

SUPPLEMENTARY MATERIAL

Methods

Determination of serum parameters

Concentrations of mast cell tryptase (2.3µg/mL), total IgE (109kU/L) and allergen-specific IgE to penicilloyl G and V, ampicilloyl, amoxicilloyl, ethylene oxide, the major birch pollen allergen Bet v 1 (4.61kUA/L) dermatophagoides pteronyssinus (4.34kUA/L) and farinae (1.34kUA/L), alpha-galactosidase, Tri a 14, Tri a 19, Cor a 8, Cor a 9, Cor a 14, and natural rubber latex were quantified by the Phadia ImmunoCAP system (Thermo Fisher Scientific, Uppsala, Sweden) according to the manufacturer's instructions (positive ImmunoCap results are indicated in parentheses).

Skin tests

Skin tests comprised skin prick (SPT) and intradermal testing (IDT) with different drugs, excipients as well as vaccines. Briefly, SPT were carried out using a sterile prick lancet, for IDT the substances were injected intradermally using a tuberculin syringe with a 21 gauge. As negative control 0.9% NaCl was applied (SPT, IDT), as a positive control 0.1% histamine (SPT). The substances were tested in various dilution stages (Table 1 and Table E1). Polyethylene glycol (PEG) 2000 and 6000 (both Sigma-Aldrich, Merck KGaA, Darmstadt, Germany) were diluted in aqua dest. Polysorbate was diluted in aqua dest. (1:10) and heated in a water bath at 37°C until completely solved. All substances were filtered sterile.

A mean wheal diameter (sum of largest and hereto vertical diameter divided by two), recorded 20 minutes after applying the test, of ≥ 3 mm and ≥ 6 mm was judged as a positive test result for SPT and IDT, respectively. To avoid interindividual variations, the same, herein trained and experienced person executed and evaluated the skin tests.

Oral challenges

Oral provocation tests were performed double-blind and placebo-controlled with individually prepared capsules of titrated doses of metamizole (starting with 50mg, maximum single dose 500mg, cumulative dose 800mg), diclofenac (starting with 5 mg, maximum single dose 100mg, cumulative daily dose 155mg) and phenoxymethylpenicillin (starting with 0.15 mega-units, maximum single dose 1.5 mega-units, cumulative daily dose 2.4 mega-units), none of them containing PEG or polysorbate.