

# [GA2-62] Population Pharmacokinetics of Epsilon-Aminocaproic Acid in Adolescents Undergoing Posterior Spinal Fusion Surgery

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Title: Population Pharmacokinetics of Epsilon-Aminocaproic Acid in Adolescents Undergoing Posterior Spinal Fusion Surgery

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## Abstract:

### Background:

The efficacy of the antifibrinolytic epsilon-aminocaproic acid (EACA) in adolescents undergoing spinal fusion surgery has been explored in several clinical trials. However, there are currently little or no pharmacokinetic data to establish an appropriate dosing regimen in this population. The aim of this study was to determine the pharmacokinetics of EACA in adolescents undergoing posterior spinal fusion surgery for scoliosis and make dosing recommendations for this population.

### Methods:

Twenty children ages 12 – 17 years old were enrolled, with 10 children in each of two groups based on diagnosis/etiology of scoliosis: an idiopathic scoliosis group and a non-idiopathic scoliosis group. Plasma EACA concentrations were determined using a validated high-performance liquid chromatography-tandem mass spectrometry assay. Previously reported pharmacokinetic data from infants undergoing craniofacial surgery were included to enhance the model. A population nonlinear mixed-effects modeling approach was used to characterize EACA pharmacokinetics.

### Results:

Population pharmacokinetic parameters of EACA were estimated using a two-compartment disposition model with weight as expressed as an allometric covariate and an age effect. Weight was referenced to 70 kg. Pharmacokinetic parameters for the typical patient were: pre/post-operative plasma drug clearance of 153 mL/min/70kg (2.1 mL/min/kg), inter-compartmental clearance of 200 mL/min/70kg (2.8 mL/kg/min), central volume of distribution of 8.78 L/70kg (0.13 L/kg) and peripheral volume of distribution of 15.8 L/70kg (0.23 L/kg). It was also estimated that the age effect reaches maturity by approximately one year of age (15.3 months). The study group did not impact drug pharmacokinetics.

### Conclusions:

EACA clearance increased with weight and age. The dependence of clearance on body weight supports current practice of weight-based EACA dosing. Based on the pharmacokinetic model developed in this study, a loading dose of 100 mg/kg followed by a CIVI of 40 mg/kg/hr is appropriate to maintain target plasma EACA concentrations in adolescents with idiopathic and non-idiopathic scoliosis undergoing posterior spinal fusion surgery. This recommended infusion rate is four times what has been used in prior efficacy studies in this population; the effect of this higher dosing strategy needs to be explored.

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