Bumblebee venom allergy as an emerging occupational allergy: safety and efficacy of bumblebee venom immunotherapy in a large single-center cohort

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Background
Bumblebees (BB) are widely used for crop pollination, which has led to an increase in the number of cases of (occupational) bumblebee venom (BBV) allergy among BB farm and greenhouse workers. From 1995 to 2015, aqueous BBV extract for venom immunotherapy (VIT) was available intermittently (ALK, The Netherlands). Data about the effectiveness of the currently available BBV (Anallergo, Italy, aqueous and depot venom, shelf life 6 vs. 24 months) are lacking. This study assessed the safety and efficacy of previously and presently available BBV in a single-center cohort of patients with BBV allergy.

Method
A retrospective analysis of all BBV-allergic patients who started BB VIT was performed. Parameters on tolerability and re-stings were prospectively collected, with follow-up until February 2024. The safety and efficacy of the previous and current VIT protocol for start-up were evaluated. Maintenance therapy was performed with progressively increasing injection intervals up to 24 weeks.

Results
Between March 1998 and May 2022, 36 patients were started on BB VIT (n=16 between 1998-2008 and n=20 between 2016 and 2022). 33/36 patients (91.7%) were stung in an occupational setting (25 BB farm workers (M/F=2/23), 8 greenhouse workers (M/F=6/2)) and 3 (8.3%, M/F=2/1) during outdoor activities. Severe grade III-IV reactions (Mueller) occurred in 4/25 (16%) of BB farm workers, 5/8 (62.5%) of greenhouse workers and 2/3 (66.7%) of non-occupational reactors. All patients had detectable BBV sIgE. Honeybee venom (HBV) and BBV sIgE double positivity was seen in 84,9% (BBV 6,78 kU/L vs. HBV 2,52 kU/L, p=0,055). During the start-up of BB VIT, systemic reactions (SR) occurred in 6/36 patients (16,7%): 1/16 (6.3%, 1 grade II SR) with ALK aqueous venom (rush scheme of 4 days), 4/11 (66.7%, grade I/II/III SR=2/1/1) with Anallergo aqueous venom (9 rush and 2 cluster schemes) vs. 1/9 (11.1%, 1 grade III SR) with depot venom (modified rush over 10 days). The median follow-up duration per patient was 5 years and 8 months (range 2 months to 23 years). The cumulative VIT duration was 295 years and 2 months (ALK vs. Anallergo: 179.8 vs. 115.37 years). 8/1544 recorded field re-stings during maintenance VIT resulted in an SR in 5/36 patients (13.9%, ALK vs. Anallergo: 3 vs. 2, failure rate of both venoms < 1%)). In 3/5 patients with a mild re-sting SR (grade I-II), increasing the interval between injections was temporarily halted and afterwards resumed (3/3 tolerating >10 subsequent re-stings). One patient with a grade III re-sting SR twice switched to another job.

Conclusion
A build-up VIT scheme with the currently available depot BBV (shelf life 2 years, always available vs. 6 months for aqueous venom, only intermittently available) over 10 days is safe and it provides rapid protection in occupational BBV allergy. Both the previously and currently available BBV for VIT are safe and effective, even with increasing injection intervals up to 24 weeks.

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