Iranian Journal of Clinical Infectious Diseases
2007;2(3):129-132

ORIGINAL ARTICLE

Evaluation of primary failure of new measles vaccine and secondary failure of previous measles vaccine after mass vaccination in military cadets in Iran

Gholamali Ghorbani[1], Kazem Ahmadi[2], Hamidreza Ghadimi[3]

[1] *Department of Infectious Diseases and Tropical Medicine, Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran*

[2] *Immunology Research Center, Baqyiatallah University of Medical Sciences , Tehran, Iran*

[3] *Medical researcher, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

ABSTRACT

Background: Measles is an acute highly infectious respiratory viral disease. It remains a leading cause of death among young children especially in developing country. Measles outbreaks occurred in Iran in recent years and soldiers and cadets have been vaccinated against it. This study was designed to evaluate primary and secondary failure of measles vaccine in cadets after mass measles vaccination.

Materials and methods: For this cross-sectional study, one month after mass vaccination in 2003, all vaccinated cadets were recruited. Eight hundred and sixty five cadets were evaluated in a simple random fashion. From each individual 5ml blood sample was obtained and checked in immunology laboratory of Baqiyatallah hospital. Antibody was checked by enzyme-linked immunosorbent assay (ELISA) for qualitative and quantitative measurement of IgG and IgM in accordance with Behring ELISA kit (Germany) instructions. Cut-off OD upper than 0.2 was considered positive and quantitative titer upper than 345 mIU/ml was considered protective.

Results: All cadets were men with a mean age of 19.0±1.1 years. IgM anti-measles antibody was positive in 0.7%. Primary failure was positive in 1.8% of individuals. Anti measles IgG antibody was positive in 97.8% of cadets. History of childhood vaccination for measles was positive in 67.7% and past history of measles was positive in 23 cases (2.6%).

Conclusion: Our results showed that secondary failure is more than 97%. Therefore, periodic studies should be performed to assess secondary failure rate in order to take preventive measures in time, of course, if its outbreaks are probable to happen.

Keywords: *Measles, Primary and secondary failure, Adult vaccination*.
(Iranian Journal of Clinical Infectious Diseases 2007;2(3):129-132).

INTRODUCTION

Measles is an acute highly infectious respiratory viral disease. Its outbreaks are seen in developing country and remain a leading cause of death among young children, despite the availability of a safe and effective vaccine. According to WHO reports, of 3-4 million people infected by measles virus every year, more than seven hundred thousand die out of whom 98% are

Received: 2 January 2006 *Accepted*: 6 February 2007
Reprint or Correspondence: Gholamali Ghorbani, MD. Department of Infectious Diseases and Tropical Medicine, Baqyiatallah University of Medical Sciences, Tehran, Iran.
E-mail: gholamalighorbani@yahoo.com

in developing countries (1,2). Measles attenuated live virus vaccine is a safe, inexpensive and complication-free way of prevention. The new type of measles vaccine recommended by CDC is live attenuated measles vaccine introduced through the respiratory tract. It may become available for practical use in 2009 (3,4).

The reason of measles outbreaks depends on vaccination coverage. If it is not high enough, outbreaks of measles occur in population. Primary failure may be seen in anyone with no antibody production following vaccination. This phenomenon, which depends on the type of vaccine, environment, cold chain and gender, is seen in 3-5% of vaccinated individuals (5).

Secondary failure of measles vaccine is a reason of measles outbreaks in young and adult population that is caused by decreasing anti measles antibody in the course of time. Secondary failure predisposes adults to measles infection if they have not been sub-clinically infected or have not had contact with measles virus before (6,7). Reduction in herd immunity against measles in people is another reason of measles outbreaks. Measles can also affect non-immunized adolescents and young adults. While measles is now rare in many industrialized countries, it remains to be a common disease in many developing countries. Hardship, complications and death caused by measles can be easily prevented by immunization (8).

Because measles outbreaks occurred in Iran in recent years and 11600 cases were reported in 2003, Iran Ministry of Health decided to perform mass vaccination in population between 5-25 years of age and also in soldiers and cadets. This mass vaccination was not a part of routine immunization program and cadets were also vaccinated against measles (2,9-10). In pervious studies on immunity of cadets against measles in Iran, it was reported that more than 22.5% had no immunity and some of them suffered from severe measles infection. For this reason this study was designed to evaluate immunity status and childhood vaccination secondary failure in cadets after recent mass measles vaccination.

PATIENTS and METHODS

This cross-sectional study was conducted on Iranian cadets in Tehran, one month after mass vaccination in 2003. All cadets recruited to this study were vaccinated and healthy. Eight hundred and sixty five cadets were evaluated for anti measles IgG and IgM antibody in a simple random fashion.

Five ml blood samples were obtained and sera were separated by centrifugation. The sera were kept at -20°C. Anti measles antibody was checked in immunology laboratory of Baqiyatallah University of Medical Sciences. Whole virus antibody was checked by enzyme-linked immuno-sorbent assay (ELISA) for qualitative and quantitative evaluation of IgG and IgM. The ELISA test for antibody was done in accordance with Enzygnost Behring ELISA kit instructions manufactured in Germany. Qualitative evaluation (cut-off OD) less than <0.1 was considered as negative and was repeated if revealed 0.1-0.2. Test results >0.2 were considered positive for IgG and IgM. The quantitative titer was measured according to international units (mIU/ml). The level of anti measles IgG antibody upper than 345 mIU/ml was considered protective. We have only determined IgM antibody qualitatively.

All patients were requested to complete an informed consent. Data were analyzed by SPSS for Windows (version 12, SPSS Inc., USA).

RESULTS

All cadets were men with a mean age of 19.0±1.1 years. IgM anti measles antibody was qualitatively positive in 0.7% of subjects. Anti measles IgG antibody or secondary failure of previous measles vaccine was positive in 97.8% of cadets. Primary failure of new vaccine was positive in 1.8% of individuals (table 1).

History of childhood vaccination for measles was positive in 67.7%. History of contact with measles patients was positive in 34 individuals (3.9%).

Twenty-three (2.6%) subjects could recall past history of measles, however, none of them were confirmed by laboratory data and diagnosis was made clinically**.**

Table 1. Prevalence of anti measles antibody in cadets after mass vaccination of measles

Antibody	Positive (%)	Negative (%)
IgG	846 (97.8%)	19 (2.2%)
IgM	6 (0.7%)	859 (99.3%)

DISCUSSION

Measles is a contagious respiratory viral infection with 80% transmission rate. It can be prevented by vaccination. Measles breakouts cost a lot to control and sometimes claim lives so the Iranian Ministry of Health and Medical Education undertook a mass vaccination program against measles in 5-25 year old population and thus 33 million people were vaccinated (2, 9-10). In this study that was achieved one month after the mass vaccination program against measles, 0.7% and 97.8% were positive for IgM and IgG, respectively, while 1.8% had no antibody. This suggests that 97% of individuals face a secondary failure which is in line with other studies in adults (6,7).

Only 0.7% of vaccinated individuals had IgM antibody which is different with other studies probably due to childhood measles vaccination. It is possible that the vaccinated cadets in this study were also vaccinated or had come in contact with measles virus in childhood.

Usually after the first contact with virus or vaccine, IgM antibody is produced within the first month but its serum level does not increase after the second contact or vaccination (5,8,11).

Pannuti CS in a study showed that IgM was positive in a very few people which was suggestive of childhood vaccination secondary failure and they had lost their serum antibody in the course of time and this is the main reason for measles outbreaks in Iranian young adults. Secondary failure happens long after the vaccination time and its rate increases as time elapses. Therefore, measles outbreaks can be prevented by re-vaccination (12,13).

Moreover, although IgM produced by contact with measles vaccine or virus decreases gradually, its epidemics in a region can cause sub clinical infections in previously vaccinated individuals which enhances herd immunity and prevents severe outbreaks. This phenomenon was obvious when measles was prevalent in Iran (2,9).

During their childhood, i.e. 15-20 years ago, vaccination coverage was low. Therefore, although unvaccinated cadets must produce IgM antibody after vaccination, this was not the case in 32% of them without history of previous vaccination due to sub clinical infections. It seems that herd immunity can prevent measles outbreaks to some extent (8).

Primary failure occurs when no antibody is produced one month after the vaccination. This study was not capable of confirming primary failure in childhood, but its rate was 2.2% in this recent vaccination when no IgM or IgG antibody was produced. The rate of primary failure in this study was lower than other studies (6,13).

Primary failure is contingent on different factor such as the type of vaccine, storage conditions, cold chain, coexisting diseases and race. In this study, factors other than strain were not studied but it seems that primary failure with Edmonston-Zagreb strain vaccine is low in Iranian race but further prospective study is needed (14).

Because measles outbreaks occur when more than 10% of the population is sensitive to measles and according to the Iranian Ministry of Health stating that more than 11600 individuals had measles before vaccination and also based on another study which was carried out before vaccination and reported a 22.5% sensitive

population, secondary failure after 15 years is relatively high. Thus, periodic studies to assess secondary failure are necessary to prevent its outbreaks (2,9,10).

Our main limitation was the fact that participants' sera were not tested before vaccination, thus, secondary failure of the previous vaccination could not be differentiated from primary failure of the recent vaccination. But if only seronegative individuals were vaccinated against measles and then anti-measles antibody was checked, the above-mentioned could be differentiated with more accuracy.

In conclusion, because of the high rate of measles vaccine secondary failure in childhood, we suggest that adults should be evaluated for immunity against measles before entering university or employment or military service and in non-immunized cases, vaccination should be achieved. In our study, measles vaccination was able to augment previously decreased IgG thus protect adults and cadets against measles. Therefore, periodic studies should be performed to assess secondary failure rate in order to take preventive measures in time, of course, if its outbreaks are probable to happen.

REFERENCES

1. World Health Organization and Unicef. Immunization summary 2005. Available at: http://www.unicef.org/publications/files/Immunization_Summary_2005.pdf

2. Loo MK, Sabahi F, Soleimanjdahi H, et al. Seroprevalence of neutralizing antibodies to measles virus in a vaccinated population in Iran, 1998. Eur J Epidemiol 2003;18(11):1085-9.

3. Liashenko VA, Iuminova NV, Krasnova VP, et al. Intranasal revaccination of children with live measles vaccine: development of local immunity. Vopr Virusol 1999;44(3):124-6.

4. Castro JF, Bennett JV, Rincon HG, et al. Evaluation of immunogenicity and side effects of triple viral vaccine (MMR) in adults, given by two routes: subcutaneous and respiratory (aerosol). Vaccine 2005; 23(8):1079-84.

5. Youwang Y, Ping W, Feng C. Serological and epidemiological effects and influence factors of primary immunization with current live attenuated measles vaccine (Hu191) among infants aged 6-15 months. Vaccine 2001;19(15-16):1998-2005.

6. Erdman DD, Heath JL, Watson JC, et al. Immunoglobulin M antibody response to measles virus following primary and secondary vaccination and natural virus infection. J Med Virol 1993;41(1):44-8.

7. Lee MS, Chien LJ, Yueh YY, et al. Measles seroepidemiology and decay rate of vaccine-induced measles IgG titers in Taiwan, 1995-1997. Vaccine 2001;19(32):4644-51.

8. Lee MS, Lee LL, Chen HY, et al. Post mass-immunization measles outbreak in Taoyuan County, Taiwan: dynamics of transmission, vaccine effectiveness, and herd immunity. Int J Infect Dis 1998;3(2):64-9.

9. Ghorbani GH, Ahmadi K,Jonaidi N. Evaluation of anti measles IgG prior to mass vaccination in cadets in Iran . Pak Med Sci J 2006;6(3):521-24.

10. Ghorbani GH. Evaluation of admitted patients with severe measles infection in Baqiyatallah hospital in Iran,2000-2002. 11th Iranian Congress on Infectious Diseases and Tropical Medicine. 2002, Tehran, Iran.

11. Trier H, Ronne T. Duration of immunity and occurrence of secondary vaccine failure following vaccination against measles, mumps and rubella. Ugeskr Laeger 1992;154(29):2008-13.

12. Paunio M, Hedman K, Davidkin I, et al. Secondary measles vaccine failures identified by measurement of IgG avidity: high occurrence among teenagers vaccinated at a young age. Epidemiol Infect 2000;124(2):263-71

13. Pannuti CS, Morello RJ, Moraes JC, et al. Identification of primary and secondary measles vaccine failures by measurement of immunoglobulin G avidity in measles cases during the 1997 Sau Paulo epidemic Clin Diagn Lab Immunol 2004;11(1):119-22.

14. Jacobson RM, Poland GA. The genetic basis for measles vaccine failure. Acta Paediatr Suppl 2004; 93(445):43-6.