Paediatric palliative care

*Anne-Sophie E Darlington, Marry M van den Heuvel-Eibrink, Jan Passchier
a.darlington@erasmusmc.nl

Department of Medical Psychology and Psychotherapy, Erasmus Medical Centre, Dr Molewaterplein 50, 3015 GE Rotterdam, Netherlands (A-SED, JP); Department of Pediatric Oncology/Hematology, Erasmus Medical Centre Sophia Children's Hospital, Rotterdam, Netherlands (MMvdH-E)

With interest and appreciation we read the Review by Stephen Liben and colleagues on paediatric palliative care (March 8, p 852).[1] It beautifully illustrates how paediatric palliative care has evolved substantially over the past years, and includes topics such as mental suffering and hope, besides death and somatic issues.

For progress in this field, many of the ideas covered by Liben and colleagues require empirical evidence. However, one challenge that was not addressed in their Review concerns the participation in research of children and families in the palliative phase. Institutional review boards often struggle with these research proposals.

In the Netherlands, the Medical Research (Human Subjects) Act prohibits trials on minors, with the exception of trials that could be of direct benefit to the patients, or in which the risk associated with participation is negligible and the burden minimal.[2]

The annual report of the Central Committee on Research Involving Human Subjects (CCMO)[3] in the Netherlands addresses this issue, outlining arguments for and against an amendment of this legal guideline. In support of this amendment, it states that terminally ill children are mentally more mature than are their healthy peers and the burden of research is minimal in view of what they have to endure in their life. The counter argument might be that participation in research actually increases the burden they already have to face.

In line with the CCMO, we propose that a debate on this issue be started without delay to find a good balance between the protection of young patients and an increase in the knowledge that is needed to improve their care.

JP was a member of the Central Committee on Research Involving Human Subjects (CCMO) from 1999 to 2007. We declare that we have no conflict of interest.

1 Liben S, Papadatou D, Wolfe J. Pediatric palliative care: challenges and emerging ideas. *Lancet* 2008; **371:** 852–64.
2 Ministerie van Volksgezondheid, Welzijn en Sport. Wet Medisch-wetenschappelijk Onderzoek (WMO): section 4, article 1. The Hague: Ministerie van Volksgezondheid, Welzijn en Sport, 1998. http://www.ggd.nl/ggdnl/uploaddb/downl_object.asp?atoom=10373&VolgNr=1 (accessed June 3, 2008).
3 Centrale Commissie Mensgebonden Onderzoek. Annual report 2006. The Hague: CCMO, 2007. http://www.ccmo-online.nl/hipe/uploads/downloads_catc/CCMO_JV_2006.pdf (June 2, 2008).

Stephen Liben and colleagues' comprehensive review of the present status of paediatric palliative care[1] fills a gap in the current knowledge of this evolving medical science. Liben and colleagues summarise the barriers for adequate paediatric palliative care in their table, thus drawing attention to the variety of issues that need improvement. We would like to add a further consideration.

According to the WHO definition, palliative care should not be limited to end-of-life situations. On the contrary, it should be considered early in the patient's management scheme and focus on the four dimensions of somatic, psychological, social, and spiritual symptom control, resulting in an improvement of the quality of life. More efforts should be made to demystify palliative care and paediatric palliative care. Every individual, and specifically first-line and second-line health-care providers, should be made aware of the fact that palliative care aims to provide comfort and improve the quality of life in line with the patient's and the family's wishes and culture.

Good clinical practice implies that patients for whom treatment fails are well informed about the trajectory of their disease and their life. Successful provision of such information demands an holistic programme with obligatory anticipation of problems, and specific education and training in palliative care (especially paediatric palliative care) for all health-care providers working in this area.

The diffusion of this knowledge and its integration into the minds of all general practitioners and organ specialists is the challenge of the future.

We declare that we have no conflict of interest.


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*Kris C P Vissers, Yvonne Engels, Constans Verhagen
K.Vissers@anes.umcn.nl

University Medical Centre St Radboud, Department of Anesthesia, Pain and Palliative Medicine, 6500 HB Nijmegen, Netherlands

1 Liben S, Papadatou D, Wolfe J. Paediatric palliative care: challenges and emerging ideas. *Lancet* 2008; **371:** 852–64.

Management of acute organophosphorus pesticide poisoning

In their Review (Feb 16, p 597),[1] Michael Eddleston and colleagues summarise the treatment of acute organophosphorus pesticide poisoning. They recommend pralidoxime chloride or obidoxime as a loading dose followed by an infusion until atropine has not been needed for 12–24 h and the patient has been extubated, as well as retreatment with the oxime in case of recurring cholinergic features. This recommendation is not evidence-based and should not be regarded as the gold standard. Eddleston and colleagues present many theoretical and practical reasons why oximes might not be useful to patients with overwhelming self-poisoning, but they do not translate these considerations into clinical practice.

A placebo-controlled trial of oxime treatment for organophosphorus pesticide poisoning showed that pralidoxime plus atropine does not have any benefit over atropine alone.[2]

The need for mechanical ventilation, median days on mechanical ventilation, median days in the intensive-care unit, frequency of the intermediate syndrome, and mortality rate were similar in each group. Additionally, a meta-analysis concluded that oxime was associated with either a null effect or possible harm.[3]

Therefore, it is time to revise the role of oximes in acute organophosphorus pesticide poisoning, and to do a large, high-quality, randomised controlled trial with appropriate stratification of patients according to baseline severity, time to presentation, and class of organophosphorus pesticide (diethyl or dimethyl), with predefined subgroup hypotheses.[4] The erythrocyte acetylcholinesterase activity and the potential for ex-vivo reactivation have to be measured for reliable interpretation.[5]

We declare that we have no conflict of interest.

*Houssem Hmouda, Chaker Ben Salem, Kamel Bouraoui
houssem_hmouda@yahoo.com

Sahloul University Hospital, 4054 Sousse, Tunisia

1 Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. *Lancet* 2008; **371:** 597–607.
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Michael Eddleston and colleagues' Review[1] on organophosphate poisoning is interesting. The burden of poisoning in Asian countries can be likened to an epidemic, with mass suicides reported from rural India by farmers who incur severe financial loss.[2] Although the key to halting this epidemic lies in improving the welfare of farmers and reducing their debt trap, certain measures could reduce case-fatality.

In several Asian countries, the sale of highly toxic insecticides is not restricted. With the advent of less toxic but equally potent insecticides, replacement of toxic insecticides with compounds such as pyrethroids and neonicotinoids that have versatile application and favourable environmental and toxicological profiles seems a good strategy.[3] The banning of class I compounds in Sri Lanka was effective in reducing case-fatality.[4] High-concentration formulations that cover several acres of land also account for severe intoxication and death. Dispensing dilute preparations of insecticide, sale regulation, and safe-storage measures need to be implemented to reduce the severity of poisoning and offer a chance for poisoned patients to reach hospital for medical assistance.[3]

Although overall case-fatality is about 15%,[1] decreased mortality of severely poisoned patients in our intensive-care unit from 14·6%[5] during 1999–2005 to 7·4% in 2006–07, suggests that it might be difficult, even with large trials, to show further mortality reductions with other treatments discussed in Eddleston and colleagues' Review.[1] However, such adjunct therapies[1,3] might affect secondary outcomes such as ventilatory requirements or hospital stay, and these need to be factored in when designing therapeutic trials on organophosphate poisoning.

We declare that we have no conflict of interest.

*John Victor Peter, George John
peterjohnvictor@yahoo.com.au

Christian Medical College and Hospital, Vellore, Tamil Nadu 632 004, India

1 Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphate poisoning. *Lancet* 2008; **371:** 597–607.
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Authors' reply

We acknowledge Houssem Hmouda and colleagues' concern that the exact role of oximes in any particular patient who has taken organophosphorus pesticides is unclear. However, the study they cite[1] was not a randomised controlled trial and used low bolus doses of pralidoxime that would not be expected to benefit patients poisoned with the dimethyl organophosphorus insecticides seen in the study. The cited meta-analysis[2] combined mostly non-randomised studies and as such is likely to be confounded by selection and performance bias.

Neither the meta-analysis nor Hmouda and colleagues consider the most recently published study,[3] which used a higher dose and recruited patients who presented early—a median of 2 h after ingestion. This study showed a benefit of pralidoxime chloride. At present, the balance of published evidence favours the *early* use of pralidoxime;[4] hence our recommendation of current WHO guidelines in the panel of management guidelines, while discussing the limitations of this advice in the text.

We also agree that further trials of pralidoxime against placebo, recording the exact pesticide ingested and the acetylcholinesterase status on admission for each individual,[5] will probably provide important information about the role of pralidoxime. We have recently completed such a study and will present its results soon.

We agree with John Victor Peter and colleagues that replacing highly toxic organophosphorus insecticides with less toxic insecticides will substantially reduce deaths from pesticide poisoning. We also agree that other public-health measures, particularly reducing the concentration of pesticide in available preparations, could have major effects.

However, the low case-fatality in Peter and colleagues' hospital does