

carefully folded as shown in *Fig. 1* helps to bring about neutral positioning as shown in *Fig. 2*. Tying both the legs also prevents the mother from carrying the baby in her waist, which is a traditional practice of carrying babies by the Indian mother. This practice can produce undue stretching of the adductor muscles and lead to weakness in the muscles.

This method can be employed either when one lower limb or when both lower limbs are involved. The normal limb will act as a splint to anchor the weak limb thus preventing undue stretching. The duration of tying both the legs together is throughout the acute period of the disease (which is usually 4 to 8 weeks) and well into the convalescent period till the child has had good return of power (Grade III and above). The usual duration recommended will be for about 3 to 5 months in most cases. Tying both the legs also prevents early ambulation which is not desirable in acute paralytic poliomyelitis.

**C.R. Banapurmath,**  
*Department of Pediatrics,*  
*J.J.M. Medical College,*  
*Davangere.*

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## Theophylline Infusion for Prevention of Apnea of Prematurity

Merchant *et al.* in their recent article(1) have suggested continuous theophylline infusion for prevention of apnea of prematurity. While such a concept is theoretically sound, certain practical aspects of their study call for further explanation.

The aims of the study were to determine the optimal dosage and factors adversely affecting serum theophylline levels—apart from studying the efficacy of theophylline in primary apnea. These would have been possible only if different dosage schedules were employed, while controlling for other variables, for determination of optimal dosage schedule and some dosage in different babies with the variables for studying factors affecting serum theophylline levels. In the absence of such attempts, meaningful conclusions cannot be drawn from the study. For example, comparison of *Figs. 1* and *2* reveals that a sizeable population of the infants in the study were small for dates. Serum levels of theophylline are higher in these infants than in appropriate for gestation infants(2) despite the elimination half lives being similar in both(3). Optimal requirement of the drug for these infants would be much lower than for other infants. Similarly, hypoxia, acidosis, total parenteral nutrition and infection adversely affect the serum theophylline levels, and unless controlled for, would alter the results of the study.

The authors have used a wide range of infusion rate (0.2 mg/kg/h to 0.38 mg/kg/h) without offering any reason for the variation. Aranda *et al.*(4) have calculated that to achieve a serum level of 10 mg/L, the

rate of administration of theophylline has to be 0.14 mg/kg/h (equivalent to 0.16 mg/kg/h of aminophylline). In view of efficacy seen at much lower levels of 2.8 to 3.9 µg/ml(5), infusion rate can be further reduced. As shown in Fig. 3, many infants in the study have indeed received an infusion rate higher than 0.3 mg/kg/h, are not less as shown in the Table. Theophylline elimination occurs by first order kinetics in a large majority of infants. But in an as yet undefined percentage, it proceeds according to zero order kinetics(6), i.e., at a constant rate regardless of serum concentration. In such infants, a small increment in the dose may lead to toxic serum levels. We are perturbed by the high incidence (14%) of toxic serum levels seen in the study. Probably some of them could have been prevented if serum levels were estimated between 48 and 72 hours, when steady state levels are achieved in most of the babies(2), and not on day 5. Life threatening complications (seizures and arrhythmias) occurring at high serum levels are difficult to treat but could be prevented by frequent monitoring(6). Hence, wide use of theophylline for prevention of apnea, without facilities for frequent monitoring is fraught with dangers and cannot be recommended. Further, we do not agree with the authors' contention that infusion is preferred over intermittent administration, since steady state levels are achieved at the same time by both methods(7) and intermittent administration in our experience has been safe and obviates potential complications inherent with prolonged intravenous infusion.

Finally, the authors have presumed apnea to be primary based on a lumbar puncture and septic work up. Since cerebrospinal fluid examination does not diagnose all cases of intraventricular hemor-

rhage(8) and anemia and metabolic abnormalities, the frequent causes of apnea have not been ruled out in these infants. We wonder how many of these cases of primary apnea were really primary.

**Raghavendra Rao,  
Anil Narang,  
Neonatal Unit,  
Department of Pediatrics,  
Post Graduate Institute of  
Medical Education and Research,  
Chandigarh 160 012.**

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## Reply

We appreciate the critical evaluation of our article. The primary aim of our report was to study the role of prophylactic infusion of aminophylline for prevention of apnea. The optimal dose is well documented in literature. *Figure 3* shows that we used aminophylline in doses ranging from 0.25 to 0.33 mg/kg/h. This study was not primarily designed to ascertain the optimal dose of aminophylline, but to use the drug in doses to maintain blood levels between 8-12. Thus a few patients, earlier in the study, received a little higher or a lower dose to titrate the steady state level. *Table III* also shows mean rate of dose infused and not rate in each case.

All patients in the study were normal preterms with no other risk factors and those with secondary apnea or those who were acidotic, or septic were excluded from the analyses. It is recommended that drug levels of theophylline are best done after five half lives, to get a steady state level. We agree with Rao and Narang that blood levels after 3 days of therapy could have detected toxic levels earlier; however, frequent drug estimations were not possible due to economic constraints.

Intermittent slow bolusing or continuous infusion of theophylline are equally effective and perhaps equally safe, provided bolusing is not done rapidly, which may increase the risk of producing toxic levels. This is precisely the reason and the point we wish to make as in most of our centres, slow bolusing with syringe pumps and blood monitoring of drug levels are not available. The chance of producing toxic levels is hence higher, than when infusing the drug as a slow continuous drip.

Finally, as mentioned under material and methods, any neonate who developed apnea was investigated to rule out a secondary cause, was treated for the same and excluded from analyses of results. A septic screen, including a lumbar puncture was done wherever secondary apnea was suspected.

While Rao and Narang have certainly raised many a pertinent point, we feel that given our circumstances, slow continuous infusions (rather than rapid bolusing) may still be more practical and less harmful in the prevention of apnea. For apneic episodes, we recommend bolusing of theophylline as it is an excellent respirogenic agent. We propose to study theophylline drug levels (when bolused versus when continuously infused) in yet another carefully designed study, where we hope to take into consideration all factors pointed out by these authors.

R.H. Merchant,  
V.S. Sakhalkar,

Department of Neonatology,  
B.J. Wadia Hospital for Children,  
Parel, Bombay 400 012.