CLINICAL PHARMACOLOGY & THERAPEUTICS

OFFICIAL PUBLICATION OF THE
American Society for Clinical Pharmacology and Therapeutics
American Society for Pharmacology and Experimental Therapeutics

VOLUME 53 NUMBER 2

MARCUS M. REIDENBERG, MD *Editor*

APPEARING IN THIS ISSUE

Abstracts of papers presented at the Ninety-fourth Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics

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CLINICAL PHARMACOLOGY & THERAPEUTICS

VOLUME 53 NUMBER 2

Mosby Year Book

TABLE OF CONTENTS

Volume 53, Number 2, Febuary 1993. CLINICAL PHARMACOLOGY & THERAPEUTICS (ISSN 0009-9236). Published monthly (six issues per volume, two volumes per year) by Mosby–Year Book, Inc., 11830 Westline Industrial Dr., St. Louis, MO 63146-3318. Second class postage paid at St. Louis, Mo., and at additional mailing offices. POSTMASTER: Send change of address to: CLINICAL PHARMACOLOGY & THERAPEUTICS, Mosby–Year Book, Inc., 11830 Westline Industrial Dr., St. Louis, MO 63146-3318, (800)325-4177, ext. 4351, or (314)453-4351. Annual subscription rates for 1993: domestic, $101.00 for individuals and $188.00 for institutions. Printed in the U. S. A.

		International surface mail		*International airmail*		
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PI-40

PHARMACOKINETICS (PK) OF ESMOLOL (ES) IN PEDIATRIC POST-CARDIAC SURGERY PATIENTS. DB Wiest, PharmD*, SS Garner, PharmD*, WE Uber, PharmD*, RM Sade*, M.D., PC Gillette, M.D.*. Depts. of Clinical Pharmacy, Surgery, & Pediatric Cardiology, Med. Univ. of South Carolina, Charleston, SC.

The PK and hemodynamics of ES were investigated in 8 children (1.3-148 mo.; median: 29.6 mo.) with acute post-cardiac surgical hypertension. Sodium nitroprusside, 2-4 μg/kg/min (mean:3.6), was discontinued 6-12 min (mean: 9 min) prior to starting ES in all patients. ES given by continuous infusion was titrated to achieve blood pressure (BP) < 90th percentile for age. ES blood samples (Cp) were obtained during and post infusion. Arterial BP, mean arterial pressure (MAP) and heart rate (HR) were simultaneously recorded with each sample time. ES was analyzed by HPLC. ES concentration-time profiles were analyzed using noncompartmental analysis. Regression analysis was used to determine significant associations ($p<.05$) between the following: 1) Cp and mean % reduction in MAP and HR; 2) age and PK parameters. Maximum dose required to control BP was 300-1000 μg/kg/min (mean: 625; median: 500). The PK results revealed the following: CL (ml/kg/min)= 134 ± 73.9; V_{ss} (L/kg)=1.02 ± 0.80; $t_{1/2}$ (min)= 4.3 ± 2.1. There was a significant correlation ($p<.001$) between ES Cp and % reduction in MAP. ES was effective in controlling acute post-operative hypertension in 8/8 patients.

PI-41

DRUG DELIVERY OF METERED DOSE INHALERS (MDI) VIA PEDIATRIC ENDOTRACHEAL TUBES (ETT). SS Garner, PharmD*, DB Wiest, PharmD*, & JW Bradley, RTT*. Depts. of Clinical Pharmacy, Pediatrics, & Respiratory Therapy, Med. Univ. of South Carolina, Charleston, SC.

Drug delivery by MDI in intubated children has not been investigated. This in-vitro study assessed albuterol (AL) delivery by MDI via pediatric ETT. The model consisted of a Hamilton Veolar® ventilator, pediatric breathing circuit, Aerovent® spacing chamber or Airlife® MDI adapter connected to an AL MDI canister, and ETT (4,5, or 6mm) cut to equal lengths (19cm). The ETT tip was fitted to an in-line stainless steel filter holder with a 0.3μ A/E filter. Ten canisters were actuated 2 times (2000 μg) into dry (4,5,and 6mm ETT) and humidified air (4 and 6mm ETT) in triplicate. Percentage AL delivery was determined by weighing the filter prior to assembly and following drug administration (balance sensitivity: ± 20μg). Significant differences (α=0.05) were determined by ANOVA and student's t test. Percentage AL delivery in dry air with and without the spacer was: 4mm: 15.5 ± 0.87 vs. 7.5 ± 1.32, 5mm: 15.8 ± 1.06 vs. 6.5 ± 0, 6mm: 15.2 ± 1.26 vs. 7.7 ± 0.29. In humidified air, delivery was: 4mm: 2.5 ± 0.84 vs. 1.3 ± 0.94 and 6mm: 5.3 ± 1.44 vs. 2.4 ± 1.36. These results indicate ETT size does not influence drug delivery. AL delivery was significantly improved with the Aerovent® spacer (mean:112%) and dry air (mean: 351%) with each ETT size studied ($p<0.01$).

PI-42

PAIN-FEVER PHARMACOKINETICS/DYNAMICS (PK/PD) IN CHILDREN. M. Kelley, MD, J. Edge, MS, S. Suzuki, MD,PhD, P. Walson, MD, Div. Clin. Pharm/Tox, Ohio State Univ., Children's Hosp., Columbus, OH.

The PK/PD of acetaminophen (APAP) and ibuprofen (IBU) were studied in 20 febrile children (5-12 yrs) with sore throat pain. The vital signs, 3 pain measures (faces, visual analog and poker-chip scales) and blood samples were collected at intervals for 10 hours after either placebo, 5 or 10 mg/kg IBU liquid or 15 mg/kg APAP elixir. Despite small numbers, PK/PD analyses (MKMODEL, Holford) revealed excellent IBU PK behavior with a sigmoid E_{max} temperature fit for the 10 mg/kg IBU. All pain responses occurred earlier than temperature, especially chips (Keq=0.016), and best fit a linear model as did APAP and IBU 5 mg/kg.

DRUG	KA min-1	Vd ml	CL ml/min	Keq min-1	EC50 mg/L
IBU5	.018	187	0.89	.004	---
IBU10	.075	200	1.45	.005	10.8
APAP	.031	867	3.90	.018	---

Such data may be useful to explain or predict clinical responses and to generate testable hypotheses.

PI-43

EFFECTIVE IRON CHELATION USING THE ORAL IRON CHELATOR, 1,2-DIMETHYL-3-HYDROXYPYRID-4-ONE (L1), IN HOMOZYGOUS ß-THALASSEMIA MAJOR (HBT) PATIENTS (PTS). D. Matsui MD*, N. Olivieri MD*, M. Berkovitch MD*, D. Templeton MD*, I. Wanless MD*, L. Blendis MD*, P. Liu MD*, G. Koren MD, The Hospital for Sick Children, Toronto, Canada.

Because iron overload and subsequent organ dysfunction results from regular transfusions in HBT pts, effective iron chelation is essential. The oral iron chelator, L1, is currently being studied. 15 pts aged 20.6±4.6 (mean±SD) years were treated with L1, 75-100 mg/kg/day, for a period of 21.8±8.2 months (mos). Compliance (% of prescribed doses taken) assessed by the Medication Event Monitoring System (MEMS) during the initial 137.9±16.4 days of therapy in the first 7 pts was 91.7±7.4%. After 16.0±7.3 mos of L1 therapy, compliance in the 15 pts remained acceptable at 81.3±14.7%. Serum ferritin (SF) has decreased from an initial value of 4370±4014 µg/L to 2833±2142 µg/L (p=0.018). Urinary iron excretion was 0.6±0.4 mg/kg/day. Compared to pts receiving subcutaneous (sc) DFO matched for SF, a decline in SF was noted in 10/14 L1-treated pts and in 3/14 DFO-treated pts over a mean period of 20 mos (Fisher's Exact p=0.021). Preliminary analysis suggests a decrease in iron by Prussian blue staining in follow-up liver biopsies in some pts as well as a reduction of cardiac iron as demonstrated by magnetic resonance imaging in 1 pt with established cardiac disease. Joint pain and swelling have been noted in 3 pts all of whom continue on L1. These data suggest that L1 is a promising agent, superior or at least comparable to sc DFO, which may be useful in the removal of excess tissue iron.