

Evaluation of creatine kinase activity in Cerebrospinal fluid of normal individuals and patients with meningitis

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Entedhar Riffat Sarhat *, Ahmed H. Alanee**, Ashoor R. Sarhat** Yaser AM. Al-Noaemi*, Jinan F. Al Dahhan

Dept. of biochemistry* & pediatrics**, College of Medicine, Tikrit University

Abstract

The present study is conducted to evaluate creatine kinase, glucose level, and protein concentration activity, in CSF of patients with meningitis in comparison with their levels in healthy persons during the period from the first of February to the last of August 2005. The aim of the study is to provide further information about the relationship between meningitis and creatine kinase activity. In addition glucose and protein CSF concentration had also been evaluated in both groups.

Twenty eight samples of CSF were collected; 10 samples represented the control group whose range between (1-13) years and 18 samples were represented the patients with meningitis group whose range between (1-10) years. Creatine kinase activity appeared significantly higher in patients with meningitis in comparison with normal individuals. It is also found that CSF protein is higher and CSF glucose is lower in infected than in the control group.

Key words: Meningitis, creatine kinase, Cerebrospinal fluid, normal individuals.

Introduction

Meningitis is as simply an inflammation of the meninges leading to several clinical patterns, usually the responsibility of the infection is shouldered by microorganism. Pathogens reach the meninges by the blood stream or occasionally by spreading from nearby sites such as the middle ear or nasal sinuses.

In pyogenic type (purulent), cells are usually polymorphs and the rest lymphocytes as in meningitis caused by *Streptococcus pneumonia*, *Neisseria meningitides*, and *Haemophilus influenzae*. The protein in the C.S.F will be more than normal and glucose is usually very little. In lymphocytic type the C.S.F contains mainly lymphocyte as in meningitis caused by viruses or Mycobacterium tuberculosis⁽¹⁾.

In Viral meningitis (aseptic) C.S.F protein is raised, and the glucose stays normal and there is no bacteria. In Tuberculous meningitis the C.S.F protein is raised, the sugar is decreased below 40mg/100ml.

It is worth mentioning that in lymphocytic meningitis the kind of the cell has little help in telling whether a patient has Tuberculous or virus meningitis. The

diagnosis of suppurative meningitis is usually easy by finding bacteria⁽⁵⁾. Unfortunately some patient with bacterial meningitis may have been partially treated with drugs before a lumbar puncture is done. This may kill some of the bacteria infecting a patient without curing him properly and make these bacteria very hard to detect in the C.S.F which then represent a health problem^(1, 2).

It is known that enzymes have a diagnostic role in the diagnosis of disease, and the increase or decrease of an enzyme activity than its normal value would be a good marker for many diseases. Recent studies indicated that creatine kinase is one of the markers that is used in the diagnosis of different pathogens cases^(3,4).

It is generally accepted that cerebrospinal fluid reflects the metabolism of the brain and spinal cord. Lesions of tissues rich in enzymes, corresponding with their damage or structural destruction, may cause enzymatic release⁽²⁾. Culebras -Fernandez reported that in human patients with CNS trauma, CSF enzyme values corresponded to the clinical severity of the injury, with the highest values occurring two to nine days after injury, and enzyme elevations

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proportional to the extent of tissue damage⁽⁵⁾.

Increased enzymes levels in cerebrospinal fluid (CSF), including creatine kinase (CK) have been reported to indicate tissue damage of the central nervous system (CNS) or altered permeability of barriers.

Elevated levels of the enzymes in CSF are usually not associated with elevated serum enzyme levels in people. Valuable information concerning CSF CK activity relative to duration and severity of clinical signs is available in the human medical literature⁽⁶⁾.

The aim of this study is to perform a rapid, sensitive, and reliable diagnostic marker for meningitis.

Material and Methods

Cerebral spinal fluid was collected from 28 patients admitted to Tikrit General Hospital in Tikrit, and Pediatric Hospital in Kirkuk, their age between 1 day- 13 years old. The clinical suspicion for diagnosis of meningitis is made by a pediatrician based on the clinical manifestations like fever, headache, neck stiffness, Kernig sign, Brudzinkski sign and bulging fontanelle in children under 18 months age.⁽²⁾

The fluid was withdrawn by lumbar puncture, using a spinal needle No.20). The patient lies on a hard bench, taking the lateral reclined position and the needle is gently placed above or beneath the fourth lumbar vertebra. The amount of withdrawn C.S.F is not fixed, but usually in the range of (1-3) ml. The CSF was examined grossly for appearance and color. Freshly collected specimens were stored at 4°C. Turbid specimens were centrifuged at 3000 RPM for 10 minutes before storage. Based on clinical manifestation and laboratory results which include qualitative and quantitative cytology as well as glucose and protein concentration, gram stain, Ziehl-Neelsen stain and culture, the C.S.F samples were divided into two groups.

Group One:

Normal control (or individual whom suspected as meningitis and the laboratory examination for them were normal), this group includes 10 individuals.

Group Two: Meningitis group in whom the clinical and lab features are suggestive of meningitis and they were divided into four groups (bacterial, viral, tuberculous and partially treated meningitis). (this group includes 18 patients)

The CSF samples were also examined for the level of CK in both study groups. The reference value for CSF CK, protein and glucose is 3%, 15-40 mg/100ml, and 2.5-4.00 mmol/L respectively.⁽²⁾

Principle

Creatine phosphate + ADP \xrightarrow{CK} Creatine + ATP

Glucose + ATP \xrightarrow{HK} Glucose-6-p + ADP

Glucose-6-p + NADP⁺ $\xrightarrow{G6P-DH}$ Glucose-6-phosphate + ADPH + H⁺

Statistical analysis: The data was done by using student t test.

Results

The CSF samples were divided into 5 groups according to the results of CSF exam and to the type of meningitis. Detailed information of all individuals included in this study is summarized in table (1).

Creatine kinase activities were measured in the cerebral spinal fluid of normal individuals and patients with meningitis. The mean Creatine kinase activity level in the C.S.F of meningitis 20.99 U/l group is significantly higher than normal control 5U/l. as shown in table (2) and Fig (1). The mean level of CK in bacterial meningitis (22 U/l) is higher than that in viral type (19.9).

The mean of total protein values was (63.055 ± 8.8 g/l) in patients with meningitis, with the mean level was higher in bacterial (65.1 g/l) than in viral type (60.2 g/l) while the mean value of normal control was (25.8 ± 8.7 g/l) as shown in table (2) and Fig (1).

The mean of glucose values was (1.096 ± 8.8 mmol/l) in patients with meningitis, with the mean level was lower in bacterial (0.98g/l) than in viral type (1.12 g/l) while the mean values in normal samples was (3.52 ± 8.7 mmol/l) as shown in table (2) and Fig (3).

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Table (1): Demographic characteristic of study population.

Group	Diagnosis	No. of patients		
		Total	Male	Female
1	Normal (control)	10	7	3
2	Tuberculous meningitis	1	1	–
3	Bacterial meningitis	5	4	1
4	Viral meningitis	11	6	5
5	Partial treated meningitis	-	-	1

Table (2): CK, total protein, and glucose concentration in CSF in patients with meningitis and control.

Groups	Patient	Control	probability
	Mean \pm S.D.	Mean \pm S.D.	
CK	20.99 \pm 4.2 U/l	5 \pm 2.5 U/l	P < 0.05
Glucose	0.972 \pm 30 mmol/l	3.52 \pm 22.9 mmol/l	P < 0.05
Total protein	63.05 \pm 8.8 g/l	25.8 \pm 8.7 g/l	P < 0.05

Discussion

The mean level of CK in patients with meningitis is higher than that in the control group. This result is in line with other study by Pancewecz⁽⁸⁾ who shows that CK activity is higher in infected CSF than in normal ones. This may be due to Brain tissue has a relatively large amount of CK activity and the elevation of various enzymes in meningitis has been reported and many mechanisms have been postulated⁽⁵⁾. CK is an intracellular enzyme released in various neurological conditions including infections and the increase in their CSF levels reflects the extent of brain injury. It has been suggested that pathological process that permits blood and plasma to reach the spinal fluid results in an increase in the enzymatic activity by virtue of the contribution of enzyme from plasma. In cases of acute meningitis there is increased outflow from serum due to injury to the blood brain barrier (BBB) resulting into exudation of plasma proteins, enzymes along with circulating leucocytes into spinal fluid^(6,7). The mean level of CK in bacterial meningitis is higher than that in viral type which is similar to that seen by Pancewecz⁽⁸⁾ which may be due to the fact

that bacterial meningitis is more severe than viral type and may lead to more tissue damage which leads to higher level of enzyme in the CSF of the patients with bacterial meningitis.

The mean glucose value is lower in the CSF of meningitis group than that in control group & this result agrees with other study by Lamerz K.⁽²⁾ who shows the same results. This is due to the fact that microorganisms in meningitis use CSF glucose as a source of energy for their metabolism which leads to decrease in its level in CSF or may be due to that normally CSF glucose represents about two-thirds of blood glucose and because of decreased oral intake in patient with meningitis this leads to decrease in the level of blood glucose that in turn leads to decrease in level of CSF glucose.⁽¹⁸⁾ It is also found that CSF glucose in bacterial meningitis is lower than that in viral one. This is similar to that found by Cutler⁽¹⁶⁾ who shows comparable results. This may be due to the same reasons above and to the fact that bacterial meningitis is a more severe infection and the patient is more toxic.

The mean protein level is higher in infected CSF samples than in that of normal controls. These results are

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similar to that of Lamerz⁽²⁾. This may be due to that infected CSF is rich in protein like gamma globulins as an immunological reaction against infection in addition to the proteins released from the damaged tissues by the infection process⁽¹⁸⁾ which leads to the total increase in the CSF proteins.

It is also found that total protein level in bacterial meningitis is higher than that in viral type. These results are also found by Lamerz and Cutler^(2,16) and this may be due to that bacterial infection is more severe than viral one and this leads to more tissue damage and more severe

immunological reaction which internally leads to a higher level of CSF proteins.

Conclusion

We conclude that CK activity is higher in patients with meningitis than in control group. More studies are required to assess its usefulness as a marker of disease activity and disease control as well as the use of it as an indicator of severity of the tissue damage.

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