Title: ISOPROTERENOL AFFECTS THE PHARMACOKINETICS OF AMINOPHYLLINE IN PATIENTS WITH STATUS ASTHMATICUS

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Introduction. The treatment of status asthmaticus is characterized by aggressive pharmacology in an attempt to avoid the complications of mechanical ventilation. Aminophylline by intravenous bolus or constant infusion is the primary drug of choice; the addition of beta adrenergic agonists, in particular isoproterenol, by inhalation and more recently by constant infusion has gained wide acceptance. It was observed that the addition of isoproterenol infusion affects the kinetics of aminophylline metabolism in patients receiving infusions of both drugs for the treatment of status asthmaticus.

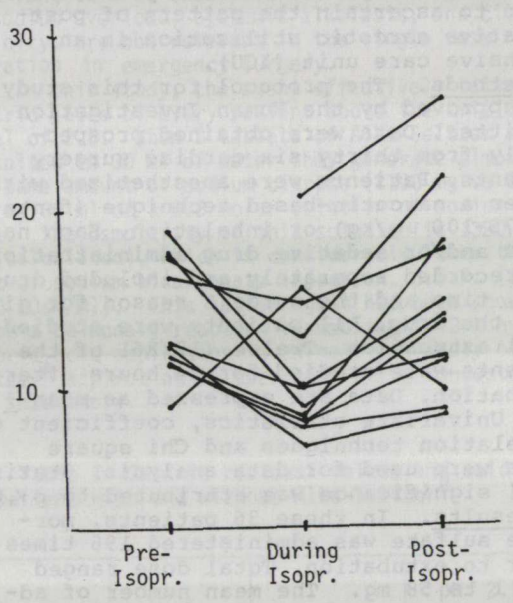
Methods. Twelve consecutive patients with severe status asthmaticus, ages two to eighteen years, were treated initially with a continuous infusion of aminophylline at a dose tailored to achieve a blood level of 15-20 mg%. When this regimen failed, an isoproterenol infusion was added at a starting dose of 0.17 mcg/kg/min and this dose was increased as required and tolerated to achieve improvement in gas exchange. When clinical improvement was demonstrated, the isoproterenol was weaned and discontinued. The mean duration of isoproterenol therapy was 37.24 ± 6.9 hours: the mean maximum infusion rate was 0.774 ± 0.03 mcg/kg/min. Aminophylline levels were closely monitored: immediately before and two hours after the isoproterenol was started; immediately before and two hours after the isoproterenol was discontinued; and as required to monitor the effects of aminophylline dose changes. To compare the effects of isoproterenol on aminophylline kinetics in these patients, an aminophylline index was created. This index is calculated as:

$$\frac{\text{the mean aminophylline level in mg\%}}{\text{the mean aminophylline dose in mg/kg/hr}}$$

Results. When the isoproterenol infusion was started, the aminophylline level decreased 3.75 ± .78 mg%. Conversely, when the isoproterenol was discontinued, the aminophylline level increased a mean of 4.27 ± .89 mg%. Aminophylline doses were altered in an attempt to maintain therapeutic levels of 15-20 mg%: the dose delivered were:

pre-isoproterenol:	1.25 ± 0.06 mg/kg/hr
during isoproterenol:	1.70 ± 0.25 mg/kg/hr
post isoproterenol:	1.46 ± 0.12 mg/kg/hr

The aminophylline indices demonstrate the relationship described in the following figure:



Numerically, this represents aminophylline indices of:

pre-isoproterenol:	13.79 ± 0.93
during isoproterenol:	11.12 ± 1.13
post isoproterenol:	14.65 ± 1.5

Conclusion. This suggests that the pharmacokinetics of aminophylline are altered by an isoproterenol administration. It is recommended that during and immediately after isoproterenol infusions, the aminophylline level should be closely monitored and the aminophylline dose adjusted accordingly.