BRIEF COMMUNICATION
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Evaluation of Interleukin 1β in Febrile Convulsion

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ABSTRACT

Febrile convulsion (FC) is the most common type of seizure in childhood that occurs in 2-5 % of the children younger than 6 years. Interleukin 1β (IL-1β) is a cytokine that contributes to febrile inflammatory responses. There are conflicting results on increasing this cytokine in serum during FC. Thus we measured IL-1ß in febrile children with or without seizure.

60 febrile children (6 months to 5 years old) were divided in two groups, one group consisted of 30 children with FC, the other group consisting of 30 children without seizure which served as control. Blood samples were collected from members of both groups and serum samples were prepared. Interleukin 1β concentrations were measured using a commercial Enzyme-linked immunosorbent assay (ELISA) kit.

We found that there was a difference in serum levels of Interleukin 1β between FC and control group but it was not significant. This result may be due to the low number of samples or the result of Interleukin 1β binding to some large proteins such as α2-macroglobolin, complement and soluble type 2 Interleukin 1 receptor, that affected the free Interleukin 1β concentration.

We could not find a significant relationship between serum Interleukin 1β concentration and FC.

Keywords: Children; Febrile convulsion; Interleukin 1β

INTRODUCTION

Febrile convulsion (FC) is the most common type of seizure in the childhood that occurs in 2-5 % of the children younger than 6 years of age.[1] Fever has an important role in the accession of this type of seizure.[2] F.C. is usually generalized and is Tonic-clonic and it occurs with rapid increment in temperature.[3] In fact, this is an excitatory response of immature brain to the fever.[4] Some reports indicated that Interleukin 1β is a cytokine contributing to febrile inflammatory response.

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Using an immature rodent model, the role of Interleukin 1β in generation of experimental febrile seizures was demonstrated.[5] Increased CSF levels of Interleukin 1β and TNF-α in febrile seizure was reported.[6] The report suggested that, in comparison with control group, IL-1β level in acute phase of febrile seizure increased but there was no significant difference in F.C delayed phase. Direct relation between plasma IL-1β concentration and fever level indicated that IL-1β has a more active role rather than other cytokines like IL-1α and TNF-α, in fever development.[6] It was found that IL-1β production by dsRNA-stimulated leukocytes in children increases and this maybe the reason of F.C development.[7] A significant allele association between F.C and IL-1β (-511) allele 2 (T) was demonstrated.[8] However, one study could not support this hypothesis that increased production of IL-1β can contribute to the pathogenesis of F.C in children.[9] Thus, it seems there are conflicting results about this subject. Thus, to determine the role of IL-1β in F.C development, we evaluated the serum level of IL-1β in two groups of febrile children with or without seizure.

MATERIALS AND METHODS

Patients

Thirty patients (6 months to 5 years old) with F.C. and 30 age-matched febrile children as control, that needed to be hospitalized, were enrolled in this study, between July 2006 and November 2008. Patients were from the pediatric Unit of hospitals affiliated to Mashhad University of Medical Sciences in Iran. Patients with malnutrition, any CNS infection, systemic diseases like heart and renal failure, liver dysfunction, allergy, malignancy, diabetes or thyroid disease were excluded from the study.

A questionnaire containing demographic data, time after fever onset, type of infection, seizure duration, seizure attack numbers, previous F.C. and familial history of F.C. was completed for all patients. All parents signed the consent prior to entry in the study.

Blood Sampling

The blood samples were taken immediately on arrival at the hospital and then were centrifuged at 4000 rpm for 15 minutes. The serum fractions were isolated and stored at -20ºC until required for analysis. There were not significant lags in processing times or alterations in collection. All samples were processed within a certain time and by the same person.

Determination of Serum Interleukin 1β Concentration

Serum Interleukin 1β levels were measured by an enzyme-linked immunosorbent assay (ELISA) kit (CLBkit-pelikine Netherland). Each assay was calibrated using an Interleukin 1β standard curve following the manufacturer's instructions. Samples were assayed in duplicate. All samples were assayed on the same day.

Statistical Analysis

Results are expressed as mean ±S.D. Cytokine serum levels, were compared by using the Mann–Whitney test ($p<0.05$ for statistical significance). Statistical calculations were performed by using SPSS for Windows, version 11.5.

RESULTS

Characteristics of the Study Population

Demographic data and infection incidence for the patients are summarized in Table 1. Seizure condition in F.C. patients is shown in Table 2.

Evaluation of Serum IL-1β in F.C. Patients vs. Control Febrile Children

Serum IL-1β levels were not significantly different in FC patients compared to febrile control patients (8.08±6.59 pg/ml in F.C. children vs. 5.68±2.98 pg/ml in febrile control children; $p=0.08$).

Evaluation of Serum IL-1β in F.C. Patients According to the Duration of Seizure

Serum IL-1β levels were not significantly different between F.C. patients with duration of seizure more than 15 minutes compared to F.C. patients with duration of seizure less than 15 minutes. (5.85±2.7 pg/ml vs. 5.65±3.06 pg/ml, respectively; $p=0.08$).

Table 1. Characteristics of the study population

Topics	With seizure	Without seizure
Age (months)	21.83±3.54	21.86±2.76
Female/Male ratio	0.507	0.500
Incidence of infection		
Gastroenteritis	21%	37%
Pneumonia	3%	27%
Viral infection	54%	13%
Otitis Media	3%	3%
UTI	3%	7%
Vaccination	3%	0%
Other	13%	13%

Table 2. Seizure condition in F.C. patients

Percent of patients with	Positive	Negative
History of previous seizure	16.6	83.30
History of familial seizure	20	80
seizure duration more than15 minutes	6.6	93.3
more than one seizure	13.3	86.6
complex seizure	20	80

Evaluation of Serum IL-1β in F.C. Patients According to the Number of Seizures

F.C. patients with seizure number more than one did not have significantly higher serum IL-1β levels in comparison with F.C. patients that had just one seizure (5.9±2.9 pg/ml vs. 3.0±2.3 pg/ml, respectively; p=0.067).

Evaluation of Serum IL-1β in F.C. Patients According to the Type of Seizure

F.C. patients with complex seizure did not have significantly higher serum IL-1β levels compared to F.C. patients with simple seizure (5.93 ±2.971 pg/ml vs. 4.66±3.066 pg/ml, respectively; p=0.42).

Evaluation of Serum IL-1β in F.C. Patients According to Type of Infection

According to Table 1, high percent of F.C. patients had viral infections such as influenza and bacterial gastroenteritis in comparison with other infections. F.C. patients with bacterial gastroenteritis had significantly higher serum IL-1β levels compared to F.C patients with other infections (8.5 ±7.98 pg/ml vs. 6.88±5.8 pg/ml, respectively; p=0.0057) but F.C. patients with viral infection did not have significantly higher serum IL-1β levels in comparison with other infections (8.68 ±5.7 pg/ml vs. 4.78±2.13 pg/ml, respectively; p=0.084).

Evaluation of Fever Level in F.C. Patients with Viral Infections such as Influenza and Bacterial Gastroenteritis in Comparison with other Infections

Bacterial gastroenteritis, in comparison with other infections, caused higher grades of fever (p =0.049) in F.C. patients.

DISCUSSION

Immune response is regulated by pro- and anti-inflammatory cytokines. Infections can cause fever and induce febrile seizure. F.C. usually occurs during fever increment.[10] In this research we evaluated serum IL-1β in two groups of febrile children with and without seizure. We found that there was no significant difference in serum IL-1β level between F.C. and febrile control group.

In both groups, fever level was mainly in the range of 38-38.5ºC. There was a history of previous F.C. in 16.6% and 20% of control and F.C. groups, respectively.

Number of patients in this research was three fold higher in comparison to the number of samples in the study by Lahat et al [9] and the same of the report by Virta et al[10] and Tomoum et al.[11] Twenty percent of F.C. patients showed complex seizure and the rest of them had the simple one. Between these two groups (with simple vs. complex seizure) also there was no significant difference in serum IL-1β levels and this is supported by results of the mentioned studies.[7,9] According to our results, high percentage of F.C. patients had viral infections such as influenza and bacterial gastroenteritis in comparison with other infections. Serum IL-1β in these patients had a direct significant relation with bacterial gastroenteritis (p=0.0057) but not with viral infections (p=0.88). This may be due to the higher fever level in this type of infection (bacterial gastroenteritis) in comparison to other infections. It is reported that IL-1 receptor antagonist/IL-1β, ratios in F.C. patients were significantly increased compared to febrile children without seizure as controls.[10] One study showed increased levels of IL-1β in plasma but not cerebrospinal fluid (CSF) during the acute phase of F.C.[6], whereas another study[12] had documented increased IL-1β levels in CSF but not in serum during this phase of F.C.

It reflects the difficulty of analysis of IL-1β in clinical samples, because free IL-1β could bind to large proteins, such as α2-macroglobolin, complement and soluble type 2 Interleukin 1 receptor.[13] An *in vitro* study showed increment of IL-1β production from lipopolysaccharide-stimulated peripheral blood mononuclear cells in febrile seizure patients[14] but another similar study had failed to demonstrate significant differences in IL-1β production.[15] In conclusion, there are conflicting results about this cytokine. In some clinical studies, such as our research, this may be due to the small sample size. Thus it seems necessary to do further investigations with larger sample size.

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