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Influenza vaccination in patients with asthma: effect on peak expiratory flow, asthma symptoms and use of medication

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This pilot study was undertaken to examine whether killed influenza vaccine causes exacerbations in asthmatic adults. Thirty-three stable asthmatics recorded peak expiratory flow (PEF), asthma symptoms, and use of asthma medication for 2 weeks, and then received killed influenza vaccine. Thereafter they recorded PEF, asthma symptoms and use of medication for a further 2 weeks. Comparison of recordings during the 2 weeks before and after vaccination revealed that influenza vaccine was not associated with reduction in PEF (P=0.76), increase in asthma symptoms (P=0.17) or use of asthma medication (P=0.58).

Similar results for PEF (P=0.49), asthma symptoms (P=0.17), and asthma medication (P=0.16) were obtained when the analysis was restricted to the 2 days before and after vaccination. © 1997 Elsevier Science Ltd.

Keywords: influenza; vaccine; peak expiratory flow; asthma

Influenza is a recognized cause of asthma complications. The Department of Health (DoH) strongly recommends annual vaccination for patients with asthma but <20% of asthmatics are immunized each year. Concerns about vaccine safety among asthmatics are exemplified by two recent reports. Bronchoprovocation tests have revealed increased bronchial reactivity in asthmatics during the first 3 days following influenza immunization. Although Stenius-Aarniala et al. observed no clinical asthma exacerbations after vaccination, conflicting results have been obtained. Accordingly the DoH is planning to undertake a multi-centre double-blind, placebo-controlled cross-over study to assess whether influenza vaccine causes asthma exacerbations. We report the results of a pilot study.

MATERIALS AND METHODS

Subjects

The study was conducted during October and November 1994 and involved 38 volunteers, with stable asthma, who were attending respiratory clinics in Leicester. The study size provided a power in excess of 80% to detect a 6% drop in mean peak expiratory flow (PEF) percentage of predicted at P<0.05. Ethical approval was obtained from the local research ethics committee. Informed consent was obtained from all patients.

Patients were told that the aim of the study is to reaffirm influenza vaccine safety in asthmatics. Each patient was given an asmaplan peak flow meter (Vitalograph Ltd; UK), a diary card and instructed to record the best of three PEF in the morning before and 15 min after medication, and last thing at night; the total number of doses of asthma medication taken every day; asthma symptoms including night cough, day-time cough, chest tightness, wheeze, shortness of breath, and sleep disturbance as a result of chest symptoms according to following score 0=absent to 3=severe. Patients were instructed to telephone the research team if they developed a drop in PEF, in order to obtain samples for virology. Nose and throat swabs were tested for presence of rhinoviruses and enteroviruses as described previously. Paired acute and convalescent sera were tested for complement fixing antibodies to adenovirus, influenza A and B, respiratory syncytial virus, parainfluenza viruses 1, 2, and 3, Mycoplasma pneumoniae, and Chlamydia psittaci; an ELISA was used to detect antibody rises to coronaviruses OC43 and 229E.

At the end of the second week patients were vaccinated with commercially available influenza vaccine for the 1994/95 season and continued to record PEF, asthma symptoms and medications, as before, for another 2 weeks.

Statistical analysis

The mean morning pre-bronchodilator (if applicable) PEF percentage of predicted values before and after
vaccination were compared using a paired t-test. The Wilcoxon signed rank test was used to compare the mean of all asthma symptom scores before and after vaccination, and the mean daily dose of asthma medication before and after vaccination.

RESULTS

Thirty three patients (17 male) with a median age 56 years (range 27–74) completed the study. These patients had mean PEF percentage of predicted of 62% (range 20–103%). Twenty-one patients (64%) required regular treatment with inhaled β2-adrenoceptor stimulants and 30 patients (91%) used inhaled steroids regularly; eight patients (24%) also took oral steroids. Eleven patients (33%) had received influenza vaccine previously.

The differences between mean pre- and post-vaccination PEFs percentage of predicted were not statistically significant for the whole study period (pre=61.9%; post=61.6%; 95% C.I. -2.3-1.7%; P=0.76), or the 2 days before and after vaccination (pre=62.1%; post=61.3%; 95% C.I. -3.2-1.5%; P=0.49).

The potential strengths and limitations of the study. The study was not controlled and the PEF meters used were not data logging or coded so there may have been a potential for incorrect recording. The patients we studied were volunteers attending a secondary centre for management of asthma and therefore may not be a representative sample of stable asthmatics. Furthermore one-third of subjects had been vaccinated previously and this may have introduced bias in that they may have been self selected as not to have had a bad response. Nevertheless the patients displayed a wide range of asthma severity with morning pre-bronchodilator PEF percentage of predicted ranging from 20% to 103%; and eight patients were maintained on oral steroids.

Inoculation of killed influenza vaccine did not cause exacerbations in this group of patients with stable asthma. This is in agreement with previous observations, but contrasts with the findings of a study undertaken by Bell et al. We examined the possibility that clinically significant deterioration in symptoms, or lung function and increased need for medication occurs during the first 1–2 days after immunization, and that comparisons of data over a longer period mask these changes. We found no support for such an explanation in our study.

Although overall there was no evidence of asthma exacerbations, one patient had a deterioration in asthma control with symptoms of upper respiratory tract infection. The association between respiratory viruses and exacerbation of asthma is well established. However, we failed to identify any respiratory viral pathogen in this case. This may have been because of the interval between onset of symptoms and sampling. However, we can not exclude an adverse reaction to the vaccine. Clearly a large placebo-controlled study is needed to demonstrate that adverse pulmonary reactions to the vaccine, if they occur, occur less frequently than the pulmonary function abnormalities that would be expected during an average winter in the absence of influenza vaccine.

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