Chloramphenicol Therapy in Pregnancy

Str—The report by Choi and Pai [1] provides useful information for treating scrub typhus in pregnancy. However, they err in reporting the class of chloramphenicol for treatment in pregnancy. The current class is C, indicating no data for safety in pregnancy. There is a wealth of clinical data [2] demonstrating that chloramphenicol is safe to use in pregnancy if it is not circulating at the time of delivery, since the drug will cause gray syndrome in neonates. It does not seem to harm the fetus, however, which makes it safe to use during most of the pregnancy. Although a drug other than chloramphenicol would be used in most situations, physicians should not be afraid to use it when necessary simply because of pregnancy.

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References

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Minocycline versus Doxycycline in the Treatment of Lyme Neuroborreliosis

Str—Dotevall and Hagberg [1] from Göteborg University (Göteborg, Sweden) deserve praise for their well-done study on oral doxycycline treatment of Lyme disease–associated facial palsy and meningitis. This study confirms that oral doxycycline is equivalent to parenteral ceftriaxone in the treatment of Lyme disease–associated palsy and/or meningitis. Experience indicates 21 days of oral doxycycline therapy is equivalent to 14 days of ceftriaxone therapy [3], and Swedish investigators have demonstrated that equivalent results are achieved with doxycycline therapy for ≈2 weeks (median, 10.8 days).

Dotevall and Hagberg correctly point out that there has been some reluctance to use oral antibiotics in the treatment of Lyme neuroborreliosis because of fear of inadequate CSF and/or CNS penetration [2, 3]. Doxycycline is preferred over conventional tetracycline for this purpose because of its lipid solubility characteristics [4–6], as stated by Dotevall and Hagberg.

Doxycycline is 5 times more lipid soluble than conventional tetracycline, which is an important determinant of permeability of the blood-brain barrier [7, 8]. Dotevall and Hagberg showed that most patients had highly elevated CSF protein levels, which is the best index of antibiotic permeability of the blood-brain barrier. Aside from emphasizing a shorter duration of therapy, these researchers stressed the use of high dosages of doxycycline (e.g., 400 mg/d) for treatment of Lyme neuroborreliosis.

It is not commonly appreciated that ill patients treated with doxycycline (e.g., patients with legionnaires’ disease) should be given a loading regimen of 200 mg iv q12h for the first 72 h, because of doxycycline’s lipid solubility characteristics and long half-life. Since 5 serum half-lives are usually required to achieve steady-state serum concentrations, and early therapeutic effect, a loading regimen rather than a loading dose permits rapid saturation of the serum. If doxycycline is administered in the usual dosage of 100 mg q12h, then it takes 4–5 days to achieve steady-state kinetics and an observable therapeutic response. In Lyme neuroborreliosis, rapid saturation of the CNS compartment is
key to the efficacy of short-course regimens (≤14 days). Doxycycline is usually given in dosages of 100 mg q12h, which means that the first week of treatment is virtually lost in achieving steady-state equilibrium, and equilibrium results require 3 weeks [7–10]. Dotevall and Hagberg correctly used 400 mg of doxycycline daily and decreased treatment time to ~10.8 days.

Because of its pharmacokinetic characteristics, doxycycline may be given at a dosage of 200 mg q12h or may be given as a single daily dose of 400 mg. Gastrointestinal upset is minimal if the tablet form of the formulation is used and taken with meals. CSF concentrations achieved with high doses of doxycycline are approximately twice those achieved with conventional dosing and are achieved more rapidly. There is no toxic liability associated with the high-dose doxycycline regimen [9, 10]. Use of 400 mg of doxycycline daily assures clinicians that CNS concentrations of doxycycline are predictably and rapidly achieved above the MIC90 for Borrelia burgdorferi [1, 6].

Dotevall and Hagberg did not use or comment on minocycline as an alternative to doxycycline. Minocycline is even more highly lipid soluble than doxycycline and has excellent CSF penetration making it potentially useful in treating Lyme neuroborreliosis [7–11]. Minocycline is 2 times more lipid soluble than doxycycline, thereby making it a potential alternative for treatment of Lyme neuroborreliosis. I have treated several patients with Lyme neuroborreliosis with minocycline, and our results are comparable with those of Dotevall and Hagberg. Because minocycline is so highly lipid soluble, 100 mg orally q12h is comparable with 400-mg daily doses of doxycycline in terms of CNS concentrations which are also in excess of the MIC90 for B. burgdorferi.

Although serum levels of doxycycline and minocycline are comparable at any given dose, there are important differences in CSF and/or CNS concentrations (figure 1) [11]. The high lipid solubility of minocycline may cause vestibular side effects in some patients. This side effect limits the administration of minocycline to 100 mg q12h rather than 200 mg q12h [7–9]. Because of this, doxycycline (400 mg daily) remains the preferred oral antibiotic for treatment of Lyme neuroborreliosis in most patients [1]. For patients for whom treatment fails (those with persistent symptoms and/or active CNS disease), minocycline may be a therapeutic option.

Dotevall and Hagberg call for a randomized trial comparing oral doxycycline to iv ceftriaxone to determine the optimal dose and/or duration of treatment for Lyme neuroborreliosis. I would suggest that minocycline also be included in such future comparative studies. Minocycline may permit a shorter duration of treatment in Lyme neuroborreliosis than high dose oral doxycycline because of its excellent CNS penetration.

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**References**


**Meningitis Due to Viridans Streptococci**

**SIR—I read with interest the article by Cabellos et al. on streptococcal meningitis in adult patients [1]. They include 2 cases of post–lumbar puncture meningitis due to viridans streptococci and Streptococcus salivarius, respectively. They emphasize the role of viridans streptococci in causing meningitis but fail to discuss their clinical importance in causing meningitis complicating lumbar puncture and myelography. In 1993, Gelfand and Abolnik reported 3 cases of streptococcal meningitis complicating diagnostic myelography and reviewed the literature [2]; 25 additional cases were found, the majority of which were due to viridans streptococci, including the case that my colleague and I reported in 1992 [3]. Baird reported 2 more cases following that review [4]. Two of the 3 cases reported by Gelfand and Abolnik were also involved in litigation [5].**

Streptococcal meningitis complicating lumbar puncture and myelography is rare. The majority of cases are due to streptococci in the viridans group. It is a fulminating illness usually occurring within 24 h after the procedure. The usual clinical