

NEWS AND COMMENTARIES

Immunotherapy for Hymenoptera venom allergy: too expensive for European health care?

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To the Editor:

Insect venom allergy is the most frequent elicitor of severe anaphylaxis in central Europe (1), accounting for the majority of anaphylactic reactions in adults, and being second as elicitor of anaphylaxis in children (2). The prevalence of insect-sting anaphylaxis varies widely between children and adults ranging from 1.5% to 3.3% and more depending on the geographic and socioeconomic background (3). Venom immunotherapy (VIT) is highly effective to cure Hymenoptera venom allergy (4) and does also improve this disease-specific quality of life (5,6).

Recently, a focus has been put on the cost-effectiveness of VIT used for treating bee and wasp venom allergy. Stimulated by the English National Health Service, the British National Institute for Health and Clinical Excellence (NICE) commissioned a study analysing the economic burden caused by VIT (7). A central aspect of this analysis was the calculation of additional costs arising from potential life-saving effects of VIT. To adjust to quality of life in gained years, Hockenhull et al. (7) used the age-dependent European Quality of Life-5 Dimensions (EQ-5D) Weighted Health Status Index population norms. Key finding of the analysis was that, compared to avoidance advice and supply with emergency kits only, VIT may cost up to £18 million per year gained if the focus is put on life-saving aspect of VIT.

With this commentary, we would like to express our concerns regarding the authors' strategy to focus on fatal reactions possibly prevented by VIT.

How can it be explained that – when referred to quality-adjusted years of life – VIT results in such astronomical costs? In medicine, economic issues include the evaluation of therapy costs. As some treated patients will live longer without getting well again, it is also essential to refer the number of years gained to the resulting quality of life. To combine both variables, a QALY (quality-adjusted life year) is calculated by multiplying the number of years gained with score points reflecting the quality of life during these years. If, for example, a therapy would gain 10 extra years for a patient not suffering from any long-term morbidity (1 score point for optimal quality of life), a QALY of 10 would be calculated. With only 2 years gained and with a significant long-term morbidity (e.g. 0.5 score points for reduced quality of life), the QALY would be 1. To calculate cost-effectiveness, treatment costs arising from an additional therapy (incremental cost-effectiveness ratio, ICER) are then referred to one QALY. Thus, for example, in comparison with a wait-and-see strategy, after a lay cardiopulmonary resuscitation, up to US \$ 500,000 will be required per QALY (8). Compared to the

numbers above calculated for VIT, this sum seems to be actually quite favourable.

If, however, a disease is comparably common (and if many affected patients need a long-term therapy thereby further increasing costs), and if, simultaneously, the same disease (such as Hymenoptera venom allergy) is rarely lethal (with a low potential of saving lives), then it will be awfully expensive to gain even one extra year. The incidence of insect-sting mortality due to early anaphylaxis is known to be low ranging from 0.03 to 0.48 fatalities per 1000,000 inhabitants per year (3). These facts must have already been clear in advance of the above-mentioned analysis, which calculated a death rate following severe anaphylaxis of 1.25% (7), and make one wonder about the reasons making the initiators of the analysis commission such an evaluation of which catastrophic results for VIT were predictable. We acknowledge the fact that Hockenhull et al. (7) also performed a subgroup analysis, where VIT was found to be cost-effective in terms of preventing fatal reactions. This subgroup contained patients stung at least five times a year. Such a patient classification, however, is quite unrealistic, because there are – fortunately – hardly or even no patients who are stung that often each year.

The approach to refer cost-effectiveness of a therapy just to survival and to a normalized quality of life (ICER per QALY) must be regarded as inappropriate for many therapies. Numerous, even very expensive, therapeutic measures are not primarily aiming at a prolongation of life, but rather at a specific improvement of quality of life. VIT also falls under this category, and assessment of cost-effectiveness is only justified against this background.

It is important to note that the above NICE analysis initially assumed no VIT-related change in utility due to anxiety (1). There is, however, some evidence that VIT significantly improves quality of life (5,6). Unfortunately, there are no results obtained by a validated utility measure of quality of life. Consequently, Hockenhull et al. (7) concluded that any health benefit from VIT is entirely due to its effectiveness in reducing systemic reactions from sting and resulting deaths. We welcome the fact that the NICE analysis also contains a separate subgroup analysis assuming that fear of sting does affect the utility of some people and that VIT reduces this anxiety and so negates this loss in quality of life. For this specific subgroup (patients with sting anxiety), it was calculated that, compared to avoidance advice and supply with emergency kits only, VIT may cost up to £23,868 per QALY. These numbers are in the range of those derived, for example, for statins used to reduce cholesterol concentrations (9).

Therefore, VIT-related reduction of anxiety should have been a major outcome parameter. It is regrettable, however, that Hockenhull et al. (7) ignored the fact that of those patients admitted to hospital after a successful resuscitation, only between 7% and 30% are discharged from hospital with good neurological outcome (10–12). Consequently, an appropriate calculation of cost-effectiveness of VIT should have also included beneficial effects of VIT on neurological morbidity potentially persisting after a severe, albeit nonlethal anaphylactic reaction.

In conclusion, we strongly argue against using crude survival data and normalized quality of life to evaluate cost-effectiveness of VIT, which is used to treat a rarely lethal but comparably common disease such as Hymenoptera venom allergy. The value of VIT can only be judged on the basis of specific effects on quality of life; any other approach will be inappropriate and suspected of being biased.

Authors' contributions

FR drafted the manuscript. All authors contributed to revisions and approved the final draft.

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Conflict of interest

The authors declare that they have no competing financial interests.

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