



Polymerase Chain Reaction for Frequent Evaluation of Enterovirus in Aseptic Meningitis

Mohammad Bagher Rahmati ¹, Parviz Tabatabaie ², Mohammad Mehdi Houshmandi ^{3*}

¹Department of Infectious Diseases, Pediatric Hospital Clinical Research Development Unit, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

²Departments of Pediatric Infectious Disease, Tehran University Of Medical Science, Tehran, Iran

³Department of Pediatric, Hormozgan University of Medical Science, Bandar Abbas, Iran

* Corresponding author's Email: mhoushmandi@gmail.com

ABSTRACT: Meningitis is one of the most common CNS emergencies. Aseptic meningitis is the most prevalent type of meningitis. The clinical features initially are not specific. Enteroviruses have more than 60 serotypes which are culpable for more than 85% of aseptic meningitis. Polymerase chain reaction (PCR) is a highly sensitive test for detection of viruses; therefore by using of this method, diagnosis of aseptic meningitis can be achieved rapidly. We can use this method even for detection of viral types, and therefore choosing the best treatment. We have evaluated 47 cases of highly suspicious to meningitis in a cross sectional manner by PCR method. We found 4 positive cases for enterovirus. It seems that, by using of PCR method we can differentiate aseptic meningitis easily and rapidly, so decreasing costs can be achieved by this method.

Key words: PCR, Enterovirus, Aseptic Meningitis, Bacterial Resistance

ORIGINAL ARTICLE

INTRODUCTION

Meningitis is one of the most common CNS emergencies which can deteriorate the patient rapidly and even can be lethal with postponing the diagnosis. Aseptic meningitis includes all types of inflammations of the brain meninges except those caused by pus producing organisms. Aseptic meningitis is usually benign. Etiology of aseptic meningitis is very includes infections - both viral and non-viral, drugs, malignancy and systemic illness (Kumar, 2005). Viral infections of the central nervous system in the tropical countries of Asia and the Indian subcontinent are different from those of the Western and developed world (Handique, 2011). Enteroviruses (EVs) are common and significant human pathogens in Asia (Chen et al., 2011). Aseptic meningitis is the most prevalent type of meningitis (Ahmed et al., 1997; Andréoletti et al., 1998; Chesky et al., 2000; Elfaitouri et al., 2005; Lee et al., 2007; Logotheti et al., 2009). Spectrum of the disease is from a mild febrile disease to a severe infectious disease with lethal complications (Andréoletti et al., 1998; Pringle, 1999; Feigin et al., 2004).

Enteroviruses have more than 60 serotypes which are responsible for more than 85% of aseptic meningitis (Berlin et al., 1993; Sawyer et al., 1994; Ahmed et al., 1997). Diagnostic work up includes blood and

cerebrospinal fluid (CSF) examination and serology for infectious meningitis, Delayed diagnosis of aseptic meningitis makes us use further lab tests, X rays and scans. It can also affect the treatment by using of non-necessary antibiotics; in adverse, rapid diagnosis can decrease non necessary antibiotic usage, decrease bacterial resistance and the treatment costs reducing, a definitive diagnosis can protect the patient from unnecessary investigations and antibiotic treatment, also a better prognosis. Polymerase chain reaction (PCR) is a highly sensitive test for detection of viruses (Thorén et al., 1994; Riding et al., 1996; Kupila et al., 2005; Peigue-Lafeuille et al., 2006), therefore by using of PCR methods for detecting, diagnosis of aseptic meningitis can be achieved rapidly. By using of this method we can even detect viral types, and therefore choosing the best treatment. Herein we want to evaluate the efficacy of PCR in rapid diagnosis of aseptic meningitis.

METHODS AND MATERIAL

This study was a descriptive study which was done in a cross sectional manner in Medical Center, university hospital of Tehran in 2008. After obtaining ethical committee approval and written informed consent from the

parents, we started our study. Admitted patients, older than 1 month, that were suspicious to meningitis were evaluated in our study. We took 1cc CSF more than common CSF tests. We used this additional CSF for detection of enterovirus by PCR analysis. For collection of data we provided questionnaires including age, gender, season of admission, CSF analysis (cell count, sugar, protein, CSF smear), CBC (WBC count, Hemoglobin, platelets), ESR, CRP and PCR results. After data collection, we used SPSS software for arrangement and analysis of data. Statistical analysis was done by descriptive analysis tests.

RESULTS

We evaluated 47 cases, 4 cases of them were positive for enterovirus, PCR results from the 47 patients selected for the evaluation are shown in Table 1. Enterovirus isolated from 2 cases lower than 1 year old, one case between 1 to 3 years old and one case between 3 to 5 years old (table 2). Patients infected by enterovirus, developed some complications such as seizure, vomiting, Rhinorrhea, irritability, diarrhea and headache (table 3). Seasonal prevalence of patients in our study (table 4).

Table 1. Positive PCR differentiated by sex

Sex	PCR (positive)	PCR (negative)	Total
Male	3	22	25
Female	1	21	22
Total	4	43	47

Table 2. Prevalence differentiated by age

Variables	0-1 year	1-3 years	3-5 years	≥ 5 years	Total
PCR +	2	1	1	0	4
PCR -	15	10	6	2	43
Total	17	11	7	2	47

Table 3. Complications in PCR (+) patients

Complications in PCR + patients	With complication	Without complication	Total
Seizure	2(50%)	2(50%)	4(100%)
Rhinorrhea	2(50%)	2(50%)	4(100%)
Diarrhea	1(25%)	3(75%)	4(100%)
Irritability	2(50%)	2(50%)	4(100%)
Vomiting	3(75%)	1(25%)	4(100%)
Headache	1(25%)	3(75%)	4(100%)
Fever	3(75%)	1(25%)	4(100%)

Table 4. Seasonal prevalence of patients in our study

Season	Spring	Summer	Autumn	Winter	Total
PCR(+)	0	3	1	0	4
PCR(-)	7	17	12	7	43
Total	7	20	13	7	47

DISCUSSION

It seems that, by using of PCR method we can differentiate aseptic meningitis easily and rapidly, so decreasing costs can be achieved by this method. In Reading and colleagues study which is done in England in 2006, they used PCR for testing 2233 CSF samples, in their study 147 cases were positive (6.5%) (Riding et al., 1996). Our positive PCR cases were 8.5(4 cases) which was compatible with their study. However in mistchenko and colleagues study, they evaluated 1242cases who were suspicious to meningitis, their positive PCR cases were about 11.5% Mistchenko et al (2006). In their study maximal positive cases were in summer and autumn Mistchenko et al (2006) just like our study (75% in summer and 25% in autumn) (table 4).

Our results were not far from the others. Comparison of PCR cost with non-necessary Radiologic Exams, non-necessary interventions and Blind antibiotic therapies, can obviously reveal that, Using of PCR method for all suspicious patients is more cost effective. In addition, by using of this method we can decrease the complications, and consequent costs will be restricted; therefore better outcome with less expense will be achieved.

It seems that we can detect types of meningitis easily by PCR, which is highly sensitive method. By using of this method we can restrict our mistakes in management of meningitis patients and therefore limitation of complications and costs can be achieved.

Acknowledgment

This article is dedicated to the memory of Dr. Seyed Ahmad Siadati, teacher, researcher and clinician who has contributed greatly to growth of the pediatric profession and improved health of children.

REFERENCES

Ahmed A, Brito F, Goto C, Hickey SM, Olsen KD, Trujillo M, McCracken GH Jr (1997). Diagnosis of Enteroviral Meningitis by Using PCR with a Colorimetric Microwell Detection Assay. *J Pediatr.* 131:393-7.

Andréoletti L, Blassel-Damman N, Dewilde A, Vallée L, Cremer R, Hober D, Wattré P(1998). Comparison of Use of Cerebrospinal Fluid, Serum, and Throat Swab Specimens in Diagnosis of Enteroviral Acute Neurologica Infection by a Rapid RNA Detection PCR Assay. *J Clin Microbiol.* 36:589-91.

Aura Kupila, et al. (2005). Diagnosis of Enteroviral Meningitis by Use of Polymerase Chain Reaction of Cerebrospinal Fluid, Stool, and Serum Specimens. *Clin Infect dis.*40:982-987.

Berlin LE, Rorabaugh ML, Heldrich F, Roberts K, Doran T, Modlin JF (1993). Aseptic meningitis in infants

- < 2 years of age: diagnosis and etiology. *J Infect Dis.*168:888-92.
- Chesky M, Scalco R, Failace L, Read S, Jobim LF (2000). Polymerase chain reaction for the laboratory diagnosis of aseptic meningitis and encephalitis. *Arq Neuropsiquiatr.* 58:836-42.
- Chen TC, Shih SR (2011) *Infect Disord Drug Targets.* Jun; 11(3):337-45.
- Elfaitouri A, Mohamed N, Fohlman J, Aspholm R, Frisk G, Friman G, Magnus L, Blomberg J(2005). Quantitative PCR-enhanced immunoassay for measurement of enteroviral immunoglobulin M antibody and diagnosis of aseptic meningitis. *Clin Diagn Lab Immunol.* 12:235-41.
- Feigin, R.D, et al (2004). *Textbook of Pediatric Infectious Disease.* 5th edition: Philadelphia: SAUNDERS.p 497-504.
- Handique SK (2011) *Neuroimaging Clin N Am.* 2011 Nov; 21(4):777-94, vii. doi: 10.1016/j.nic.07.012.
- Kumar R. (2005). *Indian J Pediatr.* Jan; 72(1):57-63.
- Lee ST, Ki CS, Lee NY (2007). Molecular characterization of enteroviruses isolated from patients with aseptic meningitis in Korea. *Arch Virol.* 152:963-70.
- Logotheti M, Pogka V, Horefti E, Papadacos K, Giannaki M, Pangalis A, Sgouras D, Mentis A(2009). Laboratory investigation and phylogenetic analysis of enter viruses involved in an aseptic meningitis outbreak in Greece during the summer of 2007. *J Clin Virol.*46:270-4.
- Mistchenko AS, et al(2006). Molecular and epidemiologic analysis of enter virus B neurological infection in Argentine children. *J Clin Virol.* 37:293-9.
- Peigue-Lafeuille H. et al (2006). From prospective molecular diagnosis of enter virus meningitis...to the prevention of antibiotic resistance. *Med Mal Infect.*36:124-31.
- Pringle CR (1999). Virus taxonomy at the XIth International Congress of Virology, Sydney, Australia. *Arch Virol.* 144:2065-2070.
- Riding MH, Stewart J, Clements GB, Galbraith DN (1996). Enter viral polymerase chain reaction in the investigation of aseptic meningitis. *J Med Virol;* 50:204.
- Sawyer MH, Holland D, Aintablian N, Connor JD, Keyser EF, Waecker NJ Jr(1994). Diagnosis of enteroviral central nervous system infection by polymerase chain reaction during a large community outbreak. *Pediatr Infect Dis J.*13:177-82.
- Thorén A, Widell A (1994). PCR for the diagnosis of enteroviral meningitis. *Scand J Infect Dis;* 26:249.