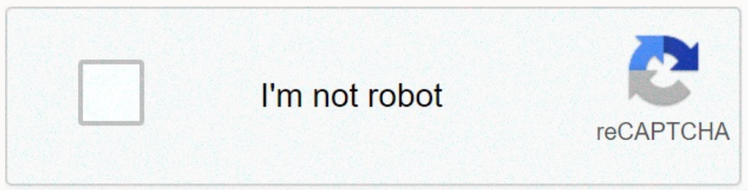

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Cryptococcus meningitis guidelines

Skip Nav Destination PDF Split View Article Content Numbers & Table Image Audio Additional Data 8 Persons Subcommittee of the National Institute of Allergy and Infectious Diseases (NIAID) Mycoses Research Group evaluated available data on cryptococcal disease treatment. The opinion on optimal treatment was based on personal experience and information in the literature. The relative strength of each recommendation was sorted by the type and degree of evidence based on the recommendation, in accordance with the previously published Guidelines of the American Society for Infectious Diseases (IDSA). The college is in person (2 times), by conference call and written reviews of each manuscript project. The choice of treatment for cryptococcus neoformans disease depends both on the anatomical places of participation and on the immune status of the host. Immunocompetent hosts with isolated lung disease may be justified by careful monitoring; in case of symptomatic infection, the prescribed treatment is fluconazole, 200-400 mg per day for 3-6 months. For persons with non-CNS isolated cryptococcaemia, positive serum cryptococcal antigen titre >1 : 8 or urinary tract or skin disease, the recommended treatment is oral azole treatment (fluconazole) for 3-6 months. In each case, in order to rule out occult meningitis, the CNS should be carefully evaluated. For those who cannot tolerate fluconazole, itraconazole (200-400 mg daily for 6-12 months) is an acceptable alternative. In patients with more severe disease, treatment with amphotericin B (0.5-1 mg/kg/d) may take 6 to 10 weeks. For otherwise healthy hosts with CNS disease, standard therapy consists of amphitheicin B, 0.7-1 mg/kg/d, as well as flucytosin, 100 mg/kg/d, 6-10 weeks. The alternative to this regimen is amtroricine B (0.7-1 mg/kg/d) and 5-flucytosin (100 mg/kg/d) for 2 weeks followed by fluconazole (400 mg/day) for at least 10 weeks. Fluconazole consolidation therapy can be continued in the same way as 6-12 months, depending on the clinical condition of the patient. HIV-negative, immunocompromised hosts should be treated in the same way as CNS disease, regardless of the location of the participation. Cryptococcal disease, which develops in patients with HIV infection, always guarantees treatment. In HIV patients with isolated lung or urinary tract disease, fluconazole 200-400 mg/d is indicated. Although the final effect of highly active antiretroviral therapy (HAART) is currently unclear, lifelong maintenance therapy is recommended for all HIV infected subjects. Itraconazole (200-400 mg/d) is an acceptable alternative among those who cannot tolerate fluconazole. In patients with more severe diseases, fluconazole (400 mg/d) and flucytosine (100-150 mg/d) can be administered for 10 weeks followed by fluconazole therapy. In patients with HIV infection and cryptococcal meningitis, induction treatment with amtrotericin B (0.7-1 mg/kg/d) and flucytosin (100 mg/kg/d for 2 weeks), followed by fluconazole (400 mg/d) for at least 10 weeks, is the treatment of choice. After 10 weeks of treatment, the dose of fluconazole can be reduced to 200 mg/d, depending on the clinical condition of the patient. Fluconazole should be continued for life. An alternative regimen for AIDS-related cryptococcal meningitis is amtroricine B (0.7-1 mg/kg/d) and 5-flucytosin (100 mg/kg/d) for 6-10 weeks followed by fluconazole maintenance therapy. Induction therapy, starting with azole alone, is usually discouraged. Amfitericin B lipid preparations amtroricine B may be replaced in patients with impaired renal function. Fluconazole (400-800 mg/d) and flucytosine (100-150 mg/kg/d) for 6 weeks are an alternative to amtroricine B, although

toxicity to this regimen is high. In all cases of cryptococcal meningitis, careful attention should be paid to the management of intracranial pressure in order to ensure an optimal clinical outcome. Introduction As with other systemic mycoses, the treatment of C. neoformansis has improved significantly over the last 2 decades. Cryptococcal disease, which was spread by 1950, was equally fatal. As many as 60-70% of patients with cryptococcal meningitis were successful in the development of polyene antifungal agents, in particular amphotericin B [1]. In the early 80's, flucytosin was identified as a daily biosimilar agent strongly exposed to C. neoformans; however, this activity was rapidly lost due to the development of resistance when the drug was used as monotherapy [2]. When flucytosin was added to amphitheericin B as a combination therapy, the overall treatment outcome improved and the duration of treatment could be reduced from 10 weeks to 4-6 weeks, depending on the host's condition [1,3]. Since the 1980s, overflowing azole antifungal drugs exposed to C. neoformans, especially itraconazole and fluconazole, have been introduced. Around the same time, the incidence of cryptococcal infections has increased dramatically due to the explosion of the AIDS epidemic worldwide and the use of stronger immunosuppressive agents in the face of an increasing number of die-hard organ transplant recipients [4]. As the overall incidence of cryptococcal disease has increased, there are also a number of treatment options that can be treated for the disease. Currently, in addition to amphitheericin B and flucytosin, other medicines, namely fluconazole, itraconazole and amfitericin B formulas can be used to treat cryptococcal infections. These agents can be used alone or in combination with other agents, the success of which varies. Some of the currently used treatment regimens have not been studied in randomised clinical trials, but are used on the basis of anecdotes or open Phase II studies. As a result, most doctors are not sure which agents to use, for which state of the underlying disease, for what combination and for what duration. It is noticeable that, despite the relatively short time of existence of AIDS, there is now more data on the treatment of AIDS-related cryptococcal meningitis than on the treatment of any other form of cryptococcal infection. Guidelines for the treatment of cryptoccoccosis in patients without HIV infection Pulmonary and non-CNS disease The presentation of pulmonary cryptococosis may range from asymptomatic nodultic disease to severe acute respiratory distress syndrome (ARDS). Classic symptoms of pneumonitis, including cough, fever, and sputum production, may be present, or pleural symptoms may be dominating. Lungs are the main way to get into infection. The presence of a positive serum cryptococcal antigen titre refers to deep tissue invasion and a high probability of spreading the disease. The body has a strong predilection to infect the CNS; however, infection has been reported in almost every organ in the body. Objectives. The purpose of treatment is to cure the infection and prevent the spread of the disease to the CNS. Options. A limited number of studies have been conducted specifically to evaluate the results of HIV negative patients with lung or non-CNS disease. Therefore, no specific treatment of choice and optimal duration of treatment were fully explained in hiv negative patients. It is clear that all immunocompromised patients should be treated, as they are at high risk of developing a disseminated infection. Patients with symptoms should be treated. Although all asymptomatic patients with positive cultures should be considered for treatment, many immunocompromisal patients with positive sputum cultures did well without treatment [5]. However, patients with non-pulmonary, eliminated (e.g. bone or skin) disease require specific antifungal therapy. Surgery should be performed in patients with persistent or refractory lung or bone disease, but it is rarely needed. Results. The desired result is the resolution or stabilisation of symptoms such as cough, shortness of breath, sputum production, chest pain, fever and chest radiographic abnormalities (infiltrates, nodules or masses). In the case of extrapulmonary, non-CNS disease, the desired result is the resolution of symptoms and signs, as well as other markers of the disease (e.g. radiographic abnormalities). Recommendations. Specific treatment of HIV-related cryptococcal lung disease are summarised in Table 1. Regardless of the treatment chosen, it is necessary that all patients with pulmonary and extrapulmonary cryptococcal disease have a lumbar puncture in order to rule out CNS infection. Immunocompromisal patients who are asymptomatic and have a pulmonary culture positive for C. neoformanus can be closely monitored or treated with fluconazole, 200-400 mg/d for 3-6 months [3, 4, 6, 7] (AIII; see section 4.4.2). Article [8] of Sobel on the definitions of categories reflecting the strength of each recommendation on its use or the strength of its use and the classes reflecting the quality of the evidence on which the recommendations are based). Immunocompotent patients with mild to moderate symptoms should be treated with fluconazole 200-400 mg/d for 6 to 12 months [3.4] (AIII). In cases where fluconazole is not an option, an acceptable alternative regimen is itraconazole, 200-400 mg/d, 6-12 months [9] (BIII). The toxicity of amphitherericin B limits its usefulness as the desired agent in the treatment of mild to moderate lung disease among immunocompetent hosts. However, if oral azole or lung disease is severe or progressive, the use of amfeticin B, 0.4 to 0.7 mg/kg/d at a total dose of 1000-2000 mg (BIII) is recommended. Ketoconazole has in vitro activity against C. neoformans, but is generally ineffective in the treatment of cryptococcal meningitis and should be used rarely, if at all, in this environment [10] (CIII). Some reports describe the successful use of flucytosin (100 mg/kg/d for 6-12 months) as a therapy for pulmonary cryptococcal disease; however, concerns about the development of resistance to flucytosin when used alone limit its use in this setting [2,5] (DII). Immunocompromised patients with non-CNS lung and extrapulmonary disease should be treated in the same way as patients with CNS disease [4.6] (AIII). Some patients are isolated cryptococcocaemia, positive serum cryptococcal antigen titre (>1 : 8) without clinical signs of disease or positive urinary culture or prostate disease. Although no retrospective or prospective studies have been conducted to investigate treatment options in such patients, they should probably be treated with antifungal therapy (AIII). Benefits and harm. Early, appropriate treatment of non-CNS lung and extrapulmonary cryptococcocal reduces morbidity and prevents progression to potentially life-threatening CNS disease. Among patients with hard organ transplantation, aggressive treatment of early cryptococcal disease can prevent the loss of the transplanted organ. Drug-related toxicity and the development of undesirable drug interactions are the main possible harm of therapeutic intervention. Costs. The cost of buying drugs is high for antifungal treatments 6-12 months. Additional costs accrue monthly in monitoring and monitoring of treatment associated with most of the recommended regimens. CNS disease cns disease is usually meningitis and in rare cases as lumps or multiple focal mass lesions (cryptococcomas). CNS disease can be associated with concurrent pneumonia or other signs of a disseminated disease, such as focal skin lesions, but most often it is a lone CNS infection without other manifestations of the disease. Whether or not CNS disease is associated with the participation of other areas of the body, the treatment remains the same. Objectives. The purpose of treatment is to cure infection (CSF sterilization) and prevention of long-term continuation of the CNS system, such as cranial nerve palsy, hearing loss and the blind. Options. In contrast to non-CNS disease, several studies have been conducted specifically to assess the results of HIV negative patients with cryptococcal meningitis. Studies evaluating the effectiveness of amphitheericin B, with or without flucytosin, have shown the optimal duration of treatment of HIV negative, immunocompromised and immunocompromised hosts. However, in the era of triazole therapy, no randomized studies in these population groups were completed. Results. The desired result is a solution to problems such as fever, headache, altered mental state, meningeal signs, increased intracranial pressure and cranial nerve disorders. In cases of CNS mass damage (cryptococcomas), the desired result is the radiographic resolution of lesions. Recommendations. Specific recommendations for the treatment of non-HIV cryptococcal meningitis are summarised in Table 1. Combination treatment of amphotericin B and flucytosin will sterilise CSF within 2 weeks of treatment in 60%-90% of patients [1.3]. Most immunocompetent patients will be successfully treated with 6 weeks of combination therapy [1.3] (AI); however, due to the requirement for (iv) therapy, long-term and relative toxicity of the regimen promoted alternatives to this method. Despite the absence of controlled clinical trial data from HIV-negative patient populations, a commonly used alternative treatment of cryptococcal meningitis in immunocompetent patients is the induction course of amphitheericine B (0.5-1 mg/kg/d) with flucytosin (100 mg/kg/d) for 2 weeks followed by consolidation therapy with fluconazole (400 mg/d) for a further 8-10 weeks [7] (BIII). This recommendation has been extrapolated from experience in the treatment of patients with HIV-related cryptococcal meningitis [11, 13]. Pilot studies investigating fluconazole with flucytosin in initial therapy have produced unsatisfactory results [7]. Therefore, initial treatment with fluconazole, even among low-risk patients, is discouraged (DIII). Waist band recommended to assess the sterilisation status of classical swine fever after 2 weeks of treatment. Patients with a positive 2-week culture may require a longer course of induction therapy. It is also not necessary to continue fluconazole (200 mg/d) for 6 to 12 months (BIII). Immunosuppressed patients, such as solid organ transplant recipients, require longer treatment [3]. Based on experience in the treatment of cryptococcal meningitis in HIV disease, it is appropriate to follow a similar strategy for induction, consolidation and inhibition, as 15-20% of failure rates with 6 weeks of treatment with amfeticin B/5-flucytosin have been reported in previous strategies [3]. After 2 weeks of treatment with amphotericin B (0.7-1 mg/kg/d), fluconazole (400-800 mg/d) is followed by 6-12 months of inhibitory therapy with a lower dose of fluconazole (200 mg/d) (BIII) for 8-10 weeks. In patients who have received long-term prednisone therapy, the reduction of the prednisone dose (or equivalent) to 10 mg/d may improve the results of antifungal therapy if possible. Amtrotericin B lipid preparations may be replaced by amfitericin B in induction phase B [12] (CIII) in both immunocompromised and immunocompromised patients with significant renal disease. In patients who are intolerant to fluconazole, itraconazole (200 mg twice daily) may be replaced (CIII). Most parencicrial lesions will respond to antifungal therapy; large (>3 cm) available CNS lesions may require surgery. All patients should be closely monitored for evidence of increased intracranial pressure and should be managed in a similar way to HIV infected patients (see below). Treatment decisions should not be based on normal or cryptococcal polysaccharide antigen titres in serum or CSF [31, 34] (AI). Since the goal is to cure after discontinuation of treatment, patients requiring depressant therapy > 1-2 years should be considered as failures. Intrathecal or intravenous amphotericin B can be used in refractory cases where systemic antifungal therapy has failed. Due to its inherent toxicity and difficulties in consumption, this treatment is recommended only in this life-saving environment [14] (CII). Benefits and harm. Early, appropriate treatment of cryptococcal meningitis reduces morbidity and mortality. Drug-related toxicity and the development of undesirable drug interactions are the main harm of therapeutic intervention. Toxic side effects of amfiberin B are common and include nausea, vomiting, chills, fever and severity, which can occur with each dose. The most troublesome toxic side effects are kidney injury, including serum creatinine elevation, hypokalemia, hypomagnesaemia and renal tubular acidosis. In addition, anaemia occurs frequently and thrombocytopenia occurs occasionally (possibly due to heparin). Serum electrolytes, renal function and bone marrow function should be closely monitored. Nevertheless, amphithenic B can be used safely and effectively; only 3% of patients will have toxic side effects requiring discontinuation within the first 2 weeks of treatment [11]. Costs. The cost of purchasing drugs is high for antifungal treatments used for 6-12 months. Additional costs accrue to the daily, weekly and monthly monitoring of treatment associated with most of the recommended regimens. Guidelines for the treatment of lung and CNS cryptococcoxosis in patients with HIV infection therapy for AIDS-related cryptococcal pneumonia are expected to announce the onset of the spread of the disease. Cryptococcal pneumonia is usually characterized by fever and cough, which produces poor sputum. There is little distinction between cryptococcal pneumonia and other atypical pneumonia causes in HIV-infected patients. Except for typical skin lesions (which mimic molluscum contagiosum) associated with distributed cryptococcoccocosis, history, physical examination or routine laboratory tests, there may not be signs that indicate cryptococcal disease. However, due to the possible serious consequences of not noticing this disease, it is necessary to assess aids patients with pneumonia due to a possible fungal infection. Sputum fungal culture, blood fungal culture and serum cryptococcal antigen test are appropriate laboratory tests in any HIV infected patient, pneumonia and CD4+ T lymphocyte count <200 cells/ml.= if= any= test= is= positive= for= c.= neofor mans,= then= a= csf= examination= is= recommended= to= exclude= cryptococcal= meningitis.objectives.= the= goal= of= treatment= is= control= of= the= infection= and= prevention= of= of= of= disease= to= the= cns.options=there= are= no= controlled= clinical= trials= the= results= of therapy= for= aids-related [2].= indeed,= studies= have= have= been= conducted= that= specifically= rated= outcomes= among= hiv-infected= patients= with= pulmonary= or= non-cns= disease.= therefore= the= specific treatment= of= has= has= not= fully= el hivucidated.= it= is= clear= that= all= all= infected patients= ,= since= they= are= high= risk= for disseminated= infection.= surgery= should= be= considered= for= patients= with= persistent= or= refractory= pulmonary= or= bone= lesions.= some= hiv-infected= patients= present= with= isolated= cryptococcemia= or= a= positive= serum= cryptococcal= antigen= titer= (==>1:8) without clinical signs of disease. Although no specific studies have been conducted to investigate the treatment of such patients, they should be treated. Results. The desired result is symptoms such as cough, shortness of breath, sputum production, chest pain, fever and abnormalities (infiltrates, masses, etc.) </200> solution or stabilization. Stabilization. radiograph. In cases of extrapulmonary, non-CNS disease, the solution to lesions is the desired result. Recommendations. Specific recommendations for the treatment of HIV-related cryptococcal lung disease are summarised in Table 2. Patients with mild to moderate symptoms or asymptomatic and with a positive culture of C. neoformans in the lungs should be treated with fluconazole, 200-400 mg/d for life [3, 4, 15] (AII); however, long-term follow-up studies are needed for the duration of treatment in the HAART era. In cases where fluconazole is not an option, an acceptable alternative is itraconazole, 400 mg/d for life [9] (CII). Possible treatment option is combination treatment with fluconazole, 400 mg/d, as well as flucytosin, 150 mg/kg/d, 10 weeks; however, the toxicity associated with this mode limits its usefulness [15] (CII). In patients with a more severe disease, amphitheirin B should be used until the symptoms are controlled, then an oral azole agent, preferably fluconazole, can be replaced (BIII). Ketoconazole is generally ineffective in the treatment of cryptoccococcosis in HIV-infected patients and should probably be avoided [10.30] (DII). Benefits and harm. Early, appropriate treatment of non-CNS lungs and extrapulmonary cryptoccocal disease in HIV infected patients reduces morbidity and prevents progression to potentially life-threatening CNS disease. Prevention of progression to cryptococcal meningitis is the main purpose of treatment in this population. Equal success cannot be predicted with the use of existing therapy; However, since mortality associated with cryptococcal meningitis can be up to 25% among aids sufferers, the use of treatments that cause even a low level of success is worth it. The undesirable effects of fluconazole monotherapy 400 mg daily are uncommon. However, flucytosin (150 mg/kg/d) is a major side effect when co-administered with fluconazole for 10 weeks in patients with HIV-related cryptococcal meningitis [16]. Dose-limiting undesirable effects (mainly gastrointestinal nature) were reported in 28% of patients leading to discontinuation of flucytosin; and a further 32% described significant side effects that did not lead to discontinuation of treatment. Costs. The cost of buying drugs is high for antifungal treatments for life. Additional costs accrue monthly by monitoring the treatment associated with most of the recommended regimens. AIDS-related cryptococcal meningitis induction therapy therapy. The recognition of cryptococcal meningitis in HIV-infected patients requires a high suspicion index. Patients usually have fever and/or headaches gradually to begin, which becomes progressively more debilitating. However, it is also important not to include cryptococcal meningitis in patients with seizures, strange behaviour, progressive dementia, or unexplained fever. Classic signs of meningeal irritation are usually absent during physical examination, and routine laboratory evaluation is rarely revealed. Due to mass damage to the brain among patients with AIDS, cns imaging should be carried out before the sampling of classical swine fever. Pending the results of imaging tests, the serum should be examined for the presence of cryptococcal polysaccharide antigen. Serum cryptococcal antigen is positive >99% in subjects with cryptococcal meningitis, usually in titres >1 : 2048 [11, 13]. It is necessary to define the presence of meningitis and its severity; there is no suitable alternative to the DEA study. Conventional tests should include: measurement of csf opening pressure (when the patient is in the position of the lateral rekuvers); collection of sufficient CSF for fungal culture (3 ml); and CSF cryptococcal antigen titre, glucose content, protein level and cell count differential (5 ml in total). Objectives. The purpose of treatment is to eradicate the infection and control increased intracranial pressure. However, the main goals are the inability to eradicate, which is a common HIV disease, long-term control of infection and the resolution of clinical signs of the disease. Options. Three antifungal drugs are useful in the treatment of cryptococcal meningitis in patients with AIDS: amphotericin B, fluconazole and flucytosin. Itraconazole is less active than fluconazole [17,33]. Due to the relatively rapid development of drug resistance, flucytosin is not used as a single agent, so it is used only in combination with amtroricine B or fluconazole. In two clinical trials, amphotericin B in combination with flucytosin was shown to be superior to amphotericin B or fluconazole monotherapy alone [11,18]. Similarly, fluconazole in combination with flucytosin appears to be superior to fluconazole alone [16,28], although this regimen is more toxic than fluconazole monotherapy. Recently, lipid formulas of amtroricine B have been tested with cryptococcal meningitis and may have some advantages in the toxicity profile against the normal amfitrycin B formula when used alone or possibly with flucyczine [12, 29]. Results. The desired result is a solution to problems such as fever, headache, altered mental state, eye signs and increased intracranial pressure. In cases of CNS mass (cryptococcoma), the resolution of violations is the desired result. Recommendations. A summary of the recommendations for the treatment of AIDS-related cryptococcal meningitis is given in Table 2. Amphetamine B (0.7-1 mg/kg iv/day ≥2 weeks) in combination with flucytosin 100 mg/kg orally 4 divided doses/day is the initial treatment of choice [11, 13, 18, 29] (DI). In cases where the flucytosine should not be used, amphotericin B alone (used at the same doses above) is an acceptable alternative [13] (OS). After 2 weeks of successful consolidation of the induction treatment period, treatment should be initiated with fluconazole (400 mg orally once daily) administered for 8 weeks or until CSF cultures are sterile [11] (AI). In cases where fluconazole cannot be given, itraconazole is an acceptable, albeit less effective, alternative [9,33] (B, I). Amphytiericin B lipid formulas appear useful and can be useful in patients with cryptococcal meningitis and renal failure [12, 18-21] (CII). The optimal dose of amfitericin B lipids was not established, but AmBisome was effective at a dose of 4 mg/kg/d [12]. Combination fluconazole (400-800 mg/d) and flucytosin (100 mg/kg/d 4 divided doses) has been shown to be effective in the treatment of AIDS-related cryptococcal meningitis [16,29]. However, due to the toxicity of this regimen, it is recommended to use only as an alternative treatment option [16] (CII). Intrathecal or intravenous amphotericin B can be used in refractory cases where systemic antifungal therapy has failed [14]. Due to its inherent toxicity and consumption difficulties, it is recommended to use only in a life-saving environment [14] (CII). In selected cases, the C. neoformansis isolate sensitivity test may be useful for patient management, especially if the initial and consistent isolates can be compared. Such a study is usually best used in cases of relapse or refractory disease. Currently, a sensitivity test for isolates is not recommended for routine patient care (CIII). Benefits and harm. Early, appropriate treatment for HIV-related cryptococcal meningitis significantly reduces the morbidity and mortality associated with this disorder. In the most recent large comparative study of this disease, the overall mortality rate was 6%; on the contrary, in previous treatment studies, mortality was between 14% and 25% [11,13]. Toxic side effects of amphitheericin B are common. The dose of flucytosin should be adjusted on the basis of haematological toxicity or, preferably, by measuring flucytosin. The toxicity associated with the use of fluconazole/flucytosin combination therapy is high [15]. Costs. The cost of buying drugs is high for antifungal treatments for life. Additional costs accrued during biweek monitoring of treatment during acute induction therapy and every other week during consolidation therapy. Maintenance therapy. Among patients with AIDS-related cryptococcal meningitis who are successfully treated, there is a high risk of relapse in the absence of maintenance therapy. This has been demonstrated in a placebo-controlled, a randomised study assessing the efficacy of fluconazole in maintenance therapy following successful primary amphotericin B alone or in combination with flucytosin in AIDS patients [23]. Three percent of fluconazole patients and 37% of placebo patients returned anywhere. Fifteen percent of patients in the placebo group developed CNS relapses compared to any relapses in the fluconazole group. Objectives. The main purpose of maintenance therapy is the prevention of relapse of cryptococcal meningitis. Options. There are 2 main elements for preventing relapse of cryptococcal meningitis: 1) control of HIV replication with a strong HAART method and (2) the use of chronic antifungal therapy to prevent microbial relapse. Prospective clinical trials and careful observational studies indicate that potent antiretroviral therapy reduces the incidence of opportunistic infections [25-27]. The prevalence of cryptococcal in these studies was too low to provide direct evidence or to confirm that antiretroviral therapy was affecting cryptococcal disease, but there was no biological reason to suspect that cryptococcococococcal control in AIDS patients would not be improved with HAART. There are three possible antifungal maintenance options: fluconazole, itraconazole and weekly or biweekly amphotericin B.Outcomes. The desired result is the persistent absence of symptoms associated with cryptococcal meningitis and the resolution or stabilization of nerve abnormalities of the skull. No laboratory or clinical study, such as a serial serum or CSF cryptococcal antigen test, is useful for monitoring microbial relapse during the maintenance phase [31, 34]. Recommendations. Aggressive antiretroviral therapy should be administered in accordance with community standards of care [35]. Long-term supportive antifungal therapy should be administered in combination with antiretroviral therapy. Oral fluconazole 200 mg/d is the most effective aids-related maintenance therapy for cryptococcal meningitis [17,24] (AI). A randomised comparative study showed an advantage of fluconazole (200 mg/d) over amphitheericine B (1 mg/kg/m) as maintenance therapy [24]. Amphitheericin B patients experienced significantly more relapses, more drug-related adverse events and more bacterial infections, including bacteraemia [24]. Fluconazole relapse rate was 2% and amtrotericin B was 17%. Therefore, due to its toxicity and difficulties in administration, amphithereticine B maintenance therapy should only be used in patients with high relapses during treatment with azole or who are intolerant to azole agents (PIs). In another randomised comparative study, fluconazole was shown to be superior to itraconazole as a maintenance therapy for cryptococcal disease [17]. This test was terminated by The Data Safety Monitoring Board showed, after preliminary results, that the incidence of KSF culture relapse in patients with fluconazole (200 mg/d) was 4% compared to a 24% relapse among recipients of itraconazole (200 mg/d) [17]. Therefore, itraconazole should be used in cases where the patient is intolerant to fluconazole or has failed to treat fluconazole (OS). It may be wise to take itraconazole 200 mg twice daily (BIII). Ketoconazole is not effective as maintenance therapy [30] (DII). Although some preliminary data suggest a lower relapse rate of opportunistic infections, patients have been successfully treated with strong antiretroviral therapy until proven otherwise, supportive cryptococcal meningitis therapy should be administered for life (AI). In selected patients who responded very well to HAART, discontinuation of secondary antifungal prophylaxis may be considered after successful inhibition of HIV virus replication (CIII) after 12 to 18 months. Benefits and harm. Prevention of relapse of cryptococcal reduces mortality and morbidity and slows the progression of HIV disease. Fluconazole is well tolerated; nausea, abdominal pain and skin rash are the most common undesirable effects. Costs. The cost of buying drugs is high for antifungal treatments for life. Additional costs are accumulated during monthly monitoring of maintenance therapy. Management of increased intracranial pressure in HIV-negative and HIV infected patients with cryptococcal meningitis, increased intracranial pressure occurs in more than 50% of patients [22]. Increased intracranial pressure is an important factor in the morbidity and mortality of cryptococcal meningitis. The increased intracranial pressure is defined as the pressure >200 mm H2O measured in the patient's straight (lateral decubitus) position. By this definition, almost three quarters of the 221 HIV-infected patients in a recent study of the NIAID-supported Mycoses study had increased intracranial pressure. A quarter of patients had baseline pressure >350 mm H2O [22]. Aggressive management of increased intracranial pressure has not been consistently used in HIV negative patients with cryptococcal meningitis, and its effect on the result is unclear. In HIV-infected patients with increased CSF pressure, a poorer clinical response was observed in patients whose pressure increased from baseline to week 2; the benefit of the management of intracranial pressure can be concluded as to the reduction in mortality in this population [22]. In addition, HIV-negative patients may have increased CSF pressure associated with meningeal inflammation, cryptocomas and communication, or very rarely obstructive hydrocephalus. Neurological signs of the focal may reflect massive lesions. HIV infected patients with elevated pressure, no clinical difference in those with normal initial pressure, except that neurological manifestations of the disease are more severe among those with a higher pressure [21, 22]. Common manifestations in this environment include papilledema, hearing loss, loss of visual acuity, pathological reflexes, severe headache and abnormal copation. The evaluation of CSF in HIV-infected patients reveals minimal inflammation (often low leukocytes; and normal glucose and protein levels), but uncontrolled growth of fungus in classical CSF. CSF antigen titres are higher, and indian ink smear is more often positive among patients with an increased opening pressure than patients with normal opening pressure. It is believed that the increased intracranial pressure in this environment is partly due to the reuptake of classical swine fever in arachnoid wool caused by high levels of fungal polysaccharide antigen or excessive growth of the body per se. The main objective of effective intracranial pressure management is to reduce morbidity and mortality associated with cryptococcal meningitis in both HIV and HIV negative patients. Options. There are several treatments to manage increased intracranial pressure (Table 3), including intermittent intermittent CSF drainage with consistent lumbar punctures, lumbar drain insert or ventricular periton shunt arrangement. Medical methods, including the use of corticosteroids, acetazolamide or mannitol, were not effective in detecting cryptococcal meningitis. Recommendations. The main intervention to reduce increased intracranial pressure is percutaneous lumbar drainage [21, 22] (DII). Radiographic imaging of the brain prior to the initial lumbar puncture is recommended to rule out space-taking damage [21] (OSI). In patients with with an initial opening pressure of normal<200 mm= h2o),= a= repeat= lumbar= puncture= should= be= performed= 2= weeks= after= therapy= to= exclude= elevated= pressure= and= to evaluate= culture= culture= status.= for= patients= with= elevated= baseline= opening= pressure,= lumbar= drainage= should= remove= enough= csf= to= reduce= the= opening= pressure= by= 50%.= patients= should= initially= undergo= daily= lumbar= to= maintain= csf= opening= pressure= in= the= normal= range=when= the= csf= pressure= is= normal= for= for= several= days ,= the= procedure= can= be= suspended.= occasionally= patients= who present= with= extremely= high= high= opening= pressures= (=>(400 mm H2O), lumbar leakage may be required, especially when lumbar punctures are often necessary or not controlled by symptoms of elevated intracranial pressure. In cases where repeated use of lumbar puncture or lumbar outflow fails to control symptoms of increased pressure or when there is persistent or progressive neurological deficits, ventricular peritoneal [21, 22] (BII). Steroid treatment has yielded mixed results in both </200> </200> hiv negative patients and its effect on results is unclear. Due to the intense fungal burden and high amount of replication in patients with HIV disease, adjunctive steroid therapy is not recommended in HIV-infected patients (DIII). Among HIV negative patients, the benefits of steroid therapy are not well known and should not be used (DIII). Acetozolamide and mannitol have not been shown to provide any clear benefit in managing the increased intracranial pressure resulting from cryptococcal meningitis (DIII). Benefits and harm. Aggressive management of increased intracranial pressure is by far the most important factor in reducing mortality and reducing the incidence of acute cryptococcal meningitis. The main risk of lumbar drainage occurs in the detection of coexistence mass damage and obstructive hydrocephalus, which is a fairly rare complication of cryptococcal disease. Due to prolonged external lumbar drainage, patients are at high risk of bacterial infection. Ventriculoperitoneal can become a second-hand infected with bacteria; however, this is an uncommon complication. Secondary shunt infection with C. neoformans usually does not occur if antifungal therapy has been initiated. Costs. Lumbar punctures are relatively inexpensive. Lumbar outflows are usually used in the parameters of the intensive care unit, which are associated with higher costs. To house a ventricular peritoneal shunt requires neurosurgical intervention with general anesthesia, which is an expensive but potentially life-saving procedure. Indications 1, , et al. Amphotericin B comparison separately and in combination with flucytosin in the treatment of cryptococcal meningitis, , vol. (pg. -)3, , et al. 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