in these groups of treatment were significantly reduced (P<0.01) (4). For example: a boy of 9 years old was admitted to our ward because of septic shock, BE, hernia with respiratory failure. The 2 syndromes of shock and BE occurred alternatively for 3 or 2 time. The 4% NaHCO$_3$ 790 mL and 20% mannitol 200 mL, ethacrynic acid 20 mg etc. were given in the first 14 hrs of his admission to promote the “Replenishment of body fluid together with dehydration” according to the change of patients condition, and the regulation of treatment from time to time quickly, so called Bian Zhan Lun Zhi (BZLZ) fluid therapy (4). This was the case who was given the largest dose of 4% NaHCO$_3$ and was cured in these groups.

Together with the use of hypertonic NaHCO$_3$, there were the unified clinical diagnostic criteria of BE of children (21) and BZLZ fluid therapy etc. in these research groups. One of the important point, a special doctor or experienced nurse was arranged to watch the patient from time to time for the first 24 hrs to regulate the therapy. There were also principles of treatments of “crystallized fluid first then colloid, dehydration and correction of the acidosis together with the replenishment of the potassium, calcium and magnesium etc.” (4).

The fluid intake on the first day of the survived patients in the several subgroups various a great deal ranging of “34-201 mL/kg·d (4), 40-203 mL/kg·d (21), 32-220 mL/kg·d (22), or 50-208 mL/kg·d” (20). The lowering of the mortality of the two sub-groups were 19.66% or 17.2% respectively (P<0.01) (4).

The side effects of hypertonic NaHCO$_3$ iv together with mannitol and furosemide treatments

The important side effects in these groups were the disturbance of the blood electrolytes such as low serum K$^+$, Ca$^{2+}$ or Mg$^{2+}$ etc. The disturbance of these electrolytes occurred quickly after the treatment of mannitol, diuretics and hypertonic NaHCO$_3$ etc. And the most important one was the hypokalemia which might even endangered the patients' life (4,20). Therefore the close watch the rearrangement of treatment with the change of patient’s blood and electrolytes was very important in these treatments.

The results of these research works indicated that the BE and ICH of children tolerate the hypertonic NaHCO$_3$ together with BZLZ fluid therapy fairly well and with the lowering of the mortality of these patients (4).

Conclusion and suggestion

According to the results of the above research work of China, the treatment of BE and ICH in children with hypertonic NaHCO$_3$ and BZLZ fluid therapy showed fairly good result and with only a few treatable side effects. The effect of hypertonic NaHCO$_3$ treatment might act just as the HTS and in addition it corrected the metabolic acidosis that seems better than HTS. Since few report was seen for these treatments abroad, thus the authors give suggestion of the popularize the use of hypertonic NaHCO$_3$ for the use of clinical treatments.

Conclusions

It might be better to use hypertonic NaHCO$_3$ rather than HTS for the treatment of BE and ICH in children complicated with metabolic acidosis. Thus it is the suggestion of this paper to use the former taking place for HTS in these cases.

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

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