World Journal of Vaccines, 2016, 6, 43-45
Published Online August 2016 in SciRes. http://www.scirp.org/journal/wjv
http://dx.doi.org/10.4236/wjv.2016.63006

Relevant Facts from Aerosol Measles Vaccine Studies

Fernández de Castro Jorge, M. L. Garcia-Garcia, Jose Luis Diaz-Ortega, Deyanira Castaneda

Instituto Nacional de Salud Pública, Secretaría Nacional de Salud Pública, Cuernavaca, Mexico
Email: jorgefernandezde@aol.com

Received 22 June 2016; accepted 28 August 2016; published 31 August 2016

Abstract

Most of the facts regarding measles aerosol vaccination have been quite thoroughly dealt with in the book by S. Plotkin, *Mass Vaccination*: *Global Aspects—Progress and Obstacles* (2006 Ed) [1]. However, there are some aspects mentioned there that should perhaps have been emphasized more strongly and others that have emerged as relevant issues since then. We shall start with the quite important point that in the Sabin *et al*. [2] first study made in Monterrey, N. L., México [3], antibody reaction for recipients of respiratory-route Edmonston-Zagreb vaccines was not fully developed (100%) until six months after aerosol inhalation. At six weeks, only 90% had increased blood levels of antibody, a fact for which there is no easy explanation, but one which should be considered when dealing with serologic evaluation of measles vaccines given by aerosol in which short-term results less than encouraging. Results of the second study performed by Sabin *et al*. in Monterrey [2] establish that the percentage of sero-responses is directly dose-dependent. In turn, the dose itself depends on at least three facts: 1) concentration of virus in the vaccine used; 2) kind of nebulizer used; and 3) time of exposure. Another point to be stressed is that the vaccine used in the first trials [1]-[3], as well in the aerosol mass vaccination in México, though originally the Ickic strain attenuated in HDP, was also grown for final harvesting in HDP (MRC-5), whereas current Edmonston-Zagreb vaccines are obtained by final culture in chick embryo fibroblasts that provide 1 log more final product, more beneficial from an economic point of view, but not for adaptation to human tissues. A crucial consideration in aerosol measles mass campaigns is the lack of electricity/energy supply, particularly in rural communities. To deal with these issues, a rudimentary assembly was utilized to produce the aerosol for mass vaccinations performed during the serious Mexican epidemic of 1990-1991: a tire pump connected to a Clay-Adams nebulizer. As this equipment works only with direct current, a car battery was used to supply sufficient energy to vaccinate thousands of children.

Keywords

Immunology Immunopharmacology

How to cite this paper: de Castro Jorge, F., Garcia-Garcia, M.L., Diaz-Ortega, J.L. and Castaneda, D. (2016) Relevant Facts from Aerosol Measles Vaccine Studies. *World Journal of Vaccines*, **6**, 43-45. http://dx.doi.org/10.4236/wjv.2016.63006

1. Aerosol Vaccination Produce a Longer Immunity Period than Did Injected Immunization

In 1998, school-children of Durban, S. A. who had received Schwarz (SW) vaccine at one year of age were re-vaccinated by three methods/vaccines: aerosol-administered HDC, and SW, administered both by aerosol and Subq. route. The Measles HDC vaccine evoked a stronger and much longer lasting antibody response than did the other two and should thus provide more durable protection as reported by Dilraj *et al*. [4] [5]. In 2007, they measured antibody levels in the three study groups and proved those immunized by aerosol had a higher titer than did those vaccinated by injection. As the researchers state, "Measles re-vaccination by aerosol evokes a stronger and much long lasting antibody response than injected vaccine and should thus provide more durable protection against measles".

2. Acceptability of Aerosol vs Injection

In all the above instances of aerosol vaccination, only a very few adult participants/parents of minor participants have rejected aerosol. In fact, most participants who were given the choice, expressed preference for aerosol vaccination.

In 2015, results of the multifocal WHO trial in which 2004 Indian children were immunized, 1003 by traditional Subq injection and 1001 by aerosol, and then tested 3 months later by serology, were published. The authors regard an outcome of the aerosol group as "inconsistent" since there was a superior rate of seroconverters in the injection group (94% - 7%) versus 85.4% in the aerosol group. However, the authors reveal that those calculations were made after "multiple imputations of missing (serologic) results", which could conceivably invalidate their study. Notably, the nebulizer used (Aeroneb) is quite different from the classical device used in México, which creates nebulization by pressure and produces zero vaccine was teas opposed to the Indian trial, in which nebulization is derived from a vibrator mesh which allows at least 1/3 of the product to condense in the inferior part of the vase. This method could easily result in a dosage error. Wong-Chew [6] [7] reported a better response to aerosol measles vaccination by merely prolonging exposure time from 30 seconds to one minute with same dose in primary immunization of children at 12 months of age [8] [9]. This simple change in the process could result in more favorable results in future studies.

Díaz Ortega *et al*. reported in 2010 that aerosolized MMRII vaccine (Triviraten) provided a good seroresponse for measles and rubella but not for the strain Rubini (mumps) as compared to aerosolized mumps vaccine (Leningrad-Zagreb strain). In a prior study using aerosolized MMR vaccine, the aerosolized Edmonston-Zagreb (EZ) measles vaccine was significantly more immunogenic than was injected EZ vaccine, and its results were comparable to those following injected Moraten measles vaccine having twice the dosage. In these studies, the responses to rubella were comparable in the three MMR study groups but, as stated above, aerosolized Rubini vaccine was unexpectedly less immunogenic than either injected Rubini or Jerryl-Lyn strains [10]. Same author found that in an administration by aerosol of MMR II, produced by Merck Sharp & Dhome Corp. Despite high levels of baseline seropositivity to all vaccine components, seroresponses to measles, rubella and mumps occurred in 44%, 15% and 41%, respectively—outcomes that compare favorably to earlier studies of other MMR vaccines given by aerosol [11].

References

[1] Plotkin, S.A. Mass Vaccination: Global Aspects—Progress and Obstacles. Springer, Berlin, Heidelberg.

[2] Sabin, A.B., Flores, A.A., Fernandez de Castro, J., Sever, J.L., Madden, D.L., Shekarchi, I., *et al*. (1984) Successful Immunization of Children with and without Maternal Antibody by Aerosolized Measles Vaccine. II. Vaccine Comparisons and Evidence for Multiple Antibody Response. *JAMA*, **251**, 2363-2371.

[3] Sabin, A.B., Flores, A.A., Fernandez de Castro, J., Sever, J.L., Madden, D.L., Shekarchi, I., *et al*. (1983) Successful Immunization of Children with and without Maternal Antibody by Aerosolized Measles Vaccine. I. Different Results with Undiluted Human Diploid Cell and Chick Embryo Fibroblast Vaccines. *JAMA*, **249**, 2651-2662.

[4] Low, N., Bavdekar, A., Jeyaseelan, L., Hirve, S., Ramanathan, K., Andrews, N.J., Shaikh, N., Jadi, R.S., Rajagopal, A., Brown, K.E., Brown, D., Fink, J.B., John, O., Scott, P., Riveros-Balta, A.X., Greco, M., Dhere, R., Kulkarni, P.S. and Henao Restrepo, A.M. (2015) A Randomized, Controlled Trial of an Aerosolized Vaccine against Measles. *The New England Journal of Medicine*.

[5] Dilraj, A., Sukhoo, R., Cutts, F.T. and Bennett, J.V. (2007) Aerosol and Subcutaneous Measles Vaccine: Antibody

Responses 6 Years after Re-Vaccination. *Vaccine*, **25**, 4170-4174. http://dx.doi.org/10.1016/j.vaccine.2007.03.003

[6] Wong-Chew, R.M., Islas-Romero, R., Garcia-Garcia, M.L., Beeler, J.A., Audet, S., Santos-Preciado, J.I., *et al.* (2004) Induction of Cellular and Humoral Immunity after Aerosol Orsubcutaneous Administration of Edmonston-Zagreb Measles Vaccine as Primary Dose to 12-Month-Old Children. *The Journal of Infectious Diseases*, **189**, 254-257.

[7] Wong-Chew, R.M., Islas-Romero, R., Garcia-Garcia, M.L., Beeler, J.A., Audet, S., Santos-Preciado, J.I., *et al.* (2005) Immunogenicity of Aerosol Measles Vaccine Given as the Primary Measles Immunization to 9-Month-Old Mexican Children.*Vaccine*, **24**, 683-690.

[8] Fernández de Castro, J., Kumate, J., Sepúlveda, J., Ramírez-Isunza, J.M. and Valdespino-Gómez, J.L. La vacunación anti-sarampionosa en México por el método de aerosol. *Salud Publica Mex*, **39**, 53-60.

[9] Fernández de Castro, J.V., Bennett, H., Gallardo-Rincon, M.T., Muñoz, L.A., Sanchez, L.A.E.P. and Santos, J.I. (2005) Evaluation of Immunogenicity and Side Effects of Triple Viral Vaccine (MMR) in Adults, Given by Two Routes: Subcutaneous and Respiratory (Aerosol). *Vaccine*, **23**, 1079-1084. http://dx.doi.org/10.1016/j.vaccine.2004.08.018

[10] Diaz-Ortega, J.L., Bennett, J.V., Castaneda, D., Vieyrac, J.-R., Valdespino-Gomez, J.L. and de Castro, J.F. (2010) Successful Seroresponses to Measles and Rubella Following Aerosolized Triviraten Vaccine, but Poor Response to Aerosolized Mumps (Rubini) Component: Comparisons with Injected MMR. *Vaccine*, **28**, 692-698. www.elsevier.com/locate/vaccine

[11] Diaz-Ortega, J.-L., Bennett, J.V., Castaneda, D., Arellano, D.M., Martinez, D. and de Castro, J.F. (2012) Safety and Antibody Responses to Aerosolized MMR II Vaccine in Adults: An Exploratory Study. *World Journal of Vaccines*, **2**, 55-60. http://dx.doi.org/10.4236/wjv.2012.22008