Short Report

Absence of ivermectin-associated excess deaths

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Ivermectin belongs to a group of semisynthetic compounds derived from the soil bacterium *Streptomyces avermitilis*. It was released in 1981, and by the end of the decade had been used in at least 77 countries for control of parasites in agricultural animals (CAMPBELL, 1985, 1988). After its registration for human onchocerciasis in 1987, the number of annual treatments reached 9·2 million in 1993 and continues to grow rapidly (WHO, 1995). Recent clinical trials have shown that ivermectin is also effective against lymphatic filariasis, indicating treatment of millions more people affected by that disease (OTTESEN & CAMBELL, 1994; WHO, 1997). Ivermectin is also effective against ectoparasites such as head lice (DUNNE *et al.*, 1991) and scabies mites (SULLIVAN *et al.*, 1997), and causes mortality in mosquitoes which have bitten people treated with the drug (WILSON, 1993).

In a recent study, ivermectin was associated with excess deaths when used to treat scabies in a long-term care unit for elderly patients (BARKWELL & SHIELDS, 1997). Although not confirmed by subsequent reports (REINTJES & HOEK, 1997; COYNE & ADDISS, 1997), this finding is a cause for concern because of the very large number of people being treated with the drug.

We present here an analysis of deaths in a part of the East Sepik Province of Papua New Guinea where we maintain demographic surveillance as part of a randomized community-based trial of ivermectin plus diethylcarbamazine (DEC) versus DEC alone for lymphatic filariasis caused by *Wuchereria bancrofti* (see BOCKARIE *et al.*, 1998). Annual treatment started in 1994, and the Table lists the 67 people who died between their first treatment and the beginning of the 1997 annual round. The dose was 400 µg/kg, and those aged less than 5 years were not treated. The death rates were analysed following SMITH & MORROW (1991). The study was randomized by community rather than individual, so it was possible to change regimen as a result of changing residence, although no death occurred among such people.

There is no statistically significant difference in the death rates, with any tendency being for a reduction, not an increase, in those receiving ivermectin. The same is true if the analysis is restricted to those aged at least 60 years at first treatment (Table). The conclusions are similar if the duration of surveillance is ignored and the data analysed as a 2×2 table, as in the original report by BARKWELL & SHIELDS (1997). Had the underlying rate ratio been 3·0 as they estimated, then the statistical power of our study would have been more than 99% for the whole population, and more than 90% for those aged 60 years and over (KIRKWOOD, 1988). In other words, the failure to detect such a difference is unlikely to be due to inadequate sample size.

Table. Death rates following treatment with ivermectin plus diethylcarbamazine or diethylcarbamazine alone

Treatment[a]	No. of deaths/ person-years of surveillance[b]	Rate ratio[c]	*P*
All treated persons			
Ivermectin plus DEC	28/3259 (0·0086)	0·74 (0·45–1·20)	0·22
DEC alone	39/3344 (0·0117)		
Age ≥60 years			
Ivermectin plus DEC	6/132 (0·045)	0·54 (0·21–1·37)	0·20
DEC alone	17/202 (0·084)		

[a]DEC=diethylcarbamazine.
[b]Death rate in parentheses.
[c]95% confidence interval in parentheses.

In conclusion, we found no evidence of an increased death rate associated with ivermectin treatment, even at a much higher dose than the 150–200 µg/kg used by BARKWELL & SHIELDS (1997). This study was randomized by community, not individual, so it was not strictly designed for individually based analyses such as this. Nevertheless, the randomization has some advantages over the retrospective case–control design of BARKWELL & SHIELDS (1997), and the results provide reassurance that the excess mortality associated with ivermectin which they reported may have resulted from pharmacological interactions or other circumstances not generally pertaining in mass control programmes for onchocerciasis or lymphatic filariasis.

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