CLINICAL STUDY SYNOPSIS

Title of the study: Pharmacokinetics of Bambuterol in children with asthma.

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Publication (reference): -

Study period: January, 1988 - February, 1988

Clinical phase: 1

Objectives: To study the pharmacokinetics of bambuterol given as the hydrochloride in asthmatic children, age 6-12 years, under steady-state conditions at two dose levels, 10 and 20 mg once daily.

Study design: Double-blind, randomised, cross-over, two centres

Number of patients (total and for each treatment): 13/12/12

Diagnosis and criteria for inclusion: Asthmatic patient, judged by the investigators to be reversible and stable.

Investigational drugs, dose and mode of administration, batch No.:  
Bambuterol; 10 & 20 mg; oral; DMK 28 & DMB 102  
Placebo; - ; oral; DNC 3 & DNB 108

Duration of treatment: Each treatment 7 days, no wash-out between treatments

20th June, 1991/JR/msl
Assessment methods: Health control: Clinical laboratory tests, lung function. Physiological tests: creatinine clearance and plasma cholinesterase activity. Pharmacokinetics: plasma concentrations (0-6h) and urinary excretions (1-6h) of bambuterol and terbutaline (plasma: 0-24h; urine: 1-6h). Effects on airways: morning and evening peak expiratory flow rate (PEFR).

Statistical methods: Descriptive

Summary of results:
Physiological tests: Mean creatinine clearance per kg body weight was about 50% higher as compared with adults. Mean basal pChE activity (16.3 nmol/min/µL) agreed with data in healthy adults. Inhibition of pChE was similar or slightly higher as compared with adults: mean peak inhibition was 64% (10 mg) and 72% (20 mg).

Bambuterol was absorbed faster and possibly to a larger extent than in adults. Dose dependency in pharmacokinetics was slightly lower as compared with adults: the doubling of the dose from 10 to 20 mg increased AUC 2.6 times (3 times in adults).

Terbutaline: Normalized AUC (0-24h) (body weight times AUC) was approximately 40% lower in the children as compared with adults, owing to higher renal clearance per kg body weight (mean values: 2.6 mL/min/kg [10 mg]; 2.7 mL/min/kg [20 mg]) and, probably, a smaller transformed fraction of bambuterol.

Effects on airways: Mean PEFR after 20 mg (doses 4-7) increased by 18 L (p<0.05, n=8) as compared with run-in. Otherwise, in this small panel, PEFR was not seen to be significantly improved by bambuterol.

Adverse events were typically those associated with β₂-agonists. Hospitalization of two subjects due to asthma aggravation was, by definition, reported as serious adverse events.

Conclusion(s): Oral bambuterol doses of 10 mg twice or 20 mg once daily should be tentative safe regimens for future investigations in children. A more comprehensive study of bambuterol is required for the evaluation of effects on airways in children.

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