

subtropical areas of Central and South America. The diagnosis of the central nervous system (CNS) involvement with paracoccidioidomycosis is frequently difficult. A definitive diagnosis is usually made by the isolation of the *P. brasiliensis* from CNS biopsy or necropsy material. The presence of antibodies anti-gp43 in CSF of patients with CNS involvement in PCM may indicate disease.

Guillain barre syndrome

In the first week of neurological symptoms the CSF protein may be normal but then becomes elevated on subsequent examination. In 10% cases, CSF protein remains normal throughout the illness. Transient oligoclonal IgG bands and elevated myelin basic protein may be detected in some patients.

Subarachnoid hemorrhage

Cerebrospinal fluid adrenomedullin concentration correlates with hyponatremia and delayed ischemic neurological deficits after subarachnoid hemorrhage.

Dementia

Measuring proteins in cerebrospinal fluid (CSF) has gained wide acceptance for the differential diagnosis of dementia. Median Abeta 42 level increases in dementia and decreases in Alzheimers. S-100B protein increases during follow-up in both the diseases.

Neurocysticercosis(NCC)

It is a parasitic disease of the nervous system caused by the larva of taenia solium. The disease is an important public health problem in developing countries. The diagnostic criteria

for NCC are related to the clinical and epidemiological data, neuroimaging studies and the reactivity of immunosorbent assay (ELISA) for NCC in the serum and CSF.

CONCLUSION

Innovative approaches to treatment of diagnostically challenging neurological diseases are being widely tested. Unfortunately, research on diagnostic strategies and outcome measures on which any advances in treatment ultimately depends, has not been avidly pursued. All the currently available measurements, including CSF cytology, biochemistry, immunology and molecular markers suffer from poor sensitivity and specificity and often correlate poorly with each other. Although CSF cytological examination, performed according to a rigorous, research supported protocol, may be the optimum diagnostic and outcome measure at this time, additional research is a prerequisite for any further advances in the diagnosis of challenging CSF's.

RECOMMEDED READING

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Drug Profile

VORICONAZOLE

Voriconazole is a triazole antifungal agent, chemically, it is designated as (2R,3S)-2(2,4-difluorophenyl)-3-(5-fluoro-4-pyrimidinyl)-1(1H-1,2,4-triazol-1-yl)-2-butanol.

Indications: The Drug is indicated for use in the treatment of . (a) invasive aspergillosis; (b) fluconazole-resistant serious invasive candida infections (including *C. Krusei*); (c) esophageal candidiasis; (d) Serious fungal infections caused by *scedosporium apiospermum* (a sexual form of *pseudallescheria boydia*)

Mecanism of Action : Voriconazole is a triazole antifungal agent; its primary mode of action is by inhibition of fungal Cytochrome P-450-mediated 14 alpha-alamosterol demethylation - an essential step in fungal ergosterol biosynthesis. The accumulation of 14 alpha-methyl sterols correlates with the subsequent loss of ergosterol in the fungal cell wall and may be responsible for the antifungal activity of voriconazole. The drug has been shown to be more selective for fungal cytochrome P-450 enzymes than for various mammalian cytochrome p-450 enzyme systems.

Dosage and Administration: The pharmacokinetics of orally administered voriconazole is not affected by renal impairment. Therefore, no adjustment is necessary for oral dosing for patients with mild to severe renal impairment.

Table 1 A: Recommended Dosing Regimen in Adults and Adolescents (12 to 16 years of age)

Dose Regimen	Intravenous	Oral (tablets)	
		Patients 40 Kg and above	Patients less than 40 Kg
Loading Dose (for the first 24 hrs)	6 mg/kg every 12 hrs	400 mg every 12 hrs.	200 mg every 12 hrs.
Maintenance Dose (after first 24 hrs)	4 mg/kg twice daily	200 mg twice daily	100 mg twice daily

Voriconazole is haemodialysed with a clearance of 121 ml/min. A four hour haemodialysis session does not remove a sufficient amount of Voriconazole to warrant dose adjustment. After intravenous administration, cyclodextrin can accumulate in the kidneys, unlike after oral administration. Accumulation of the intravenous vehicle, hydroxypropyl B cyclodextrin may occur in patients with moderate or severe renal insufficiency (creatinine clearance <50 mL/min). Oral voriconazole should be administered to these patients, unless an assessment of the benefit/risk to the patient, justifies the use of intravenous voriconazole. Serum creatinine levels should be closely monitored in these patients, and if increase occurs, consideration should be given to changing to oral voriconazole therapy.

Precautions: (1) Pregnancy- teratogenic effects on the foetus. (2) Women of childbearing potential should use effective contraception with increased dose during co-administration of voriconazole with oral contraceptive. (3) The excretion of voriconazole in breast milk has not been investigated. Voriconazole should not be used by nursing mothers unless the benefit clearly outweighs the risk.

Undesirable Effects : The most frequently reported adverse events in the therapeutic trials include fever, rash, vomiting, nausea, diarrhoea, headache, sepsis, peripheral edema, abdominal pain and respiratory disorder. The treatment-related adverse events which may often need discontinuation of voriconazole therapy include (i) elevated liver enzymes, (ii) rash, (iii) visual disturbances (colour vision change, photophobia, decrease in visual field-20% cases). (iv) dermatological reaction like photosensitivity.