Review article Leptospirosis: last Treatments & Medications

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Summary

Leptospirosis is an important but often overlooked zoonotic disease that can cause significant morbidity and mortality. Although antimicrobial therapy of leptospirosis has been studied in a few randomized controlled clinical studies, these studies are limited to specific regions of the world, and few have characterized infecting strains.

Leptospira are highly susceptible to a wide variety of antimicrobials in vitro. Despite this, it is not clear what the best choice of antimicrobial agents is for human disease.

Antibiotics have been used to treat leptospirosis since penicillin first became available.

The current choices of treatment for leptospirosis include penicillin, doxycycline, cefotaxime, ceftriaxone and azithromycin. Penicillin has long been considered the treatment of choice. Doxycycline is a reasonable alternative, but concerns exist regarding its use in all patients. In milder cases, oral treatment with tetracycline, doxycycline, ampicillin, or amoxicillin should be considered. For severe cases of Leptospirosis, intravenous administration of penicillin G, amoxicillin, ampicillin, or erythromycin is recommended.

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. Among 264 patients with Leptospirosis confirmed by serologic testing or culture, the mortality rate was 5%. There were no significant differences between antibiotics with regard to associated mortality, defervescence, or time to resolution of abnormal laboratory findings. Thus doxycycline, cefotaxime, or ceftriaxone is a satisfactory alternative to penicillin G for the treatment of severe leptospirosis.

Once-daily ceftriaxone has been shown to be as effective as penicillin.

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, although adequate human trials are lacking to fully support their use.
Reducing mortality from severe leptospirosis requires prompt triage of high-risk patients and aggressive supportive care for hypotension, renal and respiratory distress, and hemorrhage.

In 2008, an outbreak of leptospirosis caused high mortality in Sri Lanka. The General Hospital, Peradeniya recorded nine deaths in May, which prompted the medical staff to change the treatment protocol. 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 and comorbidities. Therefore, early administration of MP seems advisable.

**Pulmonary involvement** in leptospirosis is emerging as a common complication of severe leptospirosis. A prospective randomized controlled trial of desmopressin or high-dose (pulse) dexamethasone as adjunctive therapy in 68 patients with pulmonary involvement associated with severe leptospirosis was conducted between July 2003 and October 2006 at five hospitals in Thailand. The results obtained in the present study do not support the use of either pulse dexamethasone or desmopressin as adjunct therapy for pulmonary involvement associated with severe leptospirosis.

Patients with nonoliguric hypokalemic renal insufficiency have a better overall prognosis and can be treated by volume and potassium repletion. Timely initiation of dialysis is critical to prevent mortality from oliguric renal insufficiency. Continuous hemofiltration is more effective than peritoneal dialysis in treating infection-associated acute renal failure.

According to some reports, patients with leptospiral renal failure, hypothesized 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). These authors also discuss the role of high-dose pulsed steroids in areas with limited resources where dialysis treatment is unavailable and would involve lengthy medical transport. The use of renal dose dopamine in conjunction with steroids or diuretics has also been described. Pulse-dose steroids may also play a role in the management of severe pulmonary disease; this finding is different from other studies.

The vasculitis due to leptospirosis in a children was responsive to intramuscular antibiotic therapy and dexamethasone treatment. This 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. Nevertheless, contrary to previous reports, treatment started after the first 4 days of illness is still effective and the duration of antimicrobial therapy is usually 7 days.