Estimation of Live Virus Content of Measles Vaccine

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Abstract: The first measles vaccine was developed in 1963 and the improved measles mumps rubella (MMR) vaccine become available in 1976 since there is no specific anti -viral drugs available for measles, the use of live attenuated measles vaccine is recommended for all children as well as passive immunization for immunocompromised individuals and pregnant women, (Banatvala et al, 2004). The potency of the live attenuated measles vaccine collected from the three level of vaccination centres were determined using cell culture titration method. The 6 different batches of the measles vaccine (ZA101X, ZA100X, ZA98X, ZA97X, ZA90X and ZA28X) collected from the tertiary storage centre (EPID) and traced down to Tertiary (UMTH), the secondary (SSH) and primary vaccination centre (YERWA) showed low/lost of potency which consequently may affect their efficacy as compared to WHO standard titre of $10^{4.0}$ ten-dose vial. This was linked to inadequate storage facility from the tertiary vaccine storage centres down to the primary vaccination centres. Poor power supply at the secondary and primary vaccination centres (lack of 24hrs standby generator/power backup) and lack of strict adherence to W. H. O. guidelines for measles vaccine storage/administration are possible factors to the low tittered vaccine obtained in this study.
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Key words: Measles vaccine; potency and storage facilities.

INTRODUCTION

Measles is an acute highly infections viral disease characterized by fever, respiratory symptoms and most distinctively maculopapular rash of the skin. Measles virus which belong to the genus morbilivirus is the aetiological causes of measles (burnet et al, 2007). Measles has a worldwide mortality rate in children less than 5years and it is worse and severe in Africa. Measles is commonest in children but may appear in older persons who have escaped it earlier in life. Infants are immune up to four or five months of age if the mother has had the disease. Immunity to the disease measles following an attack after recovery is usually lifelong. Measles is highly communicable and contagious that the slightest contact with an active case may infect a susceptible person (Gerson et al, 1998).

MATERIAL AND METHODS

The potency of live measles vaccine was determined in an *in vitro* assay using VERO cell line. The preparation to be assayed are diluted in 2% MM. Tenfold dilution steps of the virus suspensions was initially made, The subsequent dilutions for inoculation into the microtitre plates are prepared in 0.5 $\log_{10}$ steps. The range of dilutions used will depend on the type of virus and the formulation of the vaccine under test. The range chosen should include the expected titre of the vaccine type being tested but the dilution range selected should encompass at least three dilutions that will infect between 0% and 100% of the cultures inoculated.The cells are examined for the presence of a specific viral cytopathic effect (formation of multy-nucleated giant cell) on days 3–5, with a final reading on day 7. The observations are recorded and the titer in $CCID_{50}$ per human dose calculated on the basis of the final observation using karber formula: L-D(S-0.5).

Cells

Use VERO cell line .The passage level of these cells, which should be within 15 passages of the tested stock. Watch for any change in growth characteristics such as excess acidity of medium or slowing in the time taken to achieve a complete monolayer. The number of cells used in the assay is usually about 1–2 x 10^5 cells per ml of test medium. This concentration should provide a confluent monolayer in microtitre plate wells within two to three days.

MEASLES VACCINE TITRATION

The micro titre plates were labelled according to their batches and sources with acronyms. 0.05ml of the test medium was dispensed into all wells which were followed by 0.05ml serial double dilution of the reconstituted measles vaccine. Then 0.10ml of the Vero cell suspension was added to all the wells, cell controls inclusive. The plate were covered with the lid and wrapped with aluminium foil and placed in a zipper bags. They were incubated at 37ºc for 5-9 days. The control wells contain no measles vaccine. It was observed microscopically starting from day three on daily basis.

RESULT

TABLE 1: Titration of ZA100X and vaccination centres from which it was obtained

S/NO	CENTER	BATCH NO	TITER
1	GIDAN MADARA (EPID)	ZA100X	$10^{2.15}$
2	YERWA CLINIC	ZA100X	$10^{1.75}$
3	STATE SPECIALIST HOSPITAL	ZA100X	$10^{1.65}$
4	U.M.T.H	ZA100X	$10^{2.05}$

TABLE 2: Titration of ZA98X and vaccination centres from which it was obtained

S/NO	CENTER	BATCH NO	TITER
1	GIDAN MADARA (EPID)	ZA98X	$10^{2.75}$
2	YERWA CLINIC	ZA98X	$10^{2.40}$
3	STATE,SPECIALIST HOS	ZA98X	$10^{2.40}$

TABLE 3: Titration of ZA101X and vaccination centres from which it was obtained

S/NO	CENTER	BATCH NO	TITER
1	GIDAN MADARA (EPID)	ZA101X	$10^{3.15}$
2	YERWA CLINIC	ZA101X	$10^{1.70}$
3	STATE SPECIALIST HOS	ZA101X	$10^{1.80}$

TABLE 4: Titration of ZA97X and vaccination centres from which it was obtained

S/NO	CENTER	BATCH NO	TITER
1	GIDAN MADARA(EPID)	ZA97X	$10^{2.15}$
2	YERWA CLINIC	ZA97X	$10^{1.95}$

TABLE 5: Titration of ZA90X and vaccination centres from which it was obtained

S/N	CENTERS	BATCH NO	TITER
1	GIDAN MADARA (EPID)	ZA90X	$10^{3.30}$
2	YERWA CLINIC	ZA90X	$10^{1.95}$
3	S. S. H.	ZA90X	$10^{0.00}$

TABLE 6: Titration of ZA28X and vaccination centres from which it was obtained

S/N	CENTER	BATCH NO	TITER
1	GIDAN MADARA (EPID)	ZA28X	$10^{2.20}$
2	YERWA CLINIC	ZA28X	$10^{2.00}$
3	U.M.T.H	ZA28X	$10^{1.90}$

DISCUSSION

Prior to 1963, almost everyone has had measles infection before the age six and nearly 90% of infants must have had the disease before the age of fifteen. (Field virology, 2001).

WHO/UNICEF expanded program on immunization (EPI) have significantly lead to decrease in measles outbreaks and mortality, but over the years, it has been observed that measles outbreaks and mortality still occur in certain quarters even among the vaccinated populations, most recent documentation is in sub-Saharan Africa (Grais et al, 2007), Japan (Norrie et al, 2007) and United Kingdom (Batty et al, 2009).

The Expanded Programon Immunization (EPI) was aimed at eliminating measles completely from the surface of the earth by establishing herd immunity which will prevent transmission from susceptible person to the immunized groups (resistant groups).

Nigeria lunched her own immunization program on the major childhood killer diseases of which measles is one of them in 1979 and projected 100% local governments coverage by 1989. Although considerable progress was made but only 45% coverage was achieved by the end of 1989 by National program on immunization (NPI). (Nasidi et al, 1987). NPI however, documented about 538,750 cases of measles from 1999 to 2002 (Stein at al, 2003)

This has however shown that the National Program on Immunization has not gotten a full grasp on the control and complete elimination of measles from Nigeria, since even the vaccination program itself has not achieved 100% coverage with few vaccinated population coming down with measles infection.

The titre of eighteen vials of live attenuated measles vaccine of the six batches collected from the different vaccination centres (main store traced to the vaccination centres) were significantly different. Generally the vaccines at the Central Store (EPID UNIT) (which is the first port of storage for all vaccines assigned for Borno State) showed higher titres than the same batch of vaccine at the vaccination centres. This study also showed that, the titres of the different batches of vaccines at the vaccination centres were significantly different from W. H. O. standard and not from titres of the same batch of vaccines at the EPID Unit. This implies that, the low tittered vaccines could be attributed to environmental (poor storage facility, break in cold-chain and improper handling and transportation to the centres). One batch of the vaccines tested showed no cytopathic effect (CPE) ($10^{0.00}$). It's however interesting to note that, these vaccines (those with no titre) were leftovers after a day's exercise and were obtained from the State Specialist Hospital vaccination centre. It may be necessary to also state that, in these vaccination centres used for the study, leftover vaccines after a days vaccination exercise were usually preserved for further use. This practice contradicts WHO recommendation which states that, reconstituted measles vaccines should be discarded after 8 hours. Therefore, leftovers are supposed to be discarded and not otherwise as experienced in the vaccination centres studied. This probably explains the high degree of primary vaccine failure (76%) and very low sero-conversion rate of 12% reported in the same environment as this study (Baba et al, 2007). A live vaccine that could not even cause CPE cannot also induce expected immunity in the recipient.

Although the existence of maternal antibody could interfere with the sero-conversion rate of the vaccine as previously reported (Onoja et al 1990, Baba et al 2007), but the persistence of poor condition of storage, lack of proper cold chain facilities and improper handling of the vaccines during transportation from Central Store to vaccination centres, poor power supply at the secondary and primary vaccination centres (lack of 24hrs standby generator/power backup), lack of strict adherence to W. H. O. guidelines for measles vaccine use/administration and inadequate/poorly trained personnel at the vaccination centres were the observed factors that could adversely affect the

efficacy of vaccines at the rural settings as previously reported by Shohreh et al, (2005). Administering potent vaccine especially at the secondary and primary vaccination centres is necessary for a successful measles immunization in Nigeria.

CONCLUSION

The determination of the potency (titre) of measles vaccine in the three levels (tires) of vaccination Centres in Borno state was determined by cell culture titration of the 18 vials from six batches of measles vaccines. However, this study revealed that the potency of the same measles vaccines at the EPID Unit differed significantly from similar batches at vaccination centres especially secondary and primary health vaccination centres.

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