

# CEREBROSPINAL FLUID LACTIC ACID CONCENTRATION IN BACTERIAL MENINGITIS

\*SABIHA PIT, MD (UKM) MSc (Lond)

\*FARIDA JAMAL, MBBS (Dacca) MSc (Lond) MRCPPath

\*ILINA ISAHAK, MBBS (Mal) MSc (Lond)

\*\*ALI AZMAN MINHAJ, MBBS (Mal) MRCP (UK)

\*Depat. of Microbiology  
Faculty of Medicine,  
National University of Malaysia  
Jln Raja Muda  
50300 Kuala Lumpur

\*\*Department of Paediatrics  
Faculty of Medicine, UKM

## ABSTRACT

Lactic acid concentration was determined in 37 specimens of cerebrospinal fluid by gas liquid chromatography. It was found to be raised ( $\geq 30$  mg/dl) in 15 specimens from culture positive cases of bacterial meningitis and one of fungal meningitis. It was  $< 30$  mg/dl in cerebrospinal fluid from four cases of viral meningoencephalitis and 10 contaminated specimens. It was also raised in two specimens from culture negative cases. Determination of cerebrospinal fluid lactic acid concentration by gas liquid chromatography provides a useful, additional test in the diagnosis of bacterial meningitis.

## INTRODUCTION

Meningitis is a life-threatening infection. This clinical entity requires prompt diagnosis and management in order to reduce the morbidity and mortality. Problems in management are encountered in partially treated cases where the cerebrospinal fluid cytology and biochemistry are equivocal and cultures are negative.

During the last few decades, the introduction of several rapid tests such as the Limulus test, counter-immunoelectrophoresis and latex agglutination tests have aided the diagnosis of meningitis.<sup>1</sup> However, in situations where a wide range of microorganisms may be implicated as in neonatal meningitis,<sup>2</sup> these tests have limited value. Appropriate antibiotic therapy depends on the isolation of the aetiological agents. However, in many instances, the cerebrospinal fluid (CSF) may yield growth of bacteria which are probably contaminants. Interpretation of such reports may be difficult, particularly in neonates and immunocompromised patients.

Lactic acid determination in CSF has been found to be useful in situations where both clinical and laboratory interpretations are difficult. Several workers have demonstrated that lactic acid concentration in CSF raised in cases of bacterial meningitis when compared to levels in aseptic meningitis and normal controls.<sup>3,4,5,6,7</sup> However, some controversy remains.<sup>8</sup> This study was carried out to evaluate the usefulness of gas liquid chromatography for measuring the lactic acid concentration in CSF as an adjunct to other tests in the diagnosis of meningitis.

## MATERIALS AND METHODS

### Bacteriological examination

Thirty-seven CSF specimens were included in the study. These were processed and identified according to standard techniques.<sup>2,9</sup>

### Determination of lactic acid concentration

CSF samples were kept at  $-70^{\circ}\text{C}$  for various lengths of time ranging from 18 hours to four years. Blood-stained specimens were excluded. Lactic acid levels were determined by Castroni's method<sup>10</sup> based on that of Holdeman, Cato and Moore.<sup>11</sup>

The equipment used was a 5730A Hewlett Packard with a flame ionization detector (temperature  $300^{\circ}\text{C}$ ), fitted with a glass column (100–120 mesh) and packed with 10% diethyl glycol succinate on Chromosorb W-HP. The gas flow rate through the detector was 20 ml/min for nitrogen, 30 ml/min for hydrogen and 300 ml/min for air. The instrument was operated isothermally at a temperature of  $130^{\circ}\text{C}$ . A chart recorder was used to trace the acid peaks.

A volume of 0.5 ml of standard lactic acid (30 mg/dl) was added to 0.5 ml of the CSF. One ml of the standard lactic acid was used as a control, and both test and control were treated in the following manner: The samples were acidified with 0.1 ml of 50%  $\text{H}_2\text{SO}_4$  and 1.0 ml methanol added. The tubes were then capped and placed in a waterbath for 5 minutes. After the specimens were cooled at room temperature, 0.5 ml chloroform was added to each tube. Contents were mixed by gentle inversion 20 times. Fourteen microlitres of the chloroform layer were used for the gas liquid chromatographic analysis. The height of the lactic acid peaks in test samples, seen in less than five minutes, were compared with that of the standard. The concentration of the acid in test samples was calculated from the area ratio. A positive result was taken as  $\geq 30$  mg/dl and  $< 30$  mg/dl was considered negative.

## RESULTS

Table 1 shows the details of the culture positive cerebrospinal fluid samples. The lactic acid levels were markedly elevated in *Haemophilus influenzae* meningitis, in one of three cases of *Flavobacterium meningosepticum* meningitis and in one case of cryptococcal meningitis.

Table 2 shows lactic acid concentration in CSF specimens with normal cytology and biochemistry but with growth of bacteria. These specimens were obtained from infants (who presented with fits and subsequently recovered) as part of the septic workout. Therefore, the bacterial isolates were considered to be contaminants. These included *Bacillus* sp, diphtheroids, *Staphylococcus epidermidis* and alpha-haemolytic streptococci. The concentration of lactic acid in these specimens was  $< 30$  mg/dl.

Lactic acid concentrations in the CSF of four cases of viral encephalitis and meningoencephalitis was  $< 30$  mg/dl. The concentration was found to be moderately raised, 33 and 36 mg/dl in two of three cases of partially treated meningitis. The CSF in these cases showed high cell counts (50 cells/mm<sup>3</sup> and 2000 cells/mm<sup>3</sup> respectively) with predominant polymorphonuclear cells. CSF glucose levels were low and cultures yielded no growth.

## DISCUSSION

This study supports the findings of other workers on the diagnostic value of CSF lactic acid concentration in cases of meningitis. Castroni *et. al.*<sup>10</sup> using gas liquid chromatography had found elevated levels

Table 1: Lactic acid concentrations in culture positive cases of meningitis.

Organisms isolated	No. of specimens	CSF lactic acid concentration in mg/dl				
		Case 1	Case 2	Case 3	Case 4	Case 5
<i>Cryptococcus neoformans</i>	2	36	20			
<i>Streptococcus pneumoniae</i>	5	30	30	35	35	61
<i>Haemophilus influenzae</i>	5	72	84	49	60	60
<i>E. coli</i>	1	36				
<i>Enterobacter</i> sp.	1	31				
<i>Flavobacterium meningosepticum</i>	3	82	42	32		

Table 2: Lactic acid concentration in culture positive CSF but with normal cytology and biochemistry.

No. of specimens (Sp) examined	Culture	Lactic acid concentration in mg/dl				
		Sp1	Sp2	Sp3	Sp4	Sp5
5	<i>Bacillus</i> sp.	20	24	24	24	24
1	Mixed growth of <i>Bacillus</i> sp. and diphtheroids	27				
1	Mixed growth of <i>Enterobacter</i> sp. & <i>Acinetobacter</i> sp.	24				
1	Mixed growth of <i>Bacillus</i> sp. and <i>Staph. epidermidis</i>	24				
1	Alpha-haemolytic streptococcus	18				
1	<i>Flavobacterium</i> sp.	24				

of lactic acid in 16 cases with bacterial meningitis while elevation of acid was not detected in 134 patients without bacterial meningitis. According to their study, 20 mg/dl of acid was the upper limit in normal CSF while levels of 30 mg/dl or higher was associated with bacterial meningitis. In the present study,  $\geq 30$  mg/dl was used as the cut-off point.

In 15 proven cases of bacterial meningitis, the lactic acid levels were equal or greater than 30 mg/dl. The acid levels were markedly elevated in *Haemophilus influenzae* meningitis but were  $< 30$  mg/dl in cases of viral encephalitis and meningoencephalitis. However, increased lactic acid levels have been reported in severe encephalitis,<sup>12</sup> although the levels obtained were not as high as in bacterial meningitis. In two cases of cryptococcal meningitis, one had a raised lactic acid level (36 mg/dl) while the other was

found to be low (20 mg/dl). Further studies are needed to evaluate the usefulness of lactic acid determination in fungal meningitis.

Lactic acid levels in CSF may be useful in differentiating meningitis of viral and bacterial aetiology. Among the advantages of using gas liquid chromatography for lactic acid determination are short performance time and sensitivity to various genera of bacteria.<sup>5</sup> It can also be used to exclude probable bacterial contaminants in specimens. In this study, lactic acid levels were low in 10 specimens which had growth of bacteria in the absence of other features of meningitis.

Lactic acid determination was also carried out to monitor the progress of patients after antibiotic therapy.<sup>4,6</sup> In two of three cases of partially treated meningitis, the CSF lactic acid levels were found to be above 30 mg/dl. In three cases of treated meningitis, where both CSF cytology and biochemistry had reverted to normal, the lactic acid levels were also found to be <30 mg/dl.

Estimation of lactic acid in CSF by gas liquid chromatography provides a useful additional test in the diagnosis of bacterial meningitis. It may also be used in monitoring the efficacy of treatment.

## REFERENCES

- <sup>1</sup> Leading article: Partially treated pyogenic meningitis. *Br Med J* 1977; 1:340.
- <sup>2</sup> Pit, S.; Jamal, F.; Lim, V. and Abdullah, A.M. Pattern of bacterial meningitis in childhood. *Jurnal Perubatan UKM* 1981; 1: 18-20.
- <sup>3</sup> Feldman, W.E. Cerebrospinal fluid lactic acid dehydrogenase activity. *Am J Dis Child* 1975; 129: 77-80.
- <sup>4</sup> Ferguson, I.R. and Tearle, P.V. Gas liquid chromatography in the rapid diagnosis of meningitis. *J Clin Path* 1977; 30: 1163-7.
- <sup>5</sup> Hund, C.A.; Fennema, K.J. and Blzevic, D.J. Use of cerebrospinal fluid lactate levels in the diagnosis of bacterial meningitis. *Am J Med Tech* 1978; 44.1: 11-3.
- <sup>6</sup> Vanprapar, N.; Chavalittamrong, B. and Limsathayurat, N. Cerebrospinal fluid lactate in childhood purulent meningitis. *Southeast Asian J Trop Med Pub Hlth* 1983; 14.2: 186-90.
- <sup>7</sup> Wroblewski, F.; Decker, B. and Wroblewski, R. The clinical implications of spinal fluid lactic dehydrogenase activity. *N Engl J Med* 1958; 258: 635-9.
- <sup>8</sup> Berg, B.; Gardsell, P. and Skanberg, P. Cerebrospinal fluid lactate in the diagnosis of meningitis. *Scand J Infect* 1982; 14: 111-5.
- <sup>9</sup> Cowan, S.T. and Steel, K.J. *Manual for the identification of medical bacteria*. 2nd edition. Cambridge University Press, London 1975.
- <sup>10</sup> Castroni, G.; Rodriguez, W.T.; Deane, C.; Ross, S.; Kahn, W. and Puig, J.R. Rapid diagnosis of meningitis by gas liquid chromatographic analysis of CSF lactic acid. *Clin Proc Child Hospital Natl Med Center* 1975; 31: 194-201.
- <sup>11</sup> Holdeman, L.V.; Cato, E.P. and Moore, W.E.C. *Anaerobe Laboratory Manual*. 4th Ed. Anaerobe Laboratory Virginia Polytechnic Institute and State University, Blackbury, Virginia 1977; 134-6.
- <sup>12</sup> Hansen, E.L.; Kristensens, H.S.; Brodensen, D.; Paulson, O.E.; Muellert, S. and Jessen, O. Acid base pattern of cerebrospinal fluid and arterial blood in bacterial meningitis and encephalitis. *Acta Med Scand* 1975; 196: 431-7.