Phenobarbitone and febrile convulsions

The value of long term anticonvulsant prophylaxis in children who have had febrile convulsions has been debated for many years. In a recent paper in the *New England Journal of Medicine*, Farwell *et al* concluded that phenobarbitone depresses cognitive performance without preventing seizure recurrence.¹ After two years the mean intelligence quotient in children assigned to phenobarbitone treatment was 8.4 points lower than in the placebo group, and six months later the difference was 5.2 points. There was no significant difference as regards seizure recurrence over the two years in the two groups.

The data are not easy to interpret. Only children less than 12 months old or with risk factors for the development of later epilepsy² were entered into the study. At the start of the study the average Bayley mental index in those assigned to placebo was 103.6, in those assigned to phenobarbitone 104.8, and in age matched controls without seizures 113.8. The effect of phenobarbitone in depressing cognitive performance was less in the children who performed better at the outset. The results were analysed on an intention to treat basis but of 94 children assigned to placebo 29 were taking anticonvulsant treatment at two years after entry to the trial. Of 83 children in the phenobarbitone group only 53 were still taking phenobarbitone after two years. Seventy seven had intelligence testing at that time but only 46 of them were estimated on the basis of blood tests to have complied properly with treatment. Intention to treat analysis answers the question 'What happens to children assigned to treatment with drug X?'. It cannot answer the question 'What are the effects on children of taking drug X?'. Both questions are of interest. As regards the effect of phenobarbitone treatment (or rather, intention to treat) on seizure recurrence, the conclusion of this study is similar to that of the meta-analysis performed by Newton.³ That analysis showed that sodium valproate was, if anything, less effective than phenobarbitone.

A similar study was reported from Cardiff by Aldridge

Smith and Wallace in 1982,⁴ and it seems extraordinary that that study is not mentioned in the American paper. In the Welsh study the children tested at two years had taken either the prescribed drug (phenobarbitone or sodium valproate) or no treatment throughout the study period. For children who had no recurrence of febrile convulsion the difference in mean Griffiths's development quotient between those untreated and those on phenobarbitone was 2.8 at the start of the study and 7.4 at the end, a difference assessed as statistically insignificant and due to an apparently greater rise in quotient in the children who took no drug. There was a small but (statistically) significant fall in developmental quotient after two years in the children who had further convulsions and a small rise in those who didn't. The authors therefore related poor intellectual progress to recurrence of convulsions rather than to drug treatment.

What conclusions can be drawn? Phenobarbitone treatment is commonly associated with behavioural side effects and its efficacy in preventing convulsions is at least questionable especially if results are analysed on the basis of intention to treat. There may be a small fall off in cognitive performance related to phenobarbitone treatment, although the practical as opposed to statistical significance is uncertain. It seems difficult to justify phenobarbitone prophylaxis for febrile convulsions unless the recurrence risk is very high and compliance is assured.

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- 1 Farwell JR, Lee YJ, Hirtz DG, Sulzbacher SI, Ellenberg JH, Nelson KB. Phenobarbital for the febrile seizures—effects on intelligence and on seizure recurrence. *N Engl J Med* 1990;322:364–9.
- 2 Nelson KB, Ellenberg JH. Prognosis in children with febrile seizures. *Pediatrics* 1978;61:720–7.
- 3 Newton RW. Randomised controlled trials of phenobarbitone and valproate in febrile convulsions. *Arch Dis Child* 1988;63:1189–91.
- 4 Aldridge Smith, Wallace SJ. Febrile convulsions: intellectual progress in relation to anticonvulsant therapy and to recurrence of fits. *Arch Dis Child* 1982;57:104–7.