A comparison of adverse effects of two influenza vaccines, and the influence on subsequent uptake

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SUMMARY. In a study comparing the side effects of two influenza vaccines in a health centre vaccination programme involving patients in 'at risk' groups, no significant difference was found between the vaccines used or the method of administration. The majority of side effects were minor, but as many as 35 per cent of the study group reported some systemic upset after vaccination. A follow-up study a year later showed that the incidence of side effects did not appear to influence the uptake of revaccination.

Introduction

IN the past it has been accepted that the administration of any influenza vaccine was likely to produce some side effects. With the introduction of newer and more purified vaccines, the manufacturers have claimed that reactogenic problems are less. Various studies have attempted to assess the uptake and efficacy of influenza vaccines but little work has been done to examine specifically their side effects.[1-3] It has, however, been argued that side effects from influenza vaccines are likely to produce a reduction in future uptake.[4]

The general practitioners of Howden Health Centre, Livingston have for the past eight years offered influenza vaccination to the 'at risk' groups as recommended by the Scottish Home and Health Department annual memorandum.[5] In previous years some patients have complained of side effects of vaccination either to their doctors or to other members of the health centre staff.

This study was undertaken after discussion with the doctors who wished to maintain the uptake of immunization at a high level. They were keen to obtain more accurate data on side effects and their possible influence on uptake.

The aims of the study were to compare the side effects of two influenza vaccines recommended by the Scottish Home and Health Department,[5] and to assess whether uptake of revaccination was related to the incidence of side effects and their severity.

Method

The two vaccines selected for the study were Fluvirin (Evans Medical Limited) (vaccine A) and MFV-Ject (Servier Laboratories Limited) (vaccine B). Fluvirin is an inactivated vaccine consisting of purified haemagglutinin and neuraminidase surface antigens in an aqueous suspension. It is a subunit vaccine in which the virus particles are totally disrupted and the haemagglutinin and neuraminidase particles are extracted. MFV-Ject is a split vaccine in which the virus particles are not totally disrupted in its preparation. This vaccine is prepared by zonal ultracentifugation and purified with ether.

In 1981, 462 patients were invited by letter, signed by their own general practitioners, to have influenza vaccination. Just over 80 per cent of patients (371) accepted. Of these, 259 patients attended a special vaccination clinic in the health centre and received one or other of the vaccines by the jet injection method. The other 112 patients were given vaccine from single dose prefilled syringes either in their homes or in the health centre at a time convenient to them. Neither the patients nor the two practice nurses who administered the vaccine in the clinic knew which of the two vaccines was being used and the patients were randomly allocated to each nurse. It was not feasible to use this double-blind technique for those patients who were unable to attend the clinic.

Short postal questionnaires, timed to arrive on the third or fourth day after vaccination, were sent by individual general practitioners to establish whether their patients had experienced any side effects within the first three days. Stamped and addressed envelopes were provided. Patients were asked about the possible reactions specifically mentioned in the literature of the manufacturers, namely redness at the injection site, stiffness in the arm, pain in the arm, feeling 'off colour' (malaise), headache, shivering or fever. They were also asked to state any other symptoms that they had experienced. A question about diarrhoea was included in an attempt to establish the reliability of the replies. Completed questionnaires were returned by 323 patients (87 per cent) and punch cards (feature cards) were used for the analysis of results.

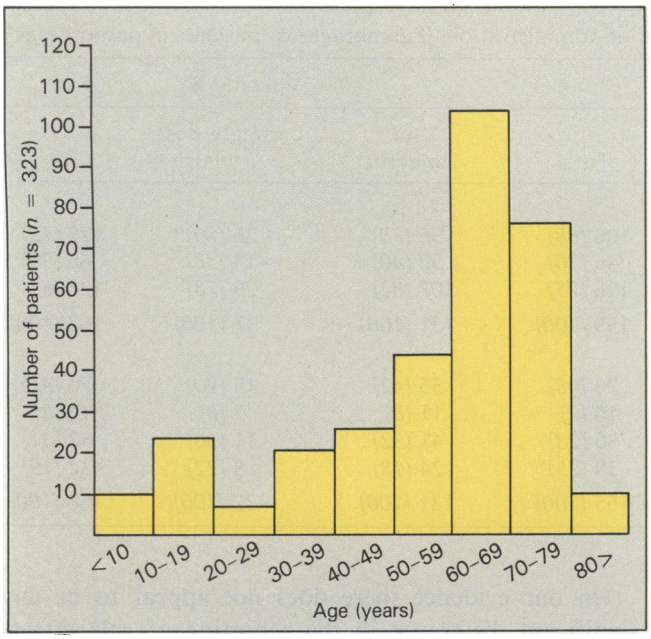

Figure 1. *Age structure of the main study population.*

In 1982 those patients who had returned questionnaires in 1981 were reviewed to assess whether there was a relationship between reported side effects and attendance for vaccination 12 months later.

Results

The age structure of the main study population—that is, 323 patients who returned questionnaires in 1981—is shown in Figure 1. The average age was 59.3 years (standard deviation (SD) = 20.4), with approximately 60 per cent over the age of 60 years. There was no significant difference in the mean ages of those who received vaccine A (59.8 years, SD = 19.3) and those who received vaccine B (58.1 years, SD = 21.5).

The vaccine used and the method of administration is set out in Table 1. The numbers were divided almost equally between the vaccines, although the majority of patients attended the clinic and were consequently given the vaccine by the jet injector method. Of those who received the vaccine by single dose vial, a larger proportion were given vaccine B.

The incidence of side effects by vaccine and by method of administration is detailed in Table 2. Overall, 252 patients (78 per cent) complained of some reaction. No statistically significant difference could be demonstrated between the vaccines ($\chi^2 = 1.76$, $P > 0.10$) or methods of administration ($\chi^2 = 1.76$, $P > 0.10$). There was an apparent tendency of vaccine B administered by the single dose vial to cause more local reactions, but the numbers were too small for any definite conclusions.

The results of a review in 1982 are shown in Table 3. Those patients (64) who were lost to follow-up came into three categories—those who had died, those who had moved away, and asthmatic patients on the list of one general practitioner who decided that this group

Table 1. Type of vaccine used and methods of administration for the 323 patients.

Vaccine	Method of administration		
	Jet injector	Single dose vial	Total
A	128	27	155
B	131	37	168
Total	259	64	323

should not be revaccinated. This meant that we were able to follow up 259 patients (80 per cent) from the original cohort. Of these, 204 patients (79 per cent) were revaccinated. Since all 259 patients had been vaccinated in 1981 this amounted to a drop in uptake of 21 per cent. There was no significant difference between those who accepted revaccination and those who refused either in the reporting of local side effects ($\chi^2 = 3.5$, $P > 0.05$) or systemic side effects ($\chi^2 = 2.21$, $P > 0.10$).

Discussion

For an influenza programme to be successful not only must the vaccines used be effective in preventing influenza but the rate of uptake must be maintained in subsequent years. With the improvements which have been made in their manufacture, few people would dispute that influenza vaccines are effective.[6] It has been suggested that any evaluation of different vaccines should also take into account the relative frequency of undesirable side effects which may in part account for the often unacceptably low acceptance rates in vaccination programmes.[4] In our study we examined the relative frequency of side effects of the two vaccines used and the effect.

We were pleased by the acceptance rate for vaccination since it has been estimated that only 20 per cent of high risk groups receive vaccination in any given year.[7] Similarly the proportion of questionnaires returned (87 per cent) compared favourably with the experience of other workers in their studies.[8]

It is always difficult to assess the subjective response of patients when an attempt is made to quantify the side effects of any medical treatment of procedure. In a previous study, questionnaires were distributed at the time of vaccination for completion over a number of days.[2] Our questionnaires were sent out with no forewarning in the hope that this would reduce the subjective element in the replies. The low incidence of diarrhoea reported (4 per cent) encouraged us to believe that the completed questionnaires reflected fairly the experiences of those who replied.

The proportion of patients who reported any reaction to the vaccines (78 per cent) was higher than in previous studies;[1-3, 8-10]. Our study population was, however, a 'high risk' group—namely the elderly and the chronic

Table 2. Side effects in patients ($n = 323$) by vaccine and method of administration. (Percentages of patients in parentheses.)

	Vaccine A			Vaccine B		
	Jet injector	Single dose vial	Total	Jet injector	Single dose vial	Total
Side effects of any kind						
Local	91 *(71)*	15 *(56)*	106 *(68)*	96 *(73)*	26 *(70)*	122 *(73)*
Systemic	38 *(30)*	8 *(30)*	46 *(30)*	52 *(40)*	14 *(38)*	66 *(39)*
Some reaction	99 *(77)*	17 *(63)*	116 *(75)*	107 *(82)*	29 *(78)*	136 *(81)*
Total	128 *(100)*	27 *(100)*	155 *(100)*	131 *(100)*	37 *(100)*	168 *(100)*
Type of reaction						
Local	61 *(48)*	9 *(33)*	70 *(45)*	55 *(42)*	15 *(40)*	70 *(42)*
Systemic only	8 *(6)*	2 *(8)*	10 *(7)*	11 *(8)*	3 *(8)*	14 *(8)*
Local + systemic	30 *(23)*	6 *(22)*	36 *(23)*	41 *(32)*	11 *(30)*	52 *(31)*
No side effects	29 *(23)*	10 *(37)*	39 *(25)*	24 *(18)*	8 *(22)*	32 *(19)*
Total	128 *(100)*	27 *(100)*	155 *(100)*	131 *(100)*	37 *(100)*	168 *(100)*

Table 3. The uptake of revaccination in 1982 by patients who had influenza vaccination in 1981.

Side effects recorded in 1981	1982 programme		
	Had vaccine	Refused vaccination	Lost to follow-up
Local only ($n = 140$)	93	18	29
Systemic only ($n = 24$)	11	9	4
Local + systemic ($n = 88$)	56	15	17
None ($n = 71$)	44	13	14
Total ($n = 323$ patients)	204	55	64

sick—in contrast to the relatively fit groups of workers or children used in these other studies. We were unable to demonstrate any significant difference in side effects either by vaccine or by method of administration. This is in contrast to the findings of Smith and colleagues, who reported more local reactions using the jet injector technique.[2]

The results of follow-up of the study population a year later suggested that previous side effects did not play a significant part in the uptake of revaccination. A more detailed study of the defaulters would have been required to establish the reasons for the 21 per cent fall in uptake.

A study of Post Office workers concluded that side effects influence immunization rates in subsequent years.[8] Our study group was in the main an 'at risk' group and it may have been that this had some bearing on the attitudes to revaccination. The letters of invitation were all signed by the patients' own general practitioners, and the clinic was based in the local health centre and staffed by practice nurses already known to the patients. These additional factors may have contributed to the good response rate despite side effects.

On our evidence there does not appear to be any significant difference in the reporting of side effects between the purified adsorbed-surface antigen vaccine (subunit vaccine) and the disrupted virus vaccine. Nevertheless, it remains important that those responsible for influenza vaccination clinics warn patients that they are likely to experience some side effects but that on the whole these will be transitory.

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