

Supplementary material

Methods

Determination of serum parameters

Concentrations of mast cell tryptase (2.3µg/mL), total IgE (109kU/L) and allergen-specific IgE to penicillin G and V, ampicillin, amoxicillin, 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.

Supplementary Table

Table E1. Skin prick test results with different drugs.

active ingredient	brand name (used for SPT)	containing PEG	MW	SPT reactivity [mm]
NSAID				
Metamizole	Novaminsulfon-ratiopharm	yes	8,000	9
Ibuprofen	Ibuprofen-ratiopharm	yes	8,000	7
Ibuprofen	Ibuflam Lichteinstein	yes	3,350	neg.
Diclofenac	Voltaren-dispers Novartis	no		neg.
ASS	ASS-ratiopharm	no		neg.
Paracetamol	Paracetamol-ratiopharm	no		neg.
Beta lactames				
Penicillin V	Penicillin-V Stada	yes	6,000	5
Sultamicillin	Sultamicillin-ratiopharm	yes	2,000	neg.
Penicillin G	Penicillin G Infectopharm	no		neg.
Ampicillin	Ampicillin-ratiopharm	no		neg.
Amoxicillin	AmoxiClav Hikma	no		neg.
Cefaclor	Panoral Eberth	no		neg.
Cefazolin	Cefazolin Hikma	no		neg.
Laxatives				
Macrogol	Kinderlax	yes	4,000	10
Macrogol	Movicol	yes	3,350	neg.

MW – molecular weight; NSAID – non-steroidale anti-inflammatory drugs; SPT – skin prick test

Figure legend

Figure E1: Positive intradermal test with (a) the COVID-19 vaccines BNT162b2 (BioNTech/Pfizer; mean wheal diameter = 11mm), and (b) AZD1222 (AstraZeneca; mean wheal diameter = 10mm), both diluted 1:100.

