

Neglected Atypical Pyridoxine Dependent Seizures

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Vitamin B6 (pyridoxine) dependent seizure (PDS) is an autosomal-recessively inherited disorder which starts within a few hours of birth or even earlier, and can cause intrauterine seizures^[1,2]. It occurs while the serum level of B6 vitamin is normal. It is the result of a defect in pyridoxine binding to its apoenzyme glutamate decarboxylase which finally leads to reduced concentrations of Gamma-aminobutyric acid (GABA). Low concentration of GABA is related to decreased seizure threshold^[3]. The frequency of PDS is unknown and limited cases have been reported worldwide^[4]. Some cases from Iran have already been reported too^[5]. Typical PDS is diagnosed according to the following criteria described by Baxter:

- 1) Seizures resistant to traditional antiepileptic treatment
- 2) Cessation of seizures with pyridoxine administration,
- 3) Complete seizure control on pyridoxine monotherapy
- 4) Recurrence of seizures upon pyridoxine withdrawal^[6].

Patients with atypical forms of PDS are more frequently reported than those with classic forms. Atypical PDS must be highly noted regarding the following specifications:

- 1) Initial response to anticonvulsants
- 2) No recurrence of attacks even after 6 weeks of pyridoxine or anticonvulsant discontinuation
- 3) Initial failure of response to pyridoxine in the first 8 months of life.

These items lead to delayed diagnosis of atypical PDS. This was the case in our following patients.

Case 1: This 6-month-old girl was admitted to emergency room of pediatrics department of Alzahra hospital in Isfahan with status epilepticus and hypothermia. The patient had recurrent tonic seizures since she was 1 month old. She was the third child of a family with three children. Her parents were not related, no family history of epilepsy or any other type of seizure was present. The other two children were healthy. Pregnancy and delivery was uneventful. Birth weight 3000 grams. Her development was delayed. With anti-epileptic drugs like phenytoin, phenobarbital and clobasam in full therapeutic dosage the seizures were temporarily controlled during several previous hospitalizations in other centers but recurred every time after discharge from hospital. EEG showed sharp waves, brain CT scan was normal. At admission, all laboratory tests were normal. Metabolic tests, amino acid chromatography with BALL method, plasma ammoniac and blood gas were normal. After admission, 100 mg intravenous vitamin B6 was given as loading dose, continued by 40mg per day orally. After 3 days, she was discharged without any seizure recurrence. Other antiepileptic drugs were gradually tapered. Under continued pyridoxine monotherapy she became completely seizure free, and at the age of 6 years she went to school with normal mental development and normal EEG.

Case 2: This patient was a 4-month-old girl, the second child of healthy unrelated parents, delivered after a normal term pregnancy by cesarean section. Birth weight was normal. No family history of epilepsy or any other type of seizure. The patient was frequently admitted to our hospital for intractable seizures: tonic seizures with upward gaze that began on 12th

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day of life. In EEG sharp waves were detected. She was treated with phenobarbital.

Two months after discharge from hospital she was readmitted for repeated attacks of tonic seizures. Physical examination revealed no abnormality.

Routine laboratory tests were normal and TORCH negative.

Anti epileptics were administered again and she was discharged on phenobarbital and phenytoin. Brain CT scan showed now in 2 months of age frontal atrophy.

Special screenings including metabolic tests, amino acid chromatography with BALL method, plasma ammoniac and blood gas were normal. In consequence, she was admitted 2 times again with tonic seizures, upward gaze, staring and excessive crying that was controlled by adding Nitrazepam to her previous drugs, but after a few days she had to be readmitted with recurrence of seizure. This time 100 mg pyridoxine was administered intravenously whereupon convulsions stopped in a few minutes. She was discharged with maintenance dose of pyridoxine 40mg/day. Convulsions stopped and EEG became normal. Other antiepileptic drugs were gradually discontinued.

After one month of treatment a period of seizure occurred again, it was due to discontinuation of pyridoxine and was controlled by re-administration of the vitamin. Now at the age of 3.5 years, the patient is completely seizure free, receiving pyridoxine monotherapy, with normal mental development.

Affected patients usually present impaired mental development especially in the case of verbal abilities. But appropriate usage of pyridoxine may prevent or even reverse this impairment provided that early neurological examinations especially head circumference is normal^[7]. In our patient early neurological examinations were normal and despite occurrence of several seizure attacks, after pyridoxine therapy ultimately proper mental development was achieved.

PDS patients usually show an EEG pattern containing sharp waves. In a few minutes after pyridoxine administration this pattern becomes normal^[7]. This was seen also in our patients.

Although the diagnosis of PDS can be confirmed by genetic and biochemical testing, clinical suspicion is the mainstay for proper diagnosis^[8].

Concluding all, the clinicians should always consider PDS in patients with intractable seizure according to the importance of early diagnosis and treatment of PDS to avoid prolonged time between presentation and diagnosis which has been around 18 months in some cases^[8].

Pyridoxine must be initiated as soon as physicians encounter these patients especially in the first two years of life.

Key words: Pyridoxine; Seizures; Vitamin B6

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Tourniquet Test Positive, High Fever and a Pediatric Case of Swine Flu

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Swine flu is the present problem of the world. In the tropical countries, swine flu is still pandemic.

The author hereby reports and discusses on a pediatric case of swine flu. The case is a 7 year-old boy (body weight 28 kg) presenting to the primary care center in Bangkok, Thailand with the complaint of high fever, non productive cough, nausea, vomiting and malaise. His body temperature was 39.2 °C. His throat was red and lung clear. The attending physician performed tourniquet test and got positive result. The boy was referred to the hospital for further proper management. At the hospital, complete blood count was done and no thrombocytopenia could be detected. In this case, the finalized diagnosis as swine flu was derived. The Real time PCR test was done to confirm new H1N1 influenza virus infection (confirmation was performed at Thai Department of Medical Science). During hospitalization, investigations done to rule out co-existing dengue fever or other infections included hemoculture, dengue serological study (paired serum test) and Chikungunya serological study (results of all tests were negative). Chest X ray was also done in this case and there was no lung involvement. This case was treated by antiviral drug (Oseltamivir 60 mg twice daily) and got full recovery within 10 days. Of interest, high fever and flu like symptoms are non significant and several tropical diseases can have this presentation. In Thailand, dengue infection is common and tourniquet test is helpful in screening and diagnosis^[1]. Indeed, the important differential diagnoses for positive tourniquet test include dengue hemorrhagic fever and some other viral hemorrhagic fever (such as Rocky mountain spotted fever and Chikungunya fever)^[2,3]. In this case, positive tourniquet test could be seen in a case of swine flu, which is not a viral hemorrhagic disease. This observation could be due to the fragile nature of the child or the exact undisclosed pathological process of the new influenza virus infection. The possible

mechanism causing tourniquet positive might be due to swine flu induced thrombocytopenia. This requires further study for clarification. Indeed, there is no similar case in the literature. For the tropical doctors in the endemic areas of dengue, it is necessary to think of swine flu in positive tourniquet test case in the present situation of pandemic swine flu^[4].

Key words: H1N1 Virus; hemorrhagic fever; Tourniquets

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Comparison of Effect and Side Effects of Acetaminophen and Ibuprofen in Treatment of Febrile Children

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Fever is a common pediatric problem accounting for 25-30% of emergency department and clinic visits each year. Although it usually indicates minor infection, it can also be a sign of serious life-threatening disease.

Acetaminophen is usually mentioned as the medication of choice, while ibuprofen is also recommended to be given for high-temperature fevers^[1]. However, due to the potential side

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effects of these medicines, the use of antipyretics for the management of pediatric fever remains controversial^[2].

In a meta-analysis of all studies in which single-dose acetaminophen or ibuprofen were measured in a randomly blinded way in children, was concluded that ibuprofen was a more effective antipyretic than acetaminophen. There was no difference in safety between the two drugs or among these two and placebo. The recommendations in the recent literature varied between the "very safe" acetaminophen to the "slightly more effective" ibuprofen, yet answering a parent's question about which drug is "better" was difficult. Single doses were compared over a period of three to 12 hours. There was less consistency in both number and nature of outcome measures^[3].

A randomized, double-blind and case-controlled clinical trial study, was performed on 100 children between six months to 12 years of age admitted in Imam Sajjad Hospital Yasuj, southwest Iran, with fever of non-serious origin. Patients were randomized equally into two groups to receive either orally 10 mg/kg acetaminophen (Case Group) or 10 mg/kg ibuprofen (Control Group). Tympanic temperatures were recorded at baseline and subsequently at 0.5, 1, 2, 3 and 4 hours from baseline. The patients were observed for 24 hrs.

Information on adverse events was collected. Normal temperature was defined as a tympanic measurement ranging between 36.5°C and 37.9°C^[4]. A total of 100 patients were randomly assigned, 50 in the acetaminophen group, 50 in the ibuprofen group. Patients with severe systemic disease were excluded. Study groups were similar in age and gender. The mean temperature change from baseline after four hours was -1.46 °C and -1.59 °C in ibuprofen and acetaminophen groups respectively.

Acetaminophen lowered the average baseline body temperature from 38.75 °C to 37.16°C after four hours treatment. Ibuprofen lowered the average baseline body temperature from 38°C to a mean temperature of 36.54°C. The mean temperature change from baseline after four hours was -1.59°C and -1.46°C in acetaminophen and ibuprofen groups respectively. It was found that in intervals of 0.5, 1, 2, 3 and 4 hours, acetaminophen has reduced 0.25, 1.06, 1.37, 1.49 and 1.59°C and ibuprofen 0.21, 0.64, 0.94, 1.04 and 1.46°C of patients' body temperature.

The main adverse events after excluding those not related to treatment were vomiting in 11

patients (22%) and 1 (2 %), diarrhea in 5 (10%) and nil, abdominal pain in 3 (6%) and nil in the ibuprofen and acetaminophen groups respectively.

In this study temperature evolution over the 4 hours of treatment was not significantly different between the two groups (95% CI; -1.03 to 0.44). Acetaminophen, compared with ibuprofen, produced a greater body temperature reduction at 1, 2, 3 hours after intervention (maximum 0.81 after the first hour;) ($P < 0.01$).

Rainsford et al and Goldman compared the two drug in two large studies: one found no difference^[5] and in the other ibuprofen was more effective than acetaminophen^[6].

Our study showed that patients who were given ibuprofen had more side effects such as diarrhea, vomiting or abdominal pain (statistically significant differences). It should be noted that several studies show that tolerability was similar in both drugs. Rainsford et al concluded that both drugs are remarkably safe as used in clinical trials^[5].

Our results demonstrated that ibuprofen is a suitable alternative to acetaminophen for reducing temperature effectively but acetaminophen is significantly better tolerated.

Key words: Acetaminophen; Ibuprofen; Fever; Children

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