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Management of Leptospirosis: A Short Review

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Abstract

Aim:
The review the various drugs used for the management of antimicrobial on leptospirosis

Objective:
To study the different mechanism involved in the treatment of leptospirosis

background:
Leptospirosis is a treatable disease, early diagnosis and treatment are important for the better result .the antimicrobial therapy in combination with supportive therapy reduce the rate of this disease.Leptospirosis is also known as 7day fever ,field fever is an infectious caused by corkscrew- shaped bacterial called leptospirosis .They are sensitive to a variety of antimicrobial agents like penicillin, cephems, amino glycosides ,tetracyclines, macrosides. Treatment of leptospirosis patient contours to be supportive management and use of appropriate antibiotics. Of this antimicrobial agents short term treatment with streptomycin leptospirosis. When penicillin, cephems, amino glycoside are used long term therapy with larges does not be required from the early stages of this disease.

Reason:
Leptospirosis can eventually lead to death and hence the anti microbial agents studied in this review will bring awareness against leptospirosis.

INTRODUCTION:

Leptospirosis is an infection caused by corkscrew-shaped bacteria called Leptospira and it is also known as field fever, rat catchers yellow and pertibial fever[1][2][3] . Leptospires are thin, fine spiral shaped organisms with hooked ends having two or more axial filaments that are responsible for the motion of the spirochete. Symptoms can range such as headaches, muscle pains, and fevers; to severe with bleeding from the lungs or meningitis.[4]If the infection causes the person to turn yellow, have kidney failure and bleeding it is then known as Weil's disease.[5]. Leptospirosis is an important but often overlooked zoonotic disease that can cause significant morbidity and mortality. Leptospira are highly susceptible to a wide variety of antimicrobials in vitro.. Antimicrobial therapy is indicated for the severe form of leptospirosis, .If antibiotics are used, they should be initiated as soon as the diagnosis of leptospirosis is considered and should be continued for a full course despite initial serologic results, because most patients are diagnosed only through acute and convalescent testing. Early treatment has been shown to offer the best clinical outcomes; results from controlled studies of treatment during the immune phase have yielded mixed results.[6][7]

CLINICAL MANIFESTATION:

The incubation period of leptospirosis is from 1 to 30 days (average 7 – 14 d). [8][9]Leptospirosis manifests with a clinical spectrum from asymptomatic infection to the severe form of Weil's disease. Most infections are asymptomatic or mildly symptomatic and self-limited. [10][11] Clinical leptospirosis typically manifests with a biphasic course, with an acute phase (anicteric form) which may last for 1 week and it is followed by the immune phase characterized by antibody production and leptospiruria. Only a minority of patients develop biphasic illness. Patients' typically present with fever of abrupt onset, headache, myalgias localized in calves, conjunctivas suffusion, photophobia, nausea, and vomiting. [12][13]Pulmonary involvement ranges from 20% to 70% and may manifest with cough, chest pain.. [14][15] Cardiac involvement is common, with electrocardiogram abnormalities in up to 50% of cases. Weil ' s disease is associated with a 5% to 15% case fatality rate. ,[16] Males experience more severe illness and have higher fatality rates compared with females. [17]Differential diagnosis of leptospirosis depends on clinical syndrome and area of acquisition of infection and may include influenza, malaria, dengue fever, viral hemorrhagic fevers, Hantavirus infection, Legionnaires ' disease, yellow fever, aseptic meningitis, sepsis, meningococcal disease, brucellosis, typhoid fever, rickettsial diseases, relapsing fever, and viral hepatitis.

MODE OF TRANSMISSION:

Human leptospiral infections may be due to the direct or indirect exposure to urine of infected animals. Moisture is an important factor of the survival of the leptospires in the environment. Other modes of transmission of infection, such as handling infected animal tissues and ingestion of contaminated food and water. Leptospires can gain entry into humans through cuts and abrasions in the skin, through intact mucous membranes (nose, mouth, eyes) and also through waterlogged skin. They may occasionally enter the human body via the inhalation of droplets of urine or through drinking-water.

After infection, leptospires appear in the blood and invade all tissues and organs. They are subsequently cleared from the body by the host's immune response to the infection. However, they may settle in the convoluted tubules of the kidneys and be shed in the urine for few weeks to several months and occasionally even longer. They are then cleared from the kidneys and other organs but may persist in the eyes for much longer time .[18]

They can be transmitted from human to human by sexual intercourse, transplacentally from the mother to the fetus and though breast milk to a child. Urine from a patient

suffering from leptospirosis should be considered infectious. As leptospires can be cultured from blood, this should be viewed as infectious for some time before the onset of symptoms and during the first 7–10 days of illness.[19].

Pathogenesis of Leptospires is that they enter the body through abrasions macerated skin or cuts, conjunctiva, or by inhalation of aerosols or of water in near-drowning or swimming immersions. The bacteria spread through the bloodstream and tissues without initial inflammatory localization. They grow in any or all tissues until their numbers are large enough to cause local or general lesions. Once antibody appears, after a period of 7-10 days , leptospires disappear from the bloodstream and tissues, except for privileged sites such as the anterior chamber of the eye, and the brain.

TREATMENT:

General management of leptospirosis includes providing symptomatic and supportive therapy, as indicated by the nature and severity of the symptoms and signs. Antibiotics have been used to treat leptospirosis . The current choices of treatment for leptospirosis include

> penicillin,
> doxycycline,
> cefotaxime,
> ceftriaxone and
> azithromycin.

Antibiotics:

Penicillin has long been considered the treatment of choice.Penicillin 6 million units daily I.V (10-14 days) [20]. In milder cases, oral treatment with tetracycline, doxycycline, ampicillin, or amoxicillin can be considered. Ampicillin and amoxicillin are also recommended in mild disease, whereas penicillin G and ampicillin are indicated for severe disease.([21]For severe cases of Leptospirosis, intravenous administration of penicillin G, amoxicillin, ampicillin, or erythromycin is mostly recommended in use .One comparative trial of the efficacy of ceftriaxone and penicillin for the treatment of severe Leptospirosis found no significant differences between the two drugs in terms of complications or mortality rates. Another open-label randomized study compared parenteral cefotaxime, penicillin G, and doxycycline for the treatment of suspected severe leptospirosis. There were no significant differences between antibiotics with regard to mortality. Thus doxycycline, cefotaxime, or ceftriaxone is a satisfactory alternative to penicillin G for the treatment of severe leptospirosis.

Ceftriaxone has the benefit of reduced frequency (once a day versus every 4 hours for parenterally administered penicillin) and the option of intravenous and intramuscular administration. It is also more cost-effective than penicillin, and in patients with penicillin allergy it may be an alternative antibiotic. A quantitative PCR assay was used to monitor the density of leptospires in the blood and in target organs (liver, kidney, lung, heart, and spleen).

Doxycycline (10mg/kg) cleared the leptospires from blood and all tissues in 2 days, except for liver, which required 3 days.

Ampicillin (100mg/kg) cleared leptospires from the host, except for kidneys and heart, which still had 102 leptospires/g at day 6. Ofloxacin (30mg/kg) was unable to clear bacteria from blood or kidneys.[22]Leptospira organisms are susceptible in vitro to chloramphenicol and to quinolone and macrolide agents. Azithromycin and clarithromycin are efficacious in experimental animals. Broth microdilution testing has shown sensitivity to macrolides, fluoroquinolones, cephalosporins, and carbapenems. Azithromycin appears promising for the treatment of less severe disease. Another option for treating leptospirosis is the fluoroquinolone antimicrobials.[23] Many of the Leptospira species tested were more sensitive to ampicillin/sublactam than to ampicillin alone.

Doxycycline is a reasonable alternative, but concerns exist regarding its use in all patients.doxycycline (200mg/week) [24]has suggest that doxycycline prophylaxis does not prevent leptospiral infection in an endemic area, but may have a significant protective effect in reducing morbidity and mortality, even in an endemic setting. [25]Chemoprophylaxis may be impractical to administer in highly endemic areas, but is likely to be useful for adventure travellers and military personnel who visit endemic areas, and also in accidental laboratory infection. [26]Assessing the utility and practicality of antileptospiral prophylaxis after severe events such as floods and hurricanes would be a valuable clinical study.[27]Leptospires are sensitive in vitro to most antimicrobial agents, but the relevance of the in-vitro findings to clinical outcome for these agents has not been assessed in clinical trials. [28]

Reducing mortality from severe leptospirosis requires prompt triage of high-risk patients and aggressive supportive care for hypotension, renal and respiratory distress, and haemorrhage.

Corticosteroids:

Addition of intravenous methylprednisolone (MP) to the treatment regimen of severely ill patients was implemented on the basis of immune mediated pathogenesis of the disease to reduce mortality. MP may reduce mortality in patients with severe leptospirosis, except in cases with established multiple organ dysfunction . Therefore, early administration of MP seems to be more advisable. Pulmonary involvement in leptospirosis is emerging as a common complication of severe leptospirosis.. Timely initiation of dialysis is critical to prevent mortality from oliguric renal insufficiency. patients with leptospiral renal failure, hypothesised to be immune complex mediated, have been successfully treated without dialysis by administering high-dose pulsed steroids (methylprednisolone 30 mg/kg/d, not to exceed 1500 mg). The vasculitis due to leptospirosis in a children was responsive to intramuscular antibiotic therapy and dexamethasone treatment. The case provides evidence that corticosteroids can be used in ruminants at moderate doses for chronic treatment without clinically relevant detrimental effects. Therapy should be initiated as early in the course of the disease as suspicion allows. The treatment started after the first 4 days of illness is still effective and the duration of antimicrobial therapy is usually 7 days.[29.]

CHEMOPROPHYLAXIS:

Pre-exposure antibiotic prophylaxis is NOT ROUTINELY RECOMMENDED. [30]However, in those individuals who intend to visit highly endemic areas and are likely to get exposed (e.g. travelers, soldiers, those engaged in water-related recreational and occupational activities), pre-exposure prophylaxis may be considered for short-term exposures. . The recommended regimen for pre-exposure prophylaxis for non-pregnant, non-lactating adults is: Doxycycline (hydrochloride and hyclate) 200 mg once weekly, to begin 1 to 2 days before exposure and continued throughout the period of exposure.[31] Currently, there is no recommended pre-exposure prophylaxis that is safe for pregnant and lactating women.Mass chemoprophylaxis with doxycycline at 200 mg/wk for 4 weeks has been used successfully for the containment of an outbreak in India in 2001[32].

Doxycycline (hydrochloride and hyclate) is the recommended post exposure chemoprophylactic agent for leptospirosis. The duration of prophylaxis depends on the degree of exposure and the presence of wounds. Individuals should continue to monitor themselves for fever and other flu-like symptoms.

Doxycycline 200 mg single dose within 24 to 72 hours for low risk exposure.

Doxycycline 200 mg once daily for 3-5 days to be started immediately within 24 to 72 hours for moderate risk exposure.

Doxycycline 200 mg once weekly until the end of exposure [Grade B] [33][34].for high risk exposure.

CONCULSION:

Leptospirosis is a disease with protean manifestation that occasionally may result in severe complication. Early institution of antimicrobial theraphy will result in lowered morbidity and mortality.prophylati antibiotics may be inducated in some instance.

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