RUBELLA VACCINE (RA27/3 STRAIN) IN AUSTRALIAN SCHOOLGIRLS

SUMMARY

The immunogenicity and reactogenicity of the RA27/3 strain of rubella vaccine was evaluated in schoolgirls 11 to 12 years old in a study from April to July, 1987. The incidence of adverse events was lower in initially seropositive girls compared to seronegative cohorts throughout the follow-up period. Overall, 22 per cent of the vaccinees reported symptoms in the first week after vaccination, the most frequent being pain at the site of injection and headache. All initially seronegative girls administered vaccine seroconverted. This vaccine is immunogenic and well-tolerated and can therefore be used without the need for pre-vaccination screening.

INTRODUCTION

The frequency of congenital rubella in Australia has decreased, primarily due to the introduction of mass rubella vaccination programs[1]. In these programs it is important and more cost-effective to vaccinate all girls of a certain age, without pre-vaccination screening for the determination of existing levels of anti-rubella virus antibodies.

The success of these programs also depends on the widespread acceptance of the vaccine to be used. Previous studies[2] have shown that the RA27/3 strain, although more immunogenic than other strains[3-5], may be particularly reactogenic — leading to an increase in the number of subjects refusing vaccination.

We have studied the reactogenicity of the RA27/3 strain rubella vaccine in both initially seronegative and seropositive schoolgirls aged 11 and 12 years. These subjects were followed up for three months to compare the frequency and severity of adverse reactions after vaccination in the two groups. The immunogenicity of the RA27/3 strain rubella vaccine was also evaluated in initially seronegative subjects.

Subjects and methods

Girls 11 and 12 years old were included in this study, irrespective of any history of rubella infection. They were recruited from April to July 1987 from 19 high schools and four randomly selected primary schools in the Illawarra area of NSW. An explanatory letter about the clinical trial was sent to the parents of each girl, and written informed consent was obtained. All subjects were healthy at the time of vaccination and had no history of allergy to neomycin and no other contra-indication to participation in the study.

Subjects were given a card to record any adverse events during the three-month period after vaccination. Local symptoms such as pain, redness and induration were evaluated for four weeks. General symptoms, including fever, rash, joint pains and headache, were recorded for the full three months.

Blood samples for the detection of anti-rubella virus antibodies were taken immediately before vaccination and again three months later. Sera were stored at −20 °C until titrated. Blood samples were assayed by Haemagglutination Inhibition Test using trypsinized human group O red blood cells according to the method of Gupta and Peterson[6]. Antibody titres are given as the reciprocal of the highest reactive dilution. Titres under 10 were regarded as seronegative, those over 20 as seropositive. Seroconversion was defined as a four-fold, or greater, rise in antibody titres.

The live attenuated RA27/3 rubella virus vaccine (Ervevax, SmithKline Biologicals) was used. The vaccine was given subcutaneously in the deltoid region in one dose.

RESULTS

Immune status of subjects before vaccination

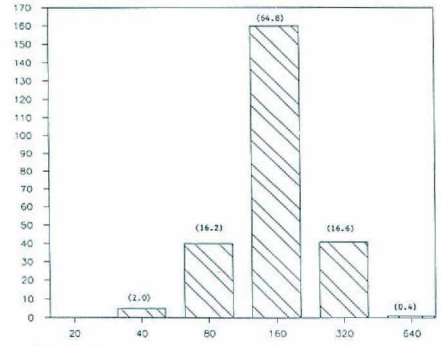
Of the 504 subjects enrolled in this study, 264 (52.4 per cent) were seronegative before vaccination. The remaining subjects had pre-vaccination anti-rubella virus titres ranging from 40 to 640 (geometric mean titre = 186).

Immunogenicity of the RA27/3 rubella vaccine

Of the initially seronegative subjects, 247 (93.6 per cent) returned for follow-up blood tests three months after vaccination. At this time, all were found to have seroconverted. The post-vaccination geometric mean antibody titre in these subjects was 157. The distribution of antibody titres is shown in Figure 5. Post-vaccination blood samples of initially seropositive girls were not assayed.

FIGURE 5

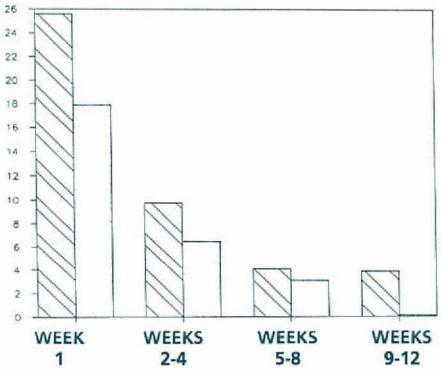
ANTI-RUBELLA ANTIBODY TITRES IN INITIALLY SERONEGATIVE ADOLESCENT GIRLS AFTER VACCINATION



RECIPROCAL RUBELLA VIRUS ANTIBODY TITRE

FIGURE 6

FREQUENCY OF SYMPTOMS AFTER VACCINATION IN ADOLESCENT GIRLS ACCORDING TO PRE-VACCINATION SEROLOGICAL STATUS



INIT. SERONEGATIVE INIT. SEROPOSITIVE

Reactogenicity of the rubella vaccine

The reactogenicity of the rubella vaccine was assessed from patient diary cards completed by the parents or children. Four hundred and seventy girls (93.3 per cent, 258 initially seronegative and 212 seropositive subjects) returned cards.

The reactogenicity of the vaccine was examined with respect to the initial immune status of the vaccinee. The follow-up period was divided in four, as shown in Figure 6. The overall reactogenicity observed in initially seropositive girls was lower than that observed in seronegative subjects. During the first week after vaccination (Week 1) 66 of 258 (25.6 per cent) initially seronegative girls reported symptoms whereas only 38 of 212 (17.9 per cent) seropositive girls did so (Table 3). In both seronegative and seropositive subjects, pain and itchiness were the most frequently reported local symptoms, experienced by 39.4 per cent and 24.0 per cent, respectively, of those girls with adverse effects after vaccination. Headache (40.4 per cent) and joint pain (17.3 per cent) were the most frequently observed general reactions. During weeks 2 to 4, the number of adverse reactions in both groups fell to below 10 per cent of all vaccinees. Nearly 4 per cent of initially seronegative girls reported symptoms 5 to 12 weeks after vaccination. It is unlikely that these events were a result of the rubella vaccine because of the general nature of the complaints (e.g. headache, dizziness, slight cough).

Discussion

This report confirms the immunogenicity of the RA27/3 strain as all 247 initially seronegative schoolgirls vaccinated during the course of the study had seroconverted at the three-month follow-up.

The adverse events observed were similar to those already reported using the same strain[2]. The most common local side-effect of vaccination was pain near the injection site, reported by 39.4 per cent of all girls with post-vaccination symptoms. Headache was also frequently reported. No severe reaction attributable to the vaccine was noted. The incidence of adverse events was lower in initially seropositive girls when compared to seronegative cohorts. The low incidence of reactions in seropositive subjects (fewer than one in five vaccinees) shows that this vaccine is safe and well-tolerated in all subjects, even those with prior evidence of rubella infection, and can therefore be used in mass immunisation programs without the need for pre-vaccination antibody screening.

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TABLE 3

SYMPTOMS OBSERVED IN THE FIRST WEEK AFTER VACCINATION

SEROLOGICAL STATUS	–	+	OVERALL %
TOTAL WITH SYMPTOMS	66/258 (25.6%)	38/212 (17.9%)	22.1
LOCAL			
pain	25	16	39.4
redness	8	4	11.5
hardness	12	4	15.4
itching	18	7	24.0
SYSTEMIC			
headache	26	16	40.4
joint pain	12	6	17.3
rash	5	2	6.7
fever	3	3	5.8
other	16	7	22.1

Editorial Comment

This study confirms a very low reaction rate with the RA27/3 strain of rubella vaccine and shows 100 per cent seroconversion in non-immune schoolgirls[1]. The RA27/3 vaccine has a slightly higher conversion rate than the other rubella vaccine strains and is included in the measles-mumps-rubella (MMR) vaccines presently available in Australia. 52.4 per cent of the 11- and 12-year-old schoolgirls in this study were seronegative before vaccination. A much higher rate of immunity to rubella can be anticipated in about 10 years, following the inclusion of MMR vaccine in the routine immunisation schedule for all infants at the age of 12 months.

The symptoms experienced by the seropositive subjects in this study may not all be due to the vaccine. An elegant double-blind, placebo-controlled, cross-over study in 581 twin pairs in Finland using MMR vaccine showed a very low true frequency of side-effects from the vaccine[2]. Some vaccines are known to cause slightly more immediate discomfort at the injection site than others, but this is transient and of little real importance as are the injection site reactions and headaches reported by these schoolgirls. The value of rubella vaccine in preventing congenital rubella infection is established[3]. Every effort should be made to encourage schoolgirls and non-immune adult women to be vaccinated.

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