

Commentary

EpiPen epidemic or good clinical practice?

Anaphylaxis is a rapidly evolving multisystem acute allergic reaction which can be considered severe when the systemic response involves the respiratory and/or cardiovascular systems. If data obtained in South Australia were to be extrapolated nationally, there are approximately 25 144 preschool and school age children in Australia who have had at least one episode of anaphylaxis.¹ Each of these children are at risk of a recurrent episode and those children with idiopathic anaphylaxis can expect to have almost three recurrent episodes each year, whilst for food and insect venom anaphylaxis one recurrent episode may occur every 2 and 7.5 years, respectively.² In addition to those children who have had a previous episode of anaphylaxis, there are a number of children who have an IgE mediated food allergy (without anaphylaxis), who are at an increased risk of anaphylaxis with subsequent exposure to the same trigger.

Parental adrenaline is indicated for the initial management of anaphylaxis because it both blocks the release and end organ effects of vasoactive mediators. Administering adrenaline as soon as possible after the onset of anaphylactic symptoms is thought to improve survival.^{3,4} Since the vast majority of childhood anaphylactic episodes occur at home, in child care or at school, it seems intuitive that an appropriate first aid anaphylaxis response should include the early administration of adrenaline. The adrenaline auto-injector or EpiPen (CSL Ltd., Parkville, Victoria, Australia) allows injectable adrenaline to be incorporated into a first aid response which can be initiated by parents and other carers.

Should all, some or none of the considerable number of Australian children at risk of anaphylaxis have an EpiPen as part of their first aid anaphylaxis plan? For paediatric allergists and pediatricians these questions are important and the reason why the viewpoint by Kemp raises many important issues for debate and further study.⁵

EPIPEN DISTRIBUTION IN AUSTRALIA

There has been an increase in EpiPen distribution in Australia.⁵ Although EpiPen distribution clearly does not equate to the number of children with EpiPens, more children are likely to have an EpiPen now than 5 years ago. Whether this is an 'epidemic' or good clinical practice is yet to be determined and calculating the optimal rate of EpiPen provision to the population is a complex task. This will depend on the number of children at risk of anaphylaxis, consensus guidelines on EpiPen prescription, the frequency of recurrent episodes of anaphylaxis, use of an EpiPen during such an episode and a number of stock control issues (such as EpiPen storage and expiry). However, even if the current crude rate of EpiPen provision (1 per 544 children) is accepted, this is still below the estimated prevalence of anaphylaxis (1 in 166 children).¹ Therefore, a counter view may be that there is still an under-distribution of EpiPens and that the current trend is required to meet optimal standards of clinical practice.

PERSPECTIVE OF ANAPHYLAXIS – MORTALITY VERSUS MORBIDITY

Fortunately, death from anaphylaxis appears to be rare but does occur as illustrated by the two childhood deaths that occurred as a result of nut anaphylaxis in New South Wales in 2002. However, the assumption that an EpiPen should only be prescribed to prevent death would be disputed by many. The rarity of this outcome, combined with potential ethical issues, will require that any evidence to support this will need to be based on retrospective case review and expert opinion rather than any form of randomized trial. What is open to a higher level of statistical evaluation is the ability of EpiPen use to prevent anaphylaxis morbidity. This can be measured in terms of medical intervention such as hospital resuscitation and admission, following anaphylaxis. Additional factors such as anaphylactic sequelae and the impact of EpiPen prescription on the quality of life of the child and family is also amenable to review.

Is there any evidence that EpiPen use is associated with a reduction in anaphylaxis morbidity? One retrospective review of 68 South Australian children with anaphylaxis who were prescribed an EpiPen suggests that EpiPen use is associated with a decrease in morbidity.² These 68 children experienced 45 recurrent episodes of anaphylaxis. For 13 of these episodes an EpiPen was used whilst in 32 episodes no EpiPen was used. Importantly, children who had an EpiPen administered were significantly less likely to have adrenaline subsequently administered and require hospital admission – 2/13 (14%) versus 15/32 (47%), $P < 0.05$, respectively.

If EpiPen use is associated with a decrease in anaphylaxis morbidity then any economic model should take this into account. Given the recurrent nature of anaphylaxis, it is likely that an economic saving could be demonstrated for EpiPen provision and use. Similarly, if the risk of anaphylaxis death is to be compared with meningococcal death, in food allergic children, so too must the risk of morbidity. Hence, it can be calculated that a child under 5 years of age, with established food anaphylaxis, would be at a 2000-fold greater risk of requiring hospital admission for a recurrent episode of anaphylaxis than for meningococcal infection.

GUIDELINES FOR EPIPEN PRESCRIPTION

Whilst the economics of EpiPen prescription are of interest to health economists, what medical practitioners and parents want to know is which children should have an EpiPen. There are currently no accepted national guidelines for EpiPen prescription. Identifying those at risk of both mortality and morbidity is appropriate. Most at risk would be those children with a past history of anaphylaxis with respiratory and/or cardiovascular involvement and a current history of persistent asthma. More difficult is determining the risk for those children who have had anaphylaxis without respiratory and/or cardiovascular involvement, those who do not have asthma and those children who have presented with a non-anaphylactic generalized allergic

reaction. The approach suggested by Kemp⁵ and based on an accumulation of additional potential risk factors seems sound if such factors can be identified. Those suggested are a good starting point for discussion but do require further analysis. For example, although death in children less than 5 years of age appears less common, can the same be said for anaphylaxis morbidity in this age group. Similarly, the majority of children who are admitted to hospital or die have nut allergy. However, given that only a minority of children with nut allergy become tolerant, the childhood prevalence of nut allergy is greater. Hence, the important question to ask is whether the death or hospitalization rate, following anaphylaxis, is greater for nuts as compared with other food allergens? Additional risk factors, that could also be considered, may include the extent of supervision of the child with regard to avoidance of triggers, the ability of the child to avoid triggers, and access to emergency medical care which may be of importance in a rural setting. Ultimately the decision to prescribe an EpiPen should be based on clinical guidelines but will also be influenced by parental anxiety and the expertise and experience of the clinician. Of equal importance is that the decision occurs within the context of a comprehensive approach which should ideally occur in a specialist allergy clinic.⁶

IMPORTANCE OF ANAPHYLAXIS EDUCATION AND ACTION PLANS

The most costly and unsatisfactory outcome for the individual child and the health system is the failure to use a prescribed EpiPen with a subsequent episode of anaphylaxis. This outcome accrues all of the costs without any of the potential benefit. In one South Australian study, the EpiPen was only used in approximately one-third of recurrent episodes, a finding which is consistent with other studies.² This was despite the EpiPen being available and in date in two-thirds of episodes. The reason(s) for the non-use of an EpiPen requires further study. Parental questionnaires indicate that parents have a poor recall of anaphylactic symptoms and how to use the EpiPen despite training. In 1996, only 36% of South Australian preschool and school anaphylactic children had an action plan, medication available at school and a teacher willing and able to administer the medication. These findings highlight the critical need for the provision of anaphylaxis education and EpiPen training, together with an anaphylaxis action plan when an EpiPen is prescribed. Since almost 1 in 5 recurrent episodes may occur away from home and without a parent present, such education and training needs to extend to other carers including school staff. Considerable progress in educating the staff of child care, preschool and school in anaphylaxis has been made in recent years in Australia.

CONCLUSIONS

There is an urgent need for further research into childhood anaphylaxis to better define the epidemiology, the most effective first aid response (including EpiPen use), and to identify further risk factors for anaphylaxis. Unfortunately, accumulating such data will take time and in the interim a uniform and coordinated national approach is required. The Australasian Society of Clinical Immunology and Allergy (ASCIA), as the professional body of allergists and clinical immunologists, has recently established an anaphylaxis working party to address these issues. The ultimate aim of the working party is to develop effective strategies to prevent anaphylaxis mortality and morbidity. The specific tasks are to develop anaphylaxis action plans, consensus guidelines for EpiPen prescription as well as anaphylaxis educational and training resources (an anaphylaxis action plan is available for use and can be obtained from the ASCIA website: <http://www.allergy.org.au>). Use of an EpiPen has a part to play in this strategy but it is still too early to say if the current trend of EpiPen prescription represents an 'epidemic' or good clinical practice.

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