CLINICAL STUDY SYNOPSIS

FINAL

Title of the study: A dose-finding study with bambuterol oral solution administered in a single dose to children (3-5 years) with asthma

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Study site: Juliana Children's Hospital, The Hague, the Netherlands

Publication (reference):

Study period: 911018-930324

Clinical phase: IIB

Objectives: The primary objective of the study was to measure the efficacy in lung function of two doses of bambuterol solution. The effect after a single dose was to be compared to a placebo solution. The primary efficacy variable was the total respiratory resistance measured with the multiple frequency oscillation technique (FOT).

Study design: The study was performed at one centre in the Netherlands. It was double-blind placebo controlled, randomized and of a cross-over design.

Number of patients (total and for each treatment): Twenty-four children (18 boys and 6 girls) with a mean age of 4.3 years (range: 3-5) were included in the study (19 patients on bambuterol 0.5mg/kg b.w., 17 on bambuterol 0.25 mg/kg b.w. and 20 on placebo).

Diagnosis and criteria for inclusion: 3 to 5 year old boys and girls. Children with chronic asthma symptoms and in need of bronchodilator therapy regularly or when necessary. A decrease in respiratory resistance at 6 Hz of ≥20% after inhalation of terbutaline 0.2 mg/kg body weight with a jet nebulizer. Informed consent.

31 October 1995

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Investigational drugs, dose and mode of administration, batch No.: Bambuterol hydrochloride oral solution 0.5 mg/mL (batch No. DRH54) and 1 mg/mL (batch No. DRH53) (black currant taste).

Reference drugs, dose and mode of administration, batch No.: Placebo for bambuterol hydrochloride oral solution with quinine hydrochloride (0.04 mg/mL) (batch No. DRH11) (black currant taste).

Duration of treatment: The study started with a run-in period of two weeks, and at visit 2 the patients were randomized into the study. The three clinic visits when a single dose was administered, were separated by wash-out periods of one week each. The single doses administered were bambuterol oral solution 0.25 mg/kg b.w., bambuterol oral solution 0.50 mg/kg b.w. and placebo oral solution, all taken in the morning.

Assessment methods: FOT measurements (primary efficacy variable resistance [R_m], and secondary efficacy variables reactance [X_m] and frequency dependence of resistance [dR_m/df]) were made before and after a single dose administration of the study drugs at visits 2, 3 and 4. At each visit, measurements were performed before medication intake (0 h) and then once every hour until 6 hours after medication intake. The measurements before medication intake were to be performed between 7 and 10 am, approximately at the same time of the day at all three visits. A variation in the FOT measurements of ≤10% (before medication intake, 0 h) was accepted. A larger variation than 10% after a second attempt would exclude the patient from further participation in the study.

Statistical methods: The data was analysed by ANOVA.

Summary of results: Treatment with both bambuterol 0.25 mg/kg b.w. and bambuterol 0.5 mg/kg b.w. resulted in a statistically significant decrease in R_m (-0.59 and -0.86 cm H_2O s/L, respectively) and a statistically significant increase in dR_m/df (3.07 and 2.73 cm H_2O s/L x 10^-2, respectively) and X_m (0.33 and 0.35 cm H_2O s/L, respectively), as compared to placebo. Further, both the systolic blood pressure and the pulse rate showed a statistically significant increase after administration of 0.5 mg/kg b.w. bambuterol as compared to placebo (3.7 mmHg and 7.7 bpm, respectively). After 0.5 mg/kg b.w., the increase in pulse rate was also statistically significantly higher as compared to 0.25 mg/kg b.w. (7.4 bpm).

Conclusion(s): Although bambuterol is intended to be used regularly, there was a statistically significant bronchodilation effect measured with FOT after a single dose of both bambuterol oral solution 0.25 and 0.5 mg/kg b.w. as compared to placebo. Both active treatments were generally well tolerated and the adverse event incidence was typical for β_2-agonists.