

Short communication

Parotid swelling due to Hoshino strain following MMR vaccination in Iranian immunization program

Majid Avijgan¹, Mandana Moghni², Seyyed Kamyar Mostafavi Zadeh³, Masoud Hafizi⁴¹ Professor of Infectious and Tropical Diseases, Iranian Traditional Medicine Research Center and Department of Infectious and Tropical Diseases, Isfahan University of Medical Sciences² Assistant Professor of Clinical Pathology, Shahr-e-kord University of Medical Sciences,³ Assistant Professor of Infectious and Tropical Diseases, Infectious and Tropical Diseases Research Center, Isfahan University of Medical Sciences.⁴ Assistant Professor of Infectious and Tropical Diseases, Department of Infectious and Tropical diseases, Shahr-e-kord University of Medical Sciences.

Abstract

This paper reports two seronegative cases of parotid swelling following MMR vaccination, which contains Hoshino strain of mumps virus. This study showed a high, (5%) potential reactogenicity induced by Hoshino strain of current MMR vaccine administered in Iranian EPI. The rate of complication of parotid swelling following national immunization against mumps is more than natural infection. Based on the results of this report, there is the first report of occurrence of parotid swelling 31 days following MMR vaccination. This reaction or complication may not be dependent on the vaccine dose, because one of cases presented parotid swelling following taking one fifth of conventional dose of vaccine. It must be considered this strain may be with high rate of complication and be the subject of change of mumps strain of this vaccine in national immunization program of Iran.

Keywords: mumps, MMR, parotid swelling, reaction, vaccine, vaccine dose.

INTRODUCTION

The introduction of mumps vaccine has been on the base of previous studies and it should be considered only in countries that have established, or are in the process of establishing, adequate programmes for the elimination of measles and the control of congenital rubella syndrome. In such countries the combination of mumps vaccine with measles and rubella vaccines is recommended^[1].

Vaccine induced-reactogenicity or complications are important subjects for selecting a vaccine.

Epidemiologic study of a vaccine's adverse e-

vents is not easy; so many countries have no reliable data. But a study results showed a high relative risk of vaccine induced meningitis for the Urabe or Hoshino strain, so that vaccines containing the Urabe or Hoshino strain have been withdrawn from use in several countries^[2]. In community-wide immunization programmes against childhood infections there is a conflict between the interests of the individual (vaccine safety and efficacy) and the interests of the community (vaccine uptake and level of herd immunity)^[3].

There was conducted a national campaign for measles and rubella but not for mumps, and since 21st March 2004, MMR (including measles, mumps and rubella) vaccine was introduced in EPI. Unfortunately before introduction of this strain in Iranian EPI, there was no reliable data in relation to adverse effect of MMR vaccination. This study is presenting complication of mumps vaccine administered in Ira-

Correspondence to: Majid Avijgan, Professor of Infectious and Tropical Diseases, Iranian Traditional Medicine Research Center and Department of Infectious and Tropical Diseases, Isfahan University of Medical Sciences.

Tel: +98 913 181 80 85 Fax: +98 311 624 15 72

Email address of corresponding author: avijgan@yahoo.com

nian EPI, and indicating that there is a high vaccine-induced complication after Hoshino strain of current MMR vaccine in Iran.

METHODS AND MATERIALS

This vaccine was manufactured by Kitasato institute, Japan, in 1970s^[4]. It has been delivered by Kitasato institute of Tokyo (Makino, S. et al. Kitasato Arch. Exp. Med. 49, 1976; 43-52), this seed virus was further developed and attenuated at Razi Institute in hen, s cell culture. The working seed is the 20th passage in HDC-MRC-5.

There conducted a study for seroprevalence of mumps among children 3-18 years old of Shahr-e-kord, Iran at 2004. This study indicated that 20% of children are seronegative and sensitive to mumps infection^[5]. (Avijgan M, Habibian R, Kheiri S. Children's mumps immunity at the beginning of mumps introduction into Iranian EPI, Sharekord. (Unpublished data in EMJH, Eastern Mediterranean Journal of Health).

These seronegative children were selected for MMR vaccination, (The same vaccine of current EPI). Forty out of 60 early seronegative children consented to be vaccinated and between them two boys involved by Parotid swelling following vaccination.

CASES REPORTS

Case number 1 :

A 13 year old male weighted 35 kg, is presented, who complicated by parotid swelling following MMR vaccination. Two months ago, during a seroprevalance study for mumps immunity^[5], (Avijgan M, Habibian R, Kheiri S. Children's mumps Immu-

nity at the beginning of mumps introduction into Iranian EPI, Sharekord. (Unpublished data in EMJH, Eastern Mediterranean Journal of Health). it was found to be seronegative to ELISA IgG mumps antibody. On the basis of EPI, his vaccination history included: BCG, Polio oral vaccine, measles, DTP, and one year ago a mixed measles and rubella vaccination during a mass campaign before introduction of MMR into EPI.

To protect against mumps, it has been taken a blood sample and injected one dose of 0.5 ml of MMR vaccine (Razi Institute of serum and vaccine, Tehran, Iran).

Unfortunately 23 days following vaccination he was admitted with the parotid swelling, and somehow redness. He had no pain, no swelling of mandible angle, no lymph adenopathy, and no dysphasia or even no problem in eating of solid material like apples, bread and rice.

Ear examination (Otoscopy) revealed swelling and redness of ear canal which worsened during otoscopy. (Both ears)

His past history and general examination were unremarkable except temperature 38.5 C. He was given acetaminophen and conservative therapy and after 3 days with complete disappearance of swelling, he was discharged home.

The laboratory data revealed: white blood cell count 4500/ml with 65% neutrophile, 29% lymphocytes and 6% LUC), platelets 250,000/ml, erythrocyte sedimentation rate 17 mm/hour, liver, kidney function tests were in normal range. There was an increased level of amylase (3 folds). The blood samples were taken in 0, 90 and 365 days following vaccination. The results of IgG and IgM of mumps, measles and rubella have been shown in table one.

Table 1: Anti bodies profile of cases against mumps, measles and rubella

Serologic tests time	Mumps Case 1		Mumps Case2		Rubella IgG		Measles IgG	
	IgM *	IgG *	IgM *	IgG *	Case 1	Case 2	Case1	Case 2
At the time of Vaccination	0.227	0.195	0.057	0.304	221 IU/ml	109 IU/ml	Positive	Positive
Simultaneous with acute phase	1.9	2.261	1.678	1.606	-	-	-	-
90 days after vaccination	1.65	3.089	1.431	2.661	-	-	-	-
12 months after Vaccination	0.696	2.470	0.753	1.770				

* The unit is in ISR (Immune Status Ratio) that the patient's ISR values are interpreted as follow: ≤ 0.90 as negative 0.91-1.09 as Equivocal ≥ 1.10 as Positive

Case number 2 :

An 11 year old male weighted 33 kg, is presented, who complicated by parotid swelling following MMR vaccination. (This case finding was similar to case number 1).

To protect against mumps, it was taken a blood sample and injected (one-fifth dose) of 0.1 ml of MMR vaccine (Razi Institute of serum and vaccine, Tehran, Iran). This reduced dose was made accidentally and by technician error.

31 days after vaccination, he admitted with the parotid swelling, pain, fullness of mandible angle, dysphasia and fever of 38.5 C. Ear examination (Otoscopy) revealed normal otoscopy. (Both ears)

His past history and general examination were unremarkable except temperature 38.5 C. He was given acetaminophen and after 4 days with complete disappearance of swelling, he was discharged home.

The laboratory data revealed; white blood cell count 6500/ml with 75% neutrophile, 24% lymphocytes and 1% LUC, platelets 183,000/ml, erythrocyte sedimentation rate 16 mm/hour, liver, kidney function tests were normal. There was an increased level of amylase (5 folds). The blood samples were taken in 0, 90 and 365 days following vaccination. The results of IgG and IgM of mumps, measles and rubella have been shown in table one.

DISCUSSION

This Paper reports two seronegative mumps cases of parotid swelling following MMR vaccination, which included Hoshino strain as mumps attenuated virus. Based on antibody profile against mumps, measles and Rubella, (Table 1) this complication could be due to mumps Hoshino strain. One study indicated IgG ELISA antibodies increase rapidly after the onset of symptoms and reached the maximal values in about third to fourth week. IgM antibodies measured by ELISA developed soon after onset of symptoms; most patients had IgM antibodies from the second day, and the highest titers were reached within the first week^[6]. At the time of vaccination (0 time), both cases of this report, had positive IgG antibodies against measles and rubella (Table 1). But their negative antibody profile against mumps changed to positive one at the acute phase and to increasing level during next months. It is clear that this complication just could be as a result of an infectious process like Hoshino mumps strain of MMR vaccine. Among 40 volunteer persons for MMR vaccination, there was two case of parotid swelling after MMR vaccine administration. The rate of parotid swelling following this kind of vaccine in EPI is reported to be as high as 5% (2 of 40 seronegative children).

Unlike measles, mumps is not considered a globally devastating disease. Nevertheless, because of its complications, it was targeted for prevention by use of a vaccine^[7]. Studies in industrialized countries have shown the incorporation of effective mumps vaccines into EPI to be highly cost effective^[1]. But the cost effectiveness of vaccine may not be cause of higher incidence rate of parotid swelling following

vaccination than natural infection.

The Hoshino strain was added to measles and rubella to form MMR vaccine to be introduced in EPI. A trivalent measles-mumps-rubella live virus vaccine, containing mumps Hoshino strain, was evaluated in a study. The vaccine induced a high seroconversion rate of 93.3%^[8] and 96.3%^[9] of initially seronegative cases for mumps virus. However, in our study in the best condition the induced seroconversion rate reached up to 80% (Avijgan M, Moghni M, Lalegani F. Reactogenicity and immunogenicity of mumps part of MMR vaccine in Iranian national immunization programme. 2005, Research deputy of Shahr-e-kord University of Medical Sciences, Iran (Unpublished data)

In general, adverse reactions to mumps vaccine are rare and mild. The most common adverse reactions are parotids and low-grade fever^[1]. Presumably, progressing vaccine-associated meningitis inhibits antibody formation^[10], and the available data suggest a potential correlation between vaccine-associated parotitis and vaccine-associated aseptic meningitis^[4]. One study summarized parotid swelling occurs 7-30 days after vaccination^[7]. In our study, one case of parotid swelling occurred 23 days following vaccination. Based on the results of this report, there is the first report of occurrence of parotiditis swelling 31 days following vaccination.

Reports of vaccine associated parotid swelling depend on the mumps vaccine strains. So that it varies from 1/90,000 (Jeryl Lynn strain, Fescharek, 1990, within 5.5 million), 1/444 (Kraigher, 1990 within 210,000 vaccines), 1/167 (Sofia-6 strain, Odisseev, 1994, 412,000 vaccines), 1/75 (Urabe strain, Santos, 2002, 2179 vaccines), 1/44 (Leningrad-3 strain, Melachenko, 1974, 1146 vaccines), 1/32 (Santos, 2002 within 2226 vaccines) and 1/18 (Leningrad-3 strain, Ivanov, 1985, 497 vaccines)^[4]. These rates are seemed to be very low but it must be considered that these reports are within general population (Immune and Non-Immune). In other word age-specific immunity is an important under-recognized factor with potential to cause rate differences among populations receiving the same strain. Persons without immunity to mumps may have a much greater risk of vaccine associated aseptic meningitis and immunity to mumps usually increases rapidly through childhood and varies among populations^[4]. So that our study shows the rate of this complication is about 1/20 of seronegative persons, which shows one of the high incidence rates of parotid swelling complications after one vaccine.

Therefore, knowledge about a population's immunity may be important in risk - benefit assessments of a particular mumps vaccine strain^[4].

We report the rate of complication of parotid swelling is more than natural infection. If it is considered that, there is about 25% seronegative to mumps among young adult (1-29 years old)^[11-13], then the estimated rate of such seronegativity (in general population), will be some about 25,000 per 100,000 population, in whom there will be about 1250 (5% rate of our study), parotid swelling following this MMR vaccine administration. So it is higher than natural parotitis which occurs following natural infection, as in most parts of the world the annual incidence of mumps is in the range 100-1000 per 100 000 population^[1]. There is always a conflict between the interests of the individual (vaccine safety and efficacy) and the interests of the community (vaccine uptake and level of herd immunity)^[3].

Another interesting finding of our study is this reaction or complication is not depends on the vaccine dose. So that in the base of our two presented cases, while one of them was administered the usual dose of vaccine (0.5 ml subcutaneously), the other one was administered one fifth of usual dose of vaccine. Also this is the first report of vaccine complication following reduced dose of vaccine.

Decisions about type of mumps vaccine and mumps vaccination strategies must consider vaccine safety issues in addition to other criteria^[14]. We suggest, improvements in MMR vaccine is needed to improve its safety, parents should have the option to have each viral component of MMR vaccine administered separately, those children who develop reaction following MMR vaccine should report their reactions to the local CDC.

CONCLUSION

This study showed a higher (5%) reactogenicity induced by Hoshino strain of current MMR vaccine administered in Iranian EPI than natural parotitis. Based on the results of this report, there is the first report of occurrence of parotitis swelling 31 days following vaccination. The other finding is this reaction is not vaccine dose dependant, the finding that it was not found in previous reports and this is the first report of vaccine complication following reduced dose of vaccine.

ACKNOWLEDGEMENT

I must thank from deputy research of Shahr-e-kord

University of Medical Sciences for their financial supports and also must thank of all persons and colleagues who helped me in this study.

REFERENCES

- 1 Available at: <http://www.who.int/wer/pdf/2001/wer7645.pdf>
- 2 **Ki M**, Park T, Yi SG, Oh JK, Choi B. Risk analysis of aseptic meningitis after measles-mumps-rubella vaccination in Korean children by using a case-crossover design. *Am J Epidemiol.* 2003; 15;157(2):158-65.
- 3 **Nokes DJ**, Anderson RM. Vaccine safety versus vaccine efficacy in mass immunization programmes. *Lancet.* 1991 Nov 23;338(8778):1309-12.
- 4 **McLean M**. The relative clinical safety of different mumps vaccine strains. A review for the Global Advisory Committee on Vaccine Safety W. H. O. *June*, 2003.
- 5 **Avijgan M**, Habibian R, Lalehgani F. Seroprevalence of Mumps Status in 3-18 years old Children of Shahr-e-kord. *Iranian Journal of Infectious Disease and Tropical Medicine.* 2005; 10 (30): 41-7.
- 6 **Ukkonen P**, Granstrom ML, Penttinen K. Mumps-specific immunoglobulin M and G antibodies in natural mumps infection as measured by enzyme-linked immunosorbent assay. *J Med Virol.* 1981; 8(2):131-42.
- 7 **Mark R**, Geier MD, Geier DA. Pediatric MMR Vaccination Safety. *Int Pediatr.* 2003; 18(2): 203-208.
- 8 **Nakayama T**, Urano T, Osano M, Nakagawa M, Maehara N, Sasaki K, et al. Evaluation of live trivalent vaccine of measles AIK-C strain, mumps Hoshino strain and rubella Takahashi strain, by virus-specific interferon-gamma production and antibody response. *Microbiol Immunol.* 1990; 34(6):497-508.
- 9 **Makino S**, Sasaki K, Nakayama T, Oka S, Urano T, Kimura M, et al. A new combined trivalent live measles (AIK-C strain), mumps (Hoshino strain), and rubella (Takahashi strain) vaccine. Findings in clinical and laboratory studies. *Am J Dis Child.* 1990;144(8):905-910.
- 10 **Goleva OV**, Kharit SM, Cherniaeva TV, Aksenov OA, Davidkin I, Kolyshkin VM. A virological description of serous meningitis in children immunized with vaccine against epidemic parotitis. *Vopr Virusol.* 2004;49(5):28-32.
- 11 **Kanbur NO**, Derman O, Kutluk T. Age-specific mumps seroprevalence of an unvaccinated population of adolescents in Ankara, Turkey. *Jpn J Infect Dis.* 2003;56(5-6):213-215.
- 12 **Aksit S**, Egemen A, Ozacar T, Kurugol Z. Mumps seroprevalence in an unvaccinated population in Izmir, Turkey. *Acta Paediatr.* 2000;89(3):370-371.
- 13 **Mossong J**, Putz L, Schneider F. Seroprevalence and force of infection of varicella-zoster virus in Luxembourg. *Epidemiol Infect.* 2004;132(6):1121-1127.
- 14 **da Silveira CM**, Kmetzsch CI, Mohrdieck R, Sperb AF, Prevots DR. The risk of aseptic meningitis associated with the Leningrad-Zagreb mumps vaccine strain following mass vaccination with measles-mumps-rubella vaccine, Rio Grande do Sul, Brazil, 1997. *Int J Epidemiol.* 2002;31(5): 978-82.