

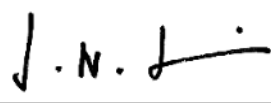


Work Practice Document: 10

Management of raised intracranial pressure

Title of study	High Dose AMBISOME® on a Fluconazole Backbone for Cryptococcal Meningitis Induction Therapy in sub-Saharan Africa: A Phase III Randomized Controlled Non-inferiority Trial		
Acronym	Ambition-cm – AMBIsome Therapy Induction OptimizatiON		
ISRCTN No.:	ISRCTN72509687		
WPD Current version	Version 1.0, 20/07/2017		
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Approved by	Joseph Jarvis CI		20/07/2017

Revision History:

Version Number	Effective Date	Reason for Change
1.0		First version

Working Practice Document 10: Management of raised intracranial pressure

Purpose

This document describes the process of managing raised intracranial pressure

References

- Perfect, J. R. et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. *Clin. Infect. Dis.* 50, 291–322 (2010).
 - Rolfes, M. A. et al. The effect of therapeutic lumbar punctures on acute mortality from cryptococcal meningitis. *Clin. Infect. Dis.* 59, 1607–1614 (2014).
 - Beardsley, J. et al. Adjunctive dexamethasone in HIV associated cryptococcal meningitis. *N. Engl. J. Med.* 374, 542–554 (2016).
 - Jarvis, J. N. et al. Determinants of mortality in a combined cohort of 501 patients with HIV-associated cryptococcal meningitis: implications for improving outcomes. *Clin. Infect. Dis.* 58, 736–745 (2014).
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Scope

This WPD applies to the process of managing raised intracranial pressure

Materials

WPD 12: Lumbar Puncture

Working Practice Document 10: Management of raised intracranial pressure

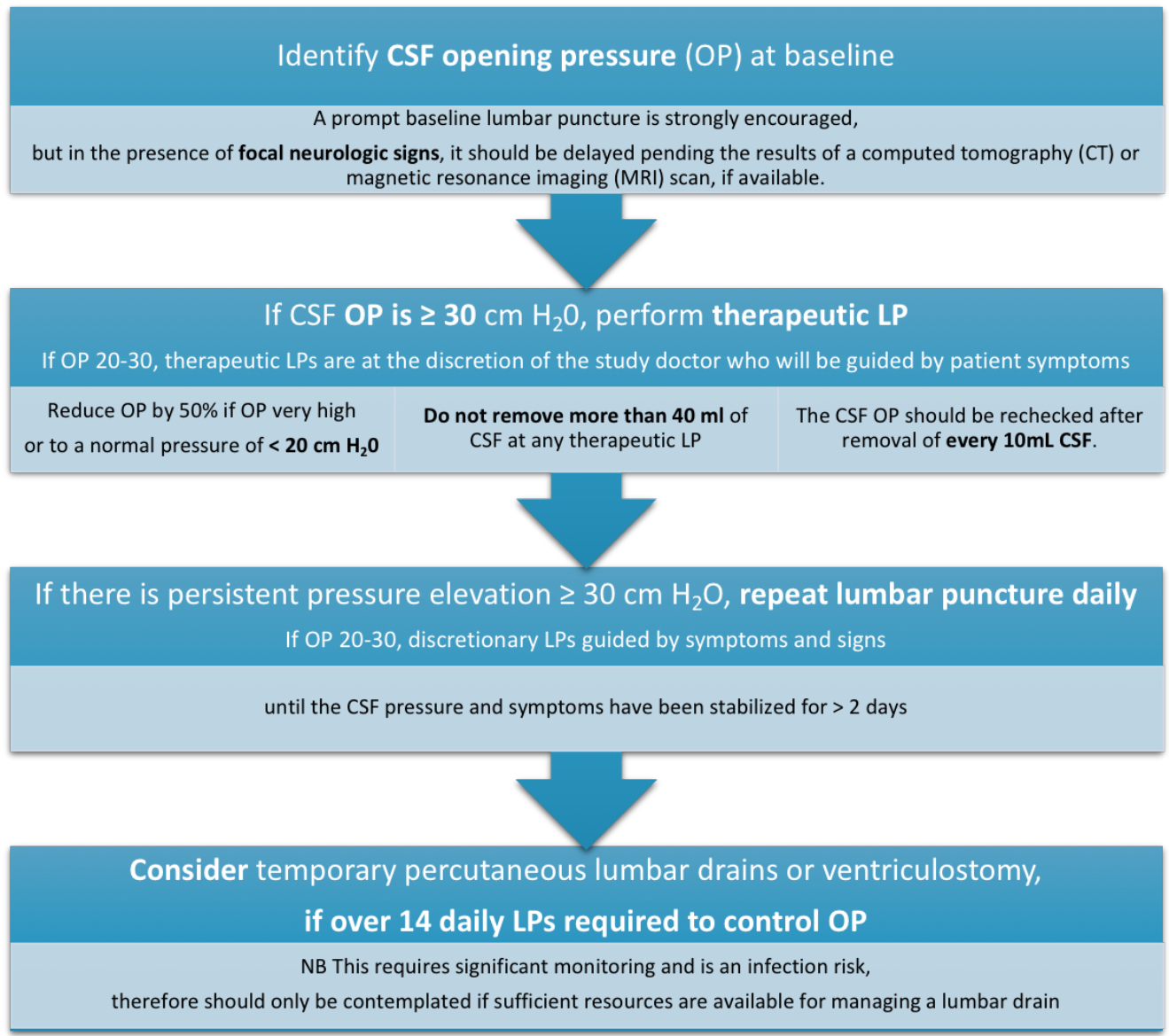
- Half of HIV-infected patients with CM have a CSF opening pressure of >25 cmH²O, with roughly a quarter of patients having a very high pressure of >35 cmH²O. High pressure is associated with worse symptoms, including headache, nausea, diplopia secondary to sixth nerve palsies, and altered mental status.
- Repeated daily therapeutic lumbar punctures are sufficient to control raised pressure in the majority of patients.
- All patients who have focal neurological signs (except VIth cranial nerve palsy which is often a false localising sign) should, if possible, have a contrast enhanced brain CT to identify mass lesions that may increase the risk of lumbar puncture. If no CT scan is available, the balance of risk favours performing a lumbar puncture.
- Cryptococcal meningitis patients should have an admission lumbar puncture CSF opening pressure recorded. Patients admitted to the study, regardless of their initial opening pressure, will undergo serial lumbar punctures on days 1, 7 and 14 of their admission.
- **The opening pressure must be measured and documented for each and every lumbar puncture.**
- Where study patients have raised intracranial pressure secondary to cryptococcal meningitis, the patient's CSF will be drained as often as required until the opening pressure normalises.
- Raised intracranial pressure is defined as a CSF opening pressure > 20 cm H²O.
- A therapeutic lumbar puncture aims to provide lumbar drainage sufficient to achieve a closing pressure ≤ 20 cm H²O or 50% of the initial opening pressure.
- **If OP >30 cm H₂O, daily therapeutic LPs should be undertaken. If OP 20-30 cm H₂O, therapeutic LPs are at the discretion of the study doctor who will be guided by patient symptoms.**
- Usually no more than 40mls CSF will be drained at any one therapeutic lumbar puncture.
- The CSF pressure should be rechecked after removal of every 10ml CSF.
- Where repeated lumbar punctures over >14 days fail to control raised intracranial pressure, and the patient is deteriorating, lumbar drains may be considered. However, the high local rates of nosocomial infection and the lack of nursing staff trained to care for such drains are important factors to take into consideration.

Please note:

- Mannitol has no proven benefit and is not recommended.
- Acetazolamide should be avoided to control increased intracranial pressure.
- Corticosteroids should not routinely be used during induction therapy for HIV-associated cryptococcal meningitis.

Working Practice Document 10: Management of raised intracranial pressure

Figure 1. Management of raised ICP diagram



Working Practice Document 10: Management of raised intracranial pressure

Training

Each staff member receives or has direct access to applicable Working Practice Documents (WPDs).

Each staff member reviews the applicable WPDs once a year.

All WPD training is documented and tracked in the training log located in the Investigator Site File (ISF)

New staff are trained on applicable WPDs within 30 days of employment and all WPDs within 90 days of employment.

Staff members whose duties fall within this WPD scope are retrained within 14 days of the approval of each WPD revision.

