Impact of fly control on childhood diarrhoea in Pakistan: community-randomised trial

D C Chavasse, R P Shier, O A Murphy, S R A Huttly, S N Cousens, T Akhtar

Summary

Background Several million children are killed each year by diarrhoeal diseases; preventive strategies appropriate for developing countries are vital. Despite strong circumstantial evidence that flies are vectors of diarrhoeal diseases, no convincing studies of the impact of fly control on diarrhoea incidence in developing countries have been reported. We undertook a randomised study of the effect of insecticide spraying on diarrhoea incidence.

Methods Six study villages were randomly assigned to two groups. Flies were controlled through insecticide application in group A in 1995 and in group B in 1996. In 1997 the effectiveness of baited fly traps was tested in group A villages. Diarrhoea episodes were monitored in children under 5 years through mothers' reports during weekly visits by a health visitor. Fly density was monitored by use of sticky fly-papers hung in sentinel compounds.

Findings During the fly seasons (March–June) of both 1995 and 1996, insecticide application practically eliminated the fly population in the treated villages. The incidence of diarrhoea was lower in the sprayed villages than in the unsprayed villages in both 1995 (mean episodes per child-year 6·3 *vs* 7·1) and 1996 (4·4 *vs* 6·5); the reduction in incidence was 23% (95% CI 11–33, p=0·007). At times other than the fly season there was no evidence of a difference in diarrhoea morbidity between sprayed and unsprayed villages. Fly density data for 1997 indicate the ineffectiveness of baited traps in this setting.

Interpretation Fly control can have an impact on diarrhoea incidence similar to, or greater than, that of the interventions currently recommended by WHO for inclusion in diarrhoeal disease control programmes in developing countries. This important finding needs confirmation in other settings in developing countries. Technologies and practices that interrupt disease transmission by flies need to be developed and promoted.

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Introduction

Diarrhoeal diseases are a leading cause of childhood mortality, accounting for 3·3 million deaths worldwide each year.[1] Preventive strategies are needed to reduce this mortality and the estimated annual morbidity of 1 billion diarrhoea episodes in children under 5 years of age.[2] An effective prevention programme will integrate a selection of proven interventions aimed at specific pathogens (such as rotavirus immunisation) or transmission routes (improved water supply and sanitation). As a step towards defining which interventions should be recommended for inclusion in national programmes, WHO published a series of reviews on the effectiveness of various candidate interventions. Three categories of intervention were defined: ineffective or intervention of limited feasibility unlikely to have a major role in control programmes; intervention for which effectiveness or feasibility remains uncertain and in need of further research; highly effective intervention with strong evidence for its feasibility.[3]

The third "highly effective" category contained seven interventions that were considered promising for inclusion in diarrhoeal disease control programmes. These were promotion of breastfeeding, improvement of weaning practices, rotavirus immunisation, cholera immunisation (in special circumstances), measles immunisation, improvement of water supply and sanitation, and promotion of personal and domestic hygiene. Of the interventions reviewed, only two reduced diarrhoea incidence by more than 5% (median reduction of many studies) in children under 5 years old.

Fly control was placed in the first "ineffective" category, despite the fact that previous studies indicated a median reduction in diarrhoea incidence of 40%.[4] Likely reasons for this decision are that many of the reviewed studies were poorly designed (with the exception of one study carried out in southern USA in the 1940s[5]) and that the sustainability of fly-control technology was unclear. If these were the reasons, fly control might, more appropriately, have been placed in the second "uncertain" category, pending further investigation.[6] Subsequently, Cohen and colleagues found a reduction in diarrhoea incidence among Israeli soldiers after fly control with yeast-baited traps.[7] Based on these promising results, and the fact that many previous intervention trials had been poorly designed, we undertook a controlled trial to investigate the impact of fly control on the incidence of childhood diarrhoea in a developing country where diarrhoea is a leading cause of childhood morbidity and mortality.

Location and methods

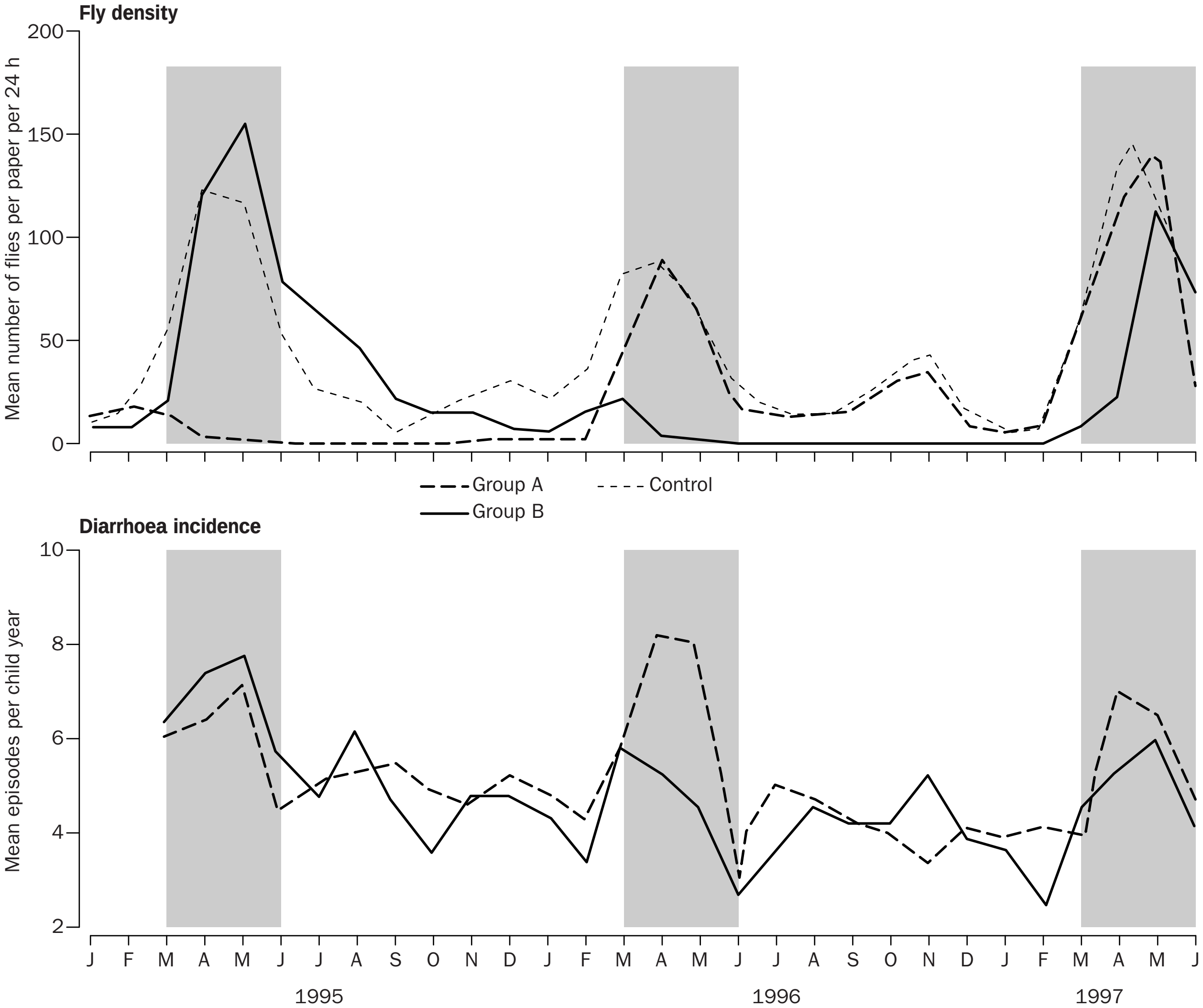
The study area comprised six study villages and two control villages near the town of Peshawar in North West Frontier Province, Pakistan. Preliminary studies showed that a seasonal peak in diarrhoea incidence between March and June coincided with a peak in fly density.[8] The villages consist of 20–40 compounds, each inhabited by two or three related families. Livestock are kept inside the compounds, giving rise to manure heaps throughout the villages, resulting in high fly-breeding potential. Domestic waste collected in Peshawar and dumped in the surrounding district is another source of flies. There are no pit latrines in these villages, so flies have ready access to diarrhoea-causing pathogens in human faeces scattered about the environment. Hence the potential exists for flies to pick up pathogens from the environment and to transmit them through

Villages	1995	1996	1997
Group A	Sprayed	Unsprayed	Traps
Group B	Unsprayed	Sprayed	No Traps
Control	Unsprayed	Unsprayed	Unsprayed

Table 1: **Study design**

London School of Hygiene and Tropical Medicine, London, UK (D C Chavasse PhD, R P Shier MSc, O A Murphy MSc, S R A Huttly MSc, S N Cousens MA)**; and Pakistan Medical Research Council, Khyber Medical College, Peshawar, Pakistan** (T Akhtar FRCP)

Correspondence to: Dr Desmond Chavasse, PSI (Malawi), c/o Population Services International, 1120 19th Street NW, Suite 600, Washington DC, 20036, USA



Fly density in group A (sprayed in 1995), group B (sprayed in 1996), and control villages, and diarrhoea incidence in children under 5 years in study villages
Shading indicates fly season.

resting and feeding on food in storage, by contaminating eating utensils and surfaces on which food is prepared, or by direct contamination of children's hands and faces.

The study took place between January, 1995, and June, 1997. The study was approved by the ethics committee of the London School of Hygiene and Tropical Medicine. Permission to proceed with the study was given by the government of North West Frontier Province and the village elders. The six study villages were divided randomly into two groups of three—village names were picked out of a hat at a meeting attended by representatives of all the villages. Flies were controlled with insecticide in villages in group A in 1995 and in villages in group B in 1996. Fly traps, based on the design of Cohen and colleagues,[7] and using a commercial bait formulation, were introduced into group A in 1997. The traps were placed in areas of the compound where flies were seen to congregate, commonly near a kitchen, an animal shed, or a manure heap. Fly density alone was monitored in a further two (control) villages. The crossover study design is summarised in table 1.

A previous study (unpublished), carried out in a neighbouring village over 4 months in 1990, found the mean number of episodes of diarrhoea per child to be 3·0. On the basis of these results, an annual incidence of at least four episodes was expected. We calculated that six villages, with about 70 children aged under 5 years in each, would give 80% power to detect, as significant at the 5% level, a 15% reduction in the mean number of episodes per child per year using a paired *t* test applied to the village rates, assuming the incidence in the absence of fly control to be four episodes per child per year, with an SD of 3.

Flies were controlled by means of ultra low volume space spraying with insecticide. The insecticide used was Aqua K-Othrine, a water-based formulation of deltamethrin, applied at a dose of 0·5–1·0 g of active ingredient per hectare by Porta-Pak sprayers (Hudson, USA). Spraying was done twice a week between March and November of each year. It was extremely popular with the villagers, because flies were regarded as being the most unpleasant household insect after mosquitoes.[8] The workers who did the spraying passed through the village on a predefined route, entering and spraying in each compound. Fly density was monitored by means of standard sticky fly-papers (yellow paper about 0·5 m long and 4 cm wide, coated in sticky gum), which were hung in areas of the compounds where fly resting sites were either suspected or identified through faecal deposits; typical sites were under the thatched roofs of animal shelters or outdoor kitchens. The number of flies stuck to the papers after 24 h was counted. During a trial period in three of the study villages in 1994, this method was found to produce more consistent estimates of fly density than the alternative Scudder grill method.[9] In each village, four sentinel compounds were selected and monitored once per week throughout the study. Over 98% of the flies caught were *Musca domestica* (house fly).

Diarrhoea incidence was monitored through mothers' reports for all children under 5 years of age in the six villages in groups A and B from February, 1995 to June, 1997. Over the course of the

Village	Mean episodes per child-year (number of episodes)		
	1995	1996	1997
Group A			
Dawa	6·8 (64)*	6·3 (60)	6·1 (66)
Dehri	6·3 (182)*	6·0 (184)	5·1 (194)
Purdil	5·8 (99)*	7·3 (157)	6·3 (144)
Whole group	6·3*	6·5	5·8
Number of child months†	666*	737	863
Group B			
Hergoni	6·8 (170)	4·2 (110)*	4·5 (128)
Miankali	7·8 (184)	4·8 (108)*	5·2 (126)
Yasinabad	6·6 (134)	4·3 (104)*	5·5 (153)
Whole group	7·1	4·4*	5·1
Number of child months‡	828	880*	963

*Sprayed villages. †Median age of children 27 months in all 3 years. ‡Median age of children 26 months in 1995, 28 months in 1996 and 1997.

Table 2: **Incidence of diarrhoea in children under 5 years during fly seasons (March–June)**

study, newborn infants were recruited and children reaching their fifth birthday were released from the study. The mothers of all eligible children consented to be involved. During weekly interviews, mothers were asked on which days since the last visit the child had had diarrhoea, if any; the mother's own definition of diarrhoea was used. During pre-testing to assess what the mothers meant by diarrhoea, stools described by mothers as "diarrhoea stools" were examined in the environment and found to be unformed liquid stools. All interviewers worked in each of the six study villages to ensure that any variation between interviewers was consistent across villages. In addition, each day a supervisor visited a random selection of compounds to interview the mothers again, without knowledge of the previous responses. If the responses obtained by the supervisor differed in any respect from those obtained by the original interviewer, both went back to the mother to repeat the interview together. In an attempt to identify any reporting bias due to the presence of the sprayers, we also monitored two other health indicators, cough and fever, which are unlikely to be affected by fly control.

Diarrhoea incidence was derived from the daily diarrhoea data; 2 days free of diarrhoea, or longer, was taken to indicate the end of an episode. The statistical analysis of the diarrhoea results had to take account of village-based rather than child-based randomisation. Therefore, we used the village as the unit of analysis. The reduction in log incidence, for the sprayed year compared with the unsprayed year, was calculated for each village. The mean reduction, calculated by the method of Hills and Armitage,[10] gave an estimate of the effect of spraying, taking the period (year) effect into account. Similarly, it also gave an estimate of any differences between years adjusted for the effect of the intervention. Transformation back to the original scale gave the results in terms of a mean rate ratio. The significance of these effects was tested by a *t* test; two-sided tests were used throughout. We confirmed the results obtained from the above analysis by fitting a Poisson regression model, taking account of the village randomisation using a generalised estimating equation approach.[11]

Results

During the study period, 4160 fly catches were done in the eight monitored villages. The number of flies caught per paper per day ranged from 0 to 675; the data on fly density in the three groups of villages over the course of the study is shown in the figure. Data from the control group show three pronounced fly seasons in March to June each year. The fly season of 1996 was less pronounced than the others; this was probably due to climatic factors affecting fly breeding. During the 1995 fly season, the mean number of flies caught per sticky paper in 24 h was three in group A (sprayed) villages, 118 in group B villages, and 88 in the control villages. After the intervention was switched in 1996, the figures were 57 in group A villages, two in group B (sprayed) villages, and 63 in the control villages. Thus, in both years, spraying was highly effective in reducing fly density. In 1997 fly densities were broadly similar in all three groups (89 in group A, 54 in group B, and 90 in the control villages), indicating the ineffectiveness of the baited fly traps.

491 children under 5 years of age were enrolled into the study during the initial survey; 214 in group A and 277 in group B. The median age was similar in the two groups (27 months and 28 months, respectively), as were the median number of families per compound (two in both groups), the median number of people living in the compound (ten in group A and nine in group B), and the baseline diarrhoea incidence during the month at the start of the study, preceding the intervention (0·4 episodes per child in both groups). A further 319 children (newborn infants or familes moving into one of the study villages) had been enrolled by the end of the study. During the course of the study, 186 children reached the age of 5 years, 24 died, and 145 moved away from the study area. At any one time, about 500 children were being followed up. The number of mothers registered in the study during the 1995 fly season was 280; an additional 48 were enrolled at the time of the 1996 fly season. Daily diarrhoea profiles were constructed for a total of 810 children who were, for all or some of the study, under 5 years of age. The figure shows the mean diarrhoea incidence by month for villages in group A and group B. Seasonal peaks in diarrhoea incidence during the fly-season months of March to June are apparent. Table 2 shows the diarrhoea incidence for the six study villages for the three fly seasons. As shown in the figure and table 2, during the 1995 fly season diarrhoea incidence was slightly lower in villages in group A (sprayed), whereas in the 1996 fly season incidence was substantially lower in group B (sprayed). In the 1997 fly season, when no effective fly control measures were in place, diarrhoea incidence was slightly lower in group B. At times when fly densities were relatively low, the two groups of villages had similar diarrhoea incidence, despite there being some carry-over effect of spraying on fly densities after the end of the fly season.

An analysis of the effect of year, adjusted for the effect of fly control, showed that there was less diarrhoea in the fly season of 1996 than in that of 1995 (mean rate ratio 0·81 [95% CI 0·70–0·93], p=0·01). An analysis of the impact of fly control, adjusted for year, indicated a substantial reduction in diarrhoea incidence associated with insecticide spraying (mean rate ratio 0·77 [0·67–0·89], p=0·007). This rate ratio is equivalent to a 23% (95% CI 11–33) reduction in diarrhoea incidence attributable to fly control. A GEE Poisson regression model gave essentially the same result (rate ratio 0·78 [0·70–0·86]; p<0·001). The effect of fly control was greater in 1996 than in 1995 (p=0·05). At times other than the fly season there was no difference between the sprayed and unsprayed groups (rate ratio 1·03 [0·84–1·27], p=0·7). There was no difference between the two groups of villages in 1997, when neither group was sprayed (rate ratio 1·15 [0·90–1·47]).

During the fly seasons there was no significant effect of spraying on the prevalence (based on days of illness) of fever (rate ratio 0·89 [0·58–1·36]; p=0·5) or cough (0·84 [0·56–1·25]; p=0·3). As previously, both these results took the effect of year into account.

Discussion

This study suggests that fly control can significantly reduce childhood diarrhoea incidence during periods of high fly densities. This effect compares favourably with some of the WHO recommended diarrhoea interventions such as immunisation. One possible explanation for this finding is reporting bias. However, there was no significant difference in the prevalence of cough or fever, two outcomes that are unlikely to be affected by the intervention.

The results of previous studies have tended to associate flies with the transmission of *Shigella* spp rather than other diarrhoea-causing pathogens.[7,12] We have few data on the causes of diarrhoea in the study villages. However, only 3·2% of children with diarrhoea were reported to be passing stools containing blood, which may indicate a relatively low rate of infection with *Shigella* spp. Variations over the study period in the frequency of different causative agents, with different propensities for flyborne transmission, could be one explanation for the apparently larger impact of fly control in 1996 than 1995. Another possible explanation could be a decline in the reporting of diarrhoea owing to apathy among the mothers. Because of the crossover design, this would cause the estimated impact to be greater for those sprayed in 1996; the estimate of the overall impact, however, would remain essentially the same.

On the basis of the results presented here, fly control, with insecticide if necessary, may be recommended in situations where high fly density is associated with a high incidence of diarrhoea—for example, during diarrhoea epidemics in refugee camps. In such camps, spraying with a water-based pyrethroid can bring about and sustain almost total fly control during the fly season.[13,14] Fly control through spraying of insecticide would, however, not be justified for long-term routine control because of the expense and the likely development of insecticide resistance. Unfortunately, baited fly traps had no appreciable impact on fly density in this setting. Some caught up to 700 flies per day, but many caught none at all; the average was insufficient to impact on the population as a whole. The traps may have been ineffective because so many sites were attractive to flies (such as scattered human faeces and manure heaps). Still, given the success of fly traps in Israel, there is no reason to assume that they would be ineffective in areas with fewer attractive sources competing with the bait. In such areas they might be suitable for routine use. More attractive baits would increase the efficacy of traps in any environment.

Environmental management, such as changing the way animal dung is kept, has the potential to reduce fly densities but, in practice, implementation of such changes through the modification of human behaviour is extremely difficult to achieve on a large scale. Restriction of fly access to pathogens (through the provision of pit latrines) and to stored food and to children (for example, by covering sleeping babies during the day[15]) could reduce the importance of flies as a transmission route; such an approach could be combined with targeted chemical and non-chemical fly control methods.[16]

Fly-borne diseases, such as diarrhoea and trachoma, are of major public health importance in developing countries. We have found fly control to be an effective method for reducing the incidence of childhood diarrhoea. However, we were not able to establish a feasible long-term method for fly control in this setting. We believe that further controlled trials should be carried out in other settings in developing countries to confirm these findings; such studies should include the collection of data on diarrhoea causes, local hygiene-related practices, environmental indicators, and fly species. Such information will help to define situations in which fly control may be recommended as an effective diarrhoea intervention. We hope that the confirmation of these important results in other areas and the development of sustainable technologies or practices for fly control or for interrupting fly transmission of pathogens will be recognised by funding agencies as a research priority.

Contributors

Desmond Chavasse selected the study site, secured the funding, designed the study, provided the entomological expertise, and supervised the project managers. Rosie Shier managed the project for the first year, set up the data collection and data management systems, and did the statistical analysis. Orla Murphy managed the project during 1996 and 1997 and designed the baited fly component of the study. Sharon Huttly and Simon Cousens helped design the study and provided technical assistance throughout the project. Tasleem Akhtar was responsible for logistical support and supervision of the local staff. All the investigators contributed to the writing of the paper.

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