Finally, there are concerns about increasing prevalence of drug resistance (including artesunate) in India(4). Though the overall cost of artemether is comparable to that of quinine, one should use artemether judiciously in selected cases to prevent an escalation of drug resistance to artemether.

The data presented in this study still does not support the use of artemether as the first choice drug for severe malaria, and quinine is still the drug of first choice in my opinion.

Sudhir Kumar,
Department of Neurological Sciences, Christian Medical College Hospital, Vellore, Tamilnadu 632 004, India.
E-mail: drsudhirkumar@yahoo.com

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Reply

The study of Petras *et al.*(1) quoted by Dr. Kumar was done on male rhesus monkey using high doses (8 mg/kg/day to 24 mg/kg/day) of arteether for 7 to 14 days. Neuropathological lesions were demonstrated only in the 14-day treated monkeys. The recommended doses and duration of therapy in humans is much less. Secondly, it may not be entirely appropriate to extrapolate results in experimental animals to humans. Moreover, a study in mouse model has demonstrated that neuropathological brain-stem damage due to intramuscular artemether is dose dependent and may be reversible(2). We do not perceive how longer duration of follow up in our study could have helped to detect neurological sequelae in the patients when they were clinically normal at discharge. A larger sample size would have definitely helped.

The study quoted on bioavailability of intramuscular artemether was done on just 26 children(3). This observation needs to be validated by larger studies.

We share Dr. Kumar's concern for emerging drug resistance and certainly do not recommend replacing quinine with artemether. We have only suggested that artemether may be a useful alternative to quinine in areas with poor medical facility for reasons already cited in the article.

Kamran Afzal,
Tabassum Shahab,
Department of Pediatrics, Jawaharlal Nehru Medical College, AMU, Aligarh 202 002, India.
E-mail: drkafzal@hotmail.com

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Treatment of Neonatal Candidiasis with Liposomal Amphotericin B

I read with interest the recent paper(1) on the treatment of neonatal candidiasis with a novel liposomal formulation of amphotericin B. Though a cheap and effective antifungal has been the dream of every clinician, I would like to draw attention to some salient features of the study.

1. It is interesting to note that this formulation is delivered in a normal saline infusion. All Amphotericin B formulations, including the conventional deoxycholate and all currently available lipid formulations carry explicit precautions regarding incompatibility of Amphotericin B and saline solutions. How does this current preparation get around this incompatibility?
2. It should also be noted that LD 50 for Ambisome® is 175 mg/kg, a more accurate value than the <17.5 mg/kg cited in the article. This is a ten-fold greater value than that of the current liposomal preparation being described.
3. To claim a 100% response rate in the assessable cases fails to consider the fact that the patients who died or were otherwise non-evaluable could have had persisting fungal infections and in fact, may have been treatment failures. This is the rationale behind an intent-to-treat analysis, where all patients who receive atleast one dose of study drug treatment must be included in the efficacy analysis. Viewed in this way according to the results presented in *Table I* of the article, 13 of 23 patients treated had favourable outcomes, a response rate of 56.5%.
4. It should also be noted that all patients in this report had infections with Candida albicans. The other reports referenced included cases of non-albicans species of Candida as well, which are known to be more difficult to treat and many require longer courses of treatment. Thus, the response rate of treatment as well as the total doses of Amphotericin B needed to treat in this paper are not appropriately comparable to those reported in the references cited.
5. Too many patients in this study have required significant amount of blood transfusion. Authors do not mention whether that was due to ongoing sepsis or an adverse effect of the drug itself.
6. Step up doses (or inability to use an optimal dose) right from the begining may be deterimental to the outcome of