

Rubella vaccine and arthritic adverse reactions: An analysis of the Vaccine Adverse Events Reporting System (VAERS) database from 1991 through 1998

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ABSTRACT

Objective.

The United States Academy of Sciences, Institute of Medicine (IOM) report - ed in 1991 that the evidence indicates a causal relationship between the currently used rubella vaccine and acute and chronic arthritis. The purpose of this study was to analyze the associated arthritic reactions reported following rubella immunization from 1991 through 1998 to the Vaccine Adverse Events Reporting System (VAERS) database.

Methods.

A certified copy of the VAERS database was obtained from the CDC. Microsoft Access was used to analyze the data - base.

Results.

The results show that rubella vaccine is associated with a number of arthritic reactions reported to the VAERS data - base.

Conclusion.

Adult female patients need to make informed decisions on whether or not rubella vaccination is right for them. Doctors and patients must together make an informed consent decision about the risk versus the benefit to the patient in their particular life situation. Additionally, those patients who have had an adverse reaction to rubella vaccination should be informed that they may seek compensation under the no-fault Vaccine Compensation Act, which is administered by the US Claims Court.

Introduction

The United States Academy of Sciences, Institute of Medicine (IOM) reported in 1991 that the evidence indicates a causal relationship between the currently used rubella vaccine and acute and chronic arthritis. They reported that the incidence rate was highest among adult women following immunization, with much lower levels noted among children, adolescents, and adult men (1).

Symptoms referable to the musculoskeletal system are among the most common side effects of natural rubella infection and rubella vaccine. The joints involved, in order of decreasing

frequency, are the fingers, knees, wrists, elbows, ankles, hips, and toes. The symptoms are frequently of sudden onset and consist of prominent stiffness and pain only; however, warmth, redness and effusions can occur, especially in the knees, fingers, and wrists. These joint symptoms usually appear within one week of the appearance of rash in natural rubella infection and within ten to twenty-eight days after vaccination (2).

It has been suggested that, given the benefits and risks of rubella vaccine in the adult population, rubella immunization should be recommended to non-immune females in the child-bearing age group, but only after appropriate counseling and the obtaining of informed consent. Those women undergoing sterilization or who are otherwise certain they will not have any more children might consider foregoing vaccination (3).

The purpose of this study was to analyze the frequency of arthritic adverse reactions after rubella vaccination and to determine if the frequency of arthritic adverse reactions was statistically significantly increased by chi-square analysis over the background rate of arthritic conditions in the US adult population.

Materials and methods

In order to further examine the association between rubella vaccination and arthritic reactions, we made a retrospective examination of the information reported to the Vaccine Adverse Events Reporting System (VAERS) database from 1991 through 1998 using Microsoft Access. VAERS is a passive epidemiological database that has been maintained by the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia since 1990. All vaccine associated adverse reactions are to be reported to this database as mandated by US law. A recent study by the CDC has helped to validate the VAERS database (4). Our recent studies have shown an association between hepatitis B vaccination and arthritic, immunological and gastroenterological symptoms based upon our analysis of the VAERS database (5-7).

Table I. Rubella vaccination and associated arthritic reactions reported to the VAERS database.

Rubella-associated arthritic reaction types	Number of reaction reports	Number of female reaction reports	Number of male reaction reports	Mean day onset time within 30 days	Mean age (years)	Incidence per million vaccinations
Arthralgia	191	170	17	10.6 ± 6.7	40.1 ± 10.6	78.0
Arthrosis	58	51	4	12.3 ± 5.3	43.1 ± 12.7	24.0
Arthritis	46	41	2	11.3 ± 7.4	37.9 ± 15.0	19.0
Joint disease	13	13	0	11.9 ± 6.8	39.4 ± 17.6	5.0

The arthritic reactions analyzed in this study included: arthrosis, arthritis, arthralgia and joint disease. The incidence rates calculated in this study were based upon the estimates of the CDC for the number of doses administered during the period examined. The CDC estimates indicate that 2,437,248 rubella vaccinations were administered during this study period. Additionally, as a control, hepatitis A vaccine associated arthritic adverse reactions reported to VAERS from 1997 through 1998 in adults were analyzed. The CDC estimates indicate that 6,038,283 hepatitis A vaccinations were administered from 1997 through 1998 to adults. The incidence rates of adult associated arthritic reactions in the hepatitis A vaccine recipients provided a background rate to compare against the incidence rates of associated arthritic reactions in rubella vaccine recipients. The use of chi-square statistical analysis determined whether the elevated incidence rates of associated arthritic reactions in rubella vaccine recipients were statistically significant.

Results

Table I summarizes the arthritic reactions reported to the VAERS in association with rubella vaccination from 1991

through 1998 among those residing in the United States. Table II analyzes the relative frequency of developing arthritic reactions after rubella vaccine and in the hepatitis A vaccine control group and determines if the elevated rate of associated arthritic conditions in rubella vaccine recipients is statistically significant.

Discussion

Our data confirms and extends the data studied by the IOM. Our study shows that rubella vaccine was associated with a large number of arthritic adverse reactions. These reactions primarily occurred in the adult female population. The incidence of developing an arthritic reaction was 126/million rubella vaccinations. The hepatitis A vaccine adult control group had an incidence rate of 3.2/million hepatitis A vaccinations. Assuming that the hepatitis A vaccine associated arthritic rate represents the background rate of developing arthritic conditions in the adult population, rubella vaccine by chi-square statistical analysis ($p < 0.01$) is statistically linked with arthritic reactions. The medical community needs to be aware of the possibility of arthritic reactions following rubella vaccine, so that they can report them to the VAERS database.

The arthritic conditions associated with rubella vaccine appear to be immune-mediated. The female to male ratio of arthritic reactions reported following immunization was 12.0/1. Additionally, the mean onset time for all the types arthritic reactions analyzed in this study was about 11 days after vaccination. This female to male ratio and the length of the mean onset time tend to suggest that the formation of antibodies is an important mechanism in the development of an adverse reaction to rubella vaccine.

The primary reason for giving rubella vaccine to adult women is to prevent Congenital Rubella Syndrome (CRS). This is an often devastating disorder of fetuses born to women who were infected with rubella virus during the first trimester of their pregnancy. Rubella and CRS have been reportable disorders since the 1960s to the CDC. From 1970 through 1979 there were 246,467 reported cases of rubella with 157 deaths and 365 cases of CRS. From 1980 through 1989 there were 11,073 cases of rubella reported with 21 deaths and 68 cases of CRS. From 1990 through 1999 there were 4,254 reported cases of rubella with 11 deaths and 99 cases of CRS (8). This data suggests that the advantages of rubella vaccine in preventing cases of rubella, rubella deaths, and cases of CRS outweighs the risks of the vaccine. Some authors have recommended universal rubella vaccination of the adult population without regard to whether the patients are male or female, whether or not they are already rubella immune, or whether or not they are likely to become pregnant (9). Others have suggested only offering rubella vaccination to non-immune females who are likely to bear children (3).

Table II. Statistical significance by chi-square of the elevated risk of rubella associated arthritic reactions.

Type of reaction	Incidence per million of rubella vaccinations	Incidence per million of hepatitis A vaccinations	Statistically significant increase after rubella vaccination
Arthralgia	78.0	2	$p < 0.01$
Arthrosis	24.0	0.7	$p < 0.01$
Arthritis	19.0	0.3	$p < 0.01$
Joint disease	5.0	0.2	$p < 0.01$

In conclusion, adult female patients need to make informed decisions as to whether or not rubella vaccination is right for them. Those females who are not immune to rubella who contemplate having children must be made aware of the potentially devastating effect that rubella syndrome may have in developing fetuses. They also should be made aware of the correlation between rubella vaccine and arthritic conditions. Adult women who are already rubella immune, who have had hysterectomies, tubal ligations or otherwise are unlikely to get pregnant, might well elect not to take the rubella vaccine because for them the risk might outweigh the benefit of the vaccine. Doctors and patients must together,

based on this information, make an informed consent decision about the risk versus the benefit to the patient in their particular life situation. Additionally, those American patients who have had an adverse reaction to rubella vaccination should be informed that they may be eligible to seek compensation under the no-fault Vaccine Compensation Act, which is administered by the US Claims Court.

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