On-line Supplemental Methods

Study Design

The first 6 patients enrolled in the study received arginine in its oral form. However due to slow enrollment and compliance issues with oral administration when patients felt ill, the protocol was amended after the first year to include an intravenous (IV) option at the same dose (100 mg/kg with a max of 10 grams/dose). All subsequently enrolled patients and parents/guardians chose the IV option, while one patient was switched from IV to oral after the intravenous catheter fell out prior to discharge. The enrollment rate into the study dramatically improved after initiation of the IV option.

Statistical Analysis: This study had 82% power at level α=0.05 to detect a 35% decrease in length of hospital stay between treatment groups of 28 subjects per group, based on the average length of stay for all admissions at Children's Hospital & Research Center Oakland in 1998 of 6 ± 3 days, using an unpaired Student's t-test. Descriptive statistics were reported as the number and percent, or the mean and standard deviation (SD). Pearson correlations were computed to examine bivariate associations. The unpaired and paired Student's *t*-test, or Fisher's exact test, were used for bivariate comparisons of the 2 arms. Narcotic records for 2 patients (randomized to placebo arm) were incomplete and were not included in the narcotic use analysis. An intent-to- treat analysis was performed using a t-test with Welch's correction to adjust for unequal variance to compare total narcotic use, length of hospital stay and pain scores at discharge in the group randomized to arginine therapy compared to placebo. Next, analysis of covariance models were used to test for differences between the 2 arms in the change from day 1 measures while adjusting for day 1 values. A *p* value ≤ 0.05 was considered statistically significant.