

Serum immunoglobulin levels in children with acute bacterial meningitis

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Abstract

To assess serum level of immunoglobulins (IgG, IgA, IgM) in children with acute bacterial meningitis before therapy and at the end of intensive antibiotic therapy and in comparison to healthy age and sex matched controls. Out of 37 cases admitted to Ibn-Al-Atheer pediatric hospital (Mosul city) between January 2005 and July 2007, 29 cases proved to be a case of *Haemophilus influenzae* meningitis. Two died during the follow up period and 27 completed the study. Also included 30 apparently healthy age and sex matched subjects taken as control group. Initially from both group (patients and control) 5ml venous blood samples were taken and assay of serum immunoglobulin (IgG, IgA, IgM) were done by single radial immunodiffusion method using commercial kits. After two weeks of intensive antibiotic therapy another blood samples were taken from the patients and assay of serum immunoglobulin levels were done using the same method and the same commercial kits. Initially before therapy there was a significant reduction in all immunoglobulin levels (IgG, IgA, IgM) in children with acute bacterial meningitis in comparison to controls. After 2 weeks of intensive antibiotic therapy, there was no significant difference in the mean serum immunoglobulin levels between the patients and controls. Acute bacterial meningitis as a disease and the intensive antibiotic therapy do affect the humoral immune response as reflected by the serum immunoglobulin levels (IgG, IgA, IgM).

مستوى الكلوبولينات المناعية لدى الاطفال المصابين بالتهاب السحايا

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المستخلص

لتحديد مستوى الكلوبولينات المناعية (IgG, IgA, IgM) في مصل دم المرضى المصابين بالتهاب السحايا البكتيري الحاد من الاطفال قبل العلاج وبعد انتهاء العلاج المكثف بالمضادات الحيوية وبالمقارنة مع مجموعة ضبط سيطرة من اصحاء ذوي اجناس و اعمار مقارنة لمجموعة المرضى. من اصل 37 مريضا ادخلوا الى مستشفى ابن الاثير للاطفال في مدينة الموصل للفترة مابين كانون الثاني 2005 وتموز 2007 ، كان هناك 29 حالة شخصت على انها التهاب سحايا بكتيري بجرثومة *Haemophilus influenzae* . اثناء حالة المتابعة توفي اثنان من المرضى و 27 مريضا شملوا الدراسة . كذلك انتخب 30 طفلا من اعمار و اجناس مقارنة من الاصحاء اتخذت كمجموعة ضبط. في البداية تم سحب 5 مل من الدم الوريدي من المجموعتين (مجموعة المرضى والضبط) وتم قياس مستوى الكلوبولينات المناعية (IgG, IgA, IgM) في مصل الدم باستخدام طريقة معينة وعدد خاصة للفحص. بالنسبة لمجموعة المرضى وبعد فترة اسبوعين من العلاج المكثف تم سحب الدم ثانية وقياس مستوى الكلوبولينات المناعية مرة اخرى باستخدام نفس طريقة الفحص ونفس عدد الفحص. في البداية قبل العلاج كان هناك نقصا معنويا في مستويات الكلوبولينات المناعية (IgG, IgA, IgM) في الاطفال الذين لديهم التهاب السحايا الحاد بالمقارنة مع مجموعة الضبط. بعد اسبوعين من العلاج المكثف بالمضادات الحيوية، لم يكن هناك فرق معنويا في مستويات الكلوبولينات المناعية (IgG, IgA, IgM) بين المرضى ومجموعة الضبط. التهاب السحايا البكتيري الحاد عند الاطفال كمرض والعلاج المكثف بالمضادات الحيوية يؤثر على الاستجابة المناعية الخلطية بدلالة التأثير على مستويات الكلوبولينات المناعية (IgG, IgA, IgM) .

Introduction

Bacterial meningitis continues to result in a significant brain injury in many affected patients, despite the use of highly active antibiotics⁽¹⁾. The pathological mechanism of central nervous system injury in human meningitis are not yet completely understood although recent studies indicates that the host's inflammatory responses are as important in brain damage as the infecting organism and toxin's⁽²⁾. Lack or impairment immunologic responses have been suggested to be involved in the pathogenesis of bacterial meningitis⁽³⁾. The aim of this study is to determine the serum immunoglobulin levels (IgG, IgA, IgM) in children with acute bacterial meningitis initially and after a course of specific antibiotic therapy, in comparison to healthy age and sex matched control.

Patients and methods

This study was conducted from January 2005 to July 2007. children with positive signs of meningitis were admitted to Ibn-Al-Atheer pediatric hospital (Mosul city) and immediately a blood and CSF samples were taken. Later positively proved cases of bacterial meningitis (from CSF culture) were selected and included in this study. Out of 37 cases admitted to hospital, 29 cases proved to be bacterial meningitis (all due to Haemophilus influenzae); two died during the follow up period and 27 cases continued the follow up. They were 8 females with 19 males with a mean \pm SD

age 4.96 ± 2.19 years (ranged between 2 and 10 years). Also included 30 apparently healthy children as a control group. They were 9 females and 21 males with a mean \pm SD age 4.76 ± 2.24 years (ranged between 2 and 10 years). Initially 5ml venous blood samples were taken from patients and control, and assay of serum levels of immunoglobulin (IgG, IgA, IgM), by Single Radial Immunodiffusion methods⁽⁴⁾, using a kit (Sanof Diagnostics Pasteur, France). After two weeks of a specific intensive antibiotic therapy with cefotaxime, another 5ml venous blood samples were taken from the patients and assay of the serum levels of immunoglobulin (IgG, IgA, IgM) were done.

Statistical analysis

All values were quoted as mean \pm SD and a P-value <0.05 was considered to be statistically significant. Unpaired t-test was used to compare results of patients initially (pretherapy) and after the intensive antibiotic therapy, with the results of the controls. Paired t-test was used to compare results of patients in the pre and post therapy stages.

Results

There was a highly significant reduction in the serum immunoglobulin IgG (P=0.03), IgA (P=0.001) and IgM (P<0.001) in children with acute bacterial meningitis before starting therapy and in comparison to controls (table 1).

Table (1): Comparison of IgG, IgA and IgM levels between cases of acute bacterial meningitis before drug therapy and the controls.

Parameters	Control(n=30)	Cases before therapy (n=27)	P-value
IgG(mg/dl)	690.67±106.48	632.96±91.31	0.030(S)
IgA(mg/dl)	253.17±66.35	200.74±37.61	0.001(S)
IgM(mg/dl)	209.67±38.12	173.33±24.96	<0.001(S)

S= significant difference

After 2 weeks of intensive antibiotic therapy, there was no significant differences in the mean immunoglobulin

levels (IgG, IgA, IgM), in such patients in comparison to the controls (table 2).

Table (2): Comparison of IgG, IgA and IgM levels between cases of acute bacterial meningitis after drug therapy and the controls.

Parameters	Control(n=30)	Cases after therapy (n=27)	P-value
IgG(mg/dl)	690.67±106.48	640.93±90.49	0.064(NS)
IgA(mg/dl)	253.17±66.35	233.52±45.74	0.203(NS)
IgM(mg/dl)	209.67±38.12	207.22±37.76	0.809(NS)

NS= no significant differences

By comparison of serum immunoglobulin levels in such patients in the pre and post therapy stage there was a highly significant differences

between levels of IgG (P=0.013), IgA (P<0.001) and IgM (P<0.001) (table 3).

Table (2): Comparison of IgG, IgA and IgM levels between cases of acute bacterial meningitis, before and after drug therapy.

Parameters	Before therapy n=27	After therapy n=27	P-value
IgG(mg/dl)	632.96±91.31	640.93±90.49	0.013(S)
IgA(mg/dl)	200.74±37.61	233.52±45.74	<0.001(S)
IgM(mg/dl)	173.33±24.96	207.22±37.76	<0.001(S)

S= significant differences

Discussion

This study shows that serum immunoglobulin levels (IgG, IgA, IgM) significantly reduced in children with

acute bacterial meningitis in the pretherapy stage in comparison to healthy controls. With therapy, the serum levels of immunoglobulin raises

to reach almost normal control values. Information with regard the effects of acute bacterial meningitis in children as a disease and the intensive antibiotic therapy on immunoglobulin levels were scanty and old. German et al, reported that the level of IgG at the beginning of the disease in patients with the generalized forms of meningococcal infection(meningitis, meningitis combined with meningococcaemia, meningococcaemia) was found to be considerably lower than in healthy subjects, and the levels of all immunoglobulin, particularly of IgA and IgM increased in the course of the disease⁽⁵⁾. Kouvalainen et al, by determining the serum levels of 5 immunoglobulin (IgG, IgA, IgM, IgD, IgE)in children with bacterial meningitis, concluded that antibodies of all the 5 immunoglobulin classes were probably involved in the defense against the causative microbes⁽³⁾. Mansour et al by comparing the immunoglobulin levels in cerebrospinal fluid and sera of 28 patients with tuberculous meningitis and 27 patients with purulent meningitis, reported that mean fluid / serum ratios of patients before therapy were significantly higher in the purulent than in the tuberculous group and with treatment all improved at varying rates with the IgM showing the fastest rate. They suggested that such findings may prove to be of prognostic aid for clinicians in the follow up of such patients⁽⁶⁾. Going with the finding of this study, Forsberg et al, reported a raise in the cerebrospinal fluid / serum index of IgM, IgG and IgA(which means a low serum immunoglobulin levels) in 11 patients with bacterial meningitis and with therapy follow up, all values of immunoglobulin in CSF and serum return to almost normal values⁽⁷⁾. Kline

MW reported that in a ten-year review of 47 patients with well-documented recurrent bacterial meningitis. Ten patients have immune deficiency (either compliment or immunoglobulin deficiencies)⁽⁸⁾. However and in contrast to our findings, Hassieb et al, reported a raise (although insignificant) in the immunoglobulin levels in all cases of bacterial meningitis⁽⁹⁾. Based on this study, the humoral immune response in children with Haemophilus influenzae meningitis seems to be affected by the disease so as by the intensive antibiotic therapy.

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