The Use Of Cerebrospinal Fluid Lactate As A Marker Of Bacterial Meningitis

Thesis

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List of abbreviations

– ADEM	acute disseminated encephalomyelitis
– AM	aseptic meningitis
– BBB	blood-brain barrier
– BM	Bacterial Meningitis
– CFR	Case Fatality Rate
– CFU	Colony-Forming Units
– CIE	Counter Immuno-Electrophoresis
– CMV	Cytomegalovirus
– CNS	Central Nervous System
– CRP	C-Reactive Protein
– CSF	Cerebrospinal fluid
– CT	Computed Tomography
– EBV	Epstein-Barr virus
– ED	Emergency department
– ESR	erythrocyte sedimentation rate
– FDA	US Food and Drug Administration
– GCSF	granulocyte colony stimulating factor
– Hib	*Haemophilus influenzae* type b
– HIV	Human immunodeficiency virus
– HSV	Herpes simplex virus
– ICP	intracranial pressure
– IHMF	International Herpes Management Forum
– IL	interleukin
– IM	Intramuscular
– IQ range	interquartile range
– IV	Intravenous
– LCMV	Lymphocytic choriomeningitis virus
– MOHP	Ministry Of Health and Population
– MRI	Magnetic Resonance Imaging
– *N. meningitides*	Neisseria meningitides

– NICE	National Institute for Health and Clinical Excellence
– OR	Odds Ratio
– PCR	polymerase chain reaction
– PCT	Procalcitonin
– PMN	Polymorphonuclear cells
– PO	Per OS
– RBC	Red Blood Cell
– *S. pneumonia*	Streptococcus pneumonia
– SEM	skin, eye and mouth disease
– SIADH	Syndrome of Inappropriate Antidiuretic Hormone secretion
– UK	United Kingdom
– US	United States
– VM	viral meningitis
– VZV	Varicella zoster virus
– WBC	White Blood Cell
– WHO	World health organization

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Introduction

Acute infection of the central nervous system (CNS) is the most likely cause of a febrile illness with manifestations of CNS involvement. Stiff neck or crying when handled suggests meningeal irritation. Bulging fontanel, headache, or vomiting suggests increased intracranial pressure. A change in consciousness, such as confusion or disorientation, is an alarming sign that suggests a disturbance of cerebral cortical function that may have many causes, including cerebral anoxia, inflammation, or edema. ***(Fisher& Boyce,*** ***)***

Infection of the CNS may be diffuse or focal. Meningitis and encephalitis are examples of diffuse infection. **Meningitis** implies primary involvement of the meninges, whereas **encephalitis** indicates brain parenchymal involvement. Because these anatomic boundaries are often not distinct, many patients have evidence of both meningeal and parenchymal involvement and should be considered to have **meningoencephalitis** ***(Prober& Dyner,*** ***)***

Encephalopathy is a generalized disorder of cerebral function that may be acute or chronic, progressive or static. The etiologies of the encephalopathies in children include infectious, toxic (carbon monoxide, drugs, lead), metabolic, genetic and ischemic causes ***(Johnston,*** ***)***

Physicians frequently care for patients who present with signs or symptoms that suggest CNS dysfunction. The differential diagnosis is broad, as disease of any organ system, when sufficiently severe, can alter CNS function. Rapid diagnosis and treatment is often necessary to prevent morbidity or mortality. Primary factors that drive the brain's susceptibility to

damage from infection are (١) inadequate room for expansion when inflammation is present;(٢) poor immune function within the blood-brain barrier;(٣) difficulty in achieving adequate antimicrobial concentrations in the cerebrospinal fluid (CSF) and parenchyma; and (٤) inability of the brain to regenerate neural tissue once cell death has occurred.***(Diebold, ٢٠٠٦)***

Classification of meningitis: ***(Fisher & Boyce, ~)***

Purulent Meningitis:

Purulent meningitis is best defined by a cerebrospinal fluid (CSF) that is cloudy and contains more than ١٠٠٠ neutrophils/mcL. Whether or not a bacterial etiology is proven by culture, purulent meningitis is almost always bacterial. When the term "meningitis" is not further modified, it usually means purulent meningitis

Nonpurulent Meningitis:

A CSF leukocyte count of ١٠- ٥٠٠/mcL, usually predominantly lymphocytes, can be defined as nonpurulent meningitis and this usually indicates a nonbacterial process (aseptic meningitis syndrome), but not always. Patients with CSF cell counts in the intermediate range (٥٠٠-١٠٠٠/mcL) can usually be classified as having presumed bacterial meningitis or aseptic meningitis syndrome on the basis of the cell count and differential, glucose, protein, Gram stain, and state of consciousness.

Despite advances in antimicrobial and general supportive therapies, CNS infections remain a significant cause of morbidity and mortality in children. Because the classic signs and symptoms are often absent, especially in younger children, diagnosing pediatric CNS infections is a challenge to the emergency department (ED). Even when such infections are

promptly diagnosed and treated, neurologic sequelae are not uncommon. Clinicians are faced with the daunting task of distinguishing the relatively few children who actually have CNS infections from the vastly more numerous children who come to the ED with less serious infections.***(Faust,*** ***)***

The beginning of this millennium has witnessed the virtual disappearance of ***Haemophilus*** invasive disease in some countries, emergence of pneumococcal strains that are resistant to multiple antibiotics, isolation of pneumococci with tolerance to vancomycin, outbreaks and clusters of meningococcal meningitis in several geographical areas, and intense research in development of effective conjugate pneumococcal and meningococcal vaccines. Bacterial meningitis has become an uncommon disease in the developed world. Unfortunately, because of limited economic resources and poor living conditions, many developing countries are still affected by the devastating consequences of this life-threatening systemic infection ***(Saez-Llorens and McCracken,*** ***)***

Accurate and rapid diagnosis of acute bacterial meningitis (BM) is essential because disease outcome depends on immediate initiation of appropriate antibiotic therapy ***(Saez-Llorens and McCracken,*** ***)***

CSF lactate is superior to the conventional methods in being rapid, not affected by antibiotic intake prior to CSF sampling and being independent of blood lactate level ***(Watson and Scott,*** ***)***

Aim of the work

To evaluate the use of CSF lactate to differentiate bacterial meningitis from viral meningitis.

Bacterial Meningitis

Definition

Meningitis is an inflammation of the leptomeninges and underlying subarachnoid cerebrospinal fluid (CSF). The inflammation may be caused by infection with viruses, bacteria, other micro-organisms, or non-infective causes ***(Razonable et al,*** ***)***

"Probable bacterial meningitis" cases were defined according to ***World Health Organization (WHO,*** ***)*** criteria as those presenting with clinical symptoms of meningitis (i.e. fever, headache, stiff neck, bulging fontanel or altered mental status) and CSF with an elevated protein (> ١٠٠ mg/dl), decreased glucose (< ٤٠ mg/dl) or leukocytosis (> ١٠٠ WBC/mm^{٣}) with at least ٨٠٪ neutrophils and lacking an identifiable bacterial pathogen. "Confirmed bacterial meningitis" cases were defined according to ***WHO*** case definition criteria : children presenting with clinical symptoms of meningitis (i.e. fever, headache, stiff neck, bulging fontanel or mental status changes) and identification of bacteria directly (by culture or PCR from blood or CSF, or by culture from the petechial lesions), or indirectly (by latex test, countercurrent immunoelectrophoresis, Phadebact (latex agglutination), or Gram stain smear of blood or CSF) ***(WHO,*** ***)***

Incidence

Bacterial meningitis remains a serious threat to global health, accounting for an estimated annual ١٧٠ ٠٠٠ deaths worldwide (***WHO,*** ***)***. Every year, bacterial meningitis epidemics affect more than ٤٠٠ million people living in the ٢١ countries of the "African meningitis belt"