BRONCHIAL PROVOCATION USING INHALED MANNITOL – A PHASE 3 TRIAL OF ADULT & PEDIATRIC ASTHMATICS & NON-ASTHMATICS

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We performed a Phase 3 study to investigate the safety and efficacy of dry powder mannitol as a bronchial provocation test for airway hyperresponsiveness in adults and children (n=592, age 6-83yrs, median 33.9 yr, median BMI 24.6, 53.7% F). For the test, FEV_1 is measured 60 sec after inhaling increasing doses of mannitol (e.g. 0,5,10,20,40,80,160,160,160mg) (Pharmaxis Ltd, Australia) from a dry powder inhaler (Plastiape, Italy) to a cumulative dose of 635mg (Anderson SD et al, AJRCCM 1997;156:758). A positive test is a fall of ≥15% in FEV_1 ($PD_{15}FEV_1$). 105 non-asthmatic (56M;49F) and 487 with a clinical diagnosis of asthma (218M;260F) based on history, spirometry, medications and response to hypertonic (4.5%) saline performed the test. The median FEV_1 % predicted was 95% (Mean±SD 95.3%±14.5). Of the 592, 434 were taking $beta_2$-agonists, 166 were taking inhaled corticosteroids (ICS), 235 were taking combination therapy, 123 were taking none of these medications. ICS and combination therapy were withheld for 12hrs and short acting $beta_2$ agonists for 8hrs before testing. 290 asthmatics were positive to mannitol with a median PD_{15} 148 mg (range: 0.2-627.8), 197 were negative. Five non-asthmatic subjects were positive to mannitol, 100 were negative. For the 197 asthmatic subjects negative to mannitol 85% were taking either ICS alone or in combination with a long acting $beta_2$ agonist. Of the 290 with a positive test 71% were taking these medications. There were no serious adverse events during or after challenge. The efficacy and safety of bronchial provocation with mannitol was demonstrated in non-asthmatic and clinically diagnosed asthmatic adults and children.

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