Cephalosporins with Clavulinic Acid

The medicine market is flooded with combination of various antibiotics with Clavulanic Acid in suspension and dispersible form like Cefpodoxime with Clavulanate, Cefixime with Clavulanate etc. I want to know whether they have any pharmacological rationality?

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REPLY

Both cefpodoxime and cefixime (3rd generation oral cephalosporins) are not currently first line drugs for any pediatric illness. The only oral antibiotic combination with clavulinic acid that is listed in pediatric drug formularies is amoxiciilin with clavulinic acid. There are no RCT's available to date that compares cefpodoxime and cefixime given alone with their respective combinations with clavulinic acid. Therefore, organisms resistant to these drugs, which must be used only as second or third line drugs, must be treated with broad spectrum antibiotics and not with their combination with clavulinic acid.

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Intravenous Immunoglobulin in Rh Hemolytic Disease of Newborn

Girish, *et al*.(1) have reported that low dose intravenous immunoglobulin (IVIG) is as efficacious as high dose IVIG in reducing the duration of phototherapy in Rh hemolytic disease of the newborn.

The trial was designed as a superiority trial; however, the authors have presented the paper as though it was a non-inferiority equivalence trial. The results show that the duration of phototherapy was longer in the low dose group (77±57 hrs) compared to the high dose group (55±49 hrs). That this difference did not achieve statistical significance only means that superiority of the high dose could not be statistically demonstrated with the sample size available. It does not mean that the low dose IVIG is equivalent in efficacy to the high dose and that one can start using the low dose to reduce the cost of therapy.

Even when viewed through the prism of a superiority trial, the sample size was inadequate and the study was underpowered. This is because the actual standard deviation was wider (49 hr) than what the authors had assumed (24 hr). For a standard deviation of 49 hrs and effect size of 24 hrs the requisite sample size was approximately 150 (assuming equal variance), and not 38. There is a distinct possibility that an adequately powered study would show that the mean difference in phototherapy duration did achieve statistical significance or was close to achieving statistical significance–quite the opposite of the authors' conclusion.

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REFERENCE

1. Girish G, Chawla D, Agarwal R, Paul VK, Deorari AK. Efficacy of two dose regimes of intravenous immunoglobulin in Rh hemolytic disease of newborn- a randomized controlled trial. Indian Pediatr 2008; 45: 653-659.

REPLY

We agree with statistical interpretation of the results made by Dr. Dutta. However, conclusions and interpretation made in our study must be viewed in light of some important facts. In absence of concrete data on duration of phototherapy in Rh hemolytic disease, calculation of sample size was based on our pilot data (unpublished). We enrolled the pre-calculated number of subjects, but because of wider dispersion of phototherapy duration, the primary outcome of our study, we were unable to reject the null hypothesis that 1 g/kg of IVIg is not better than 0.5 g/kg in reducing duration of phototherapy. Post-hoc analysis showed that the study was underpowered to detect a difference of 24 h in the duration of phototherapy- the intended difference. But the study had 80% power to detect a difference of 36 hr in the duration of phototherapy. The trend towards decreased duration of phototherapy observed in 1 g/kg IVIg group should be interpreted with caution in light of the opposite trend of longer hospital stay in the same group and the illness severity of babies. Moreover, we were unable to detect significant difference in other outcomes like number of exchange transfusions, duration of hospital stay, number of packed red blood cell transfusions and peak serum total bilirubin. Our study was not powered to detect change in these outcomes, but detecting statistically meaningful difference in an important outcome like need of exchange transfusion will need huge sample size.

Furthermore, even a small difference will achieve statistical significance if sample size is big enough. Statistical significance testing does not reflect the magnitude of the effect, and the term "statistically significant difference" does not denote that the difference between a test and control group was clinically meaningful with regard to a desired outcome. We agree that reporting of no dose-effect relationship between IVIg and duration of phototherapy may not be correct statistically, but we based our conclusions on utility of clinical benefit than what our study was powered enough to detect.

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Audit of Measles Infection in Children From a Tertiary Hospital

Measles is an acute viral infectious disease caused by measles virus. The World Health Organisation (WHO) estimates that almost 1 million deaths occur each year due to measles, the majority (85%) in Asia and Africa(1). We conducted a retrospective study of clinical profile and outcome of measles infection at private urban tertiary care childrens hospital, during the period January 2006 till December 2007. Case records of children who were admitted during the above period with clinical measles [defined as any person in whom the clinician suspects measles infection or any person with fever and maculopapular rash with cough or coryza or conjunctivitis(2)] or laboratory confirmed measles [defined as clinical measles infection with presence of measles specific IgM antibodies in serum(2)] were analyzed for age, sex, clinical features, measles immunization status, measles specific serum IgM antibodies, vitamin A supplementation status and measles related complications. During this period, 70 (0.3%) children were admitted out of 23172 hospital admissions. Of these 36 (51%) were boys and 34 (49%) were girls and the male: female ratio was 1.05:1. Fifteen (22%) children were less than one year old, 24 (34%) between one and 5 years, 23