Title: FAILURE OF ANTIBODY PRODUCTION FOLLOWING INTRA DERMAL RABIES VACCINATION IN THE MANAGEMENT OF CATEGORY III ANIMAL BITE: AN UNUSUAL CASE REPORT

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Keywords Rabies, Intra dermal rabies vaccinations, Vaccine failure, Rabies Immunoglobulin

Abstract A 11 year old boy had a category III dog bite over right great tow was treated with Purified vero cell rabies vaccine (PVRV) according to updated Thai Red Cross regimen at a district head quarter hospital of Odisha. Even after taking four dosages of vaccine through intra dermal route the protective antibodies titre (>0.5 IU/ml) could not be attained. The patient was further treated with PVRV by IM Route by the inj. Verrorab Essen regimen and Human Rabies Immunoglobulin (HRIG) Inl Berirab administered locally at the site of bite as per body weight.

Case Report

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ABSTRACT

A 11 year old boy had a category III dog bite over right great toe was treated with Purified vero cell rabies vaccine(PVRV) according to updated Thai Red Cross regimen at a District Head quarter Hospital of Odisha. Even after taking four doses of vaccine through intra dermal route, the protective antibodies titre (>0.5 IU/ mL) could not be attained. The patient was furtherre-treated with PVRV by IM Route by the inj. Verorab Essen regimen and Human Rabies Immunoglobulin (HRIG) Inj. Berirab P administered locally at the site of bite as per body weight.

Key words : Rabies, Intra-dermal rabies vaccinations, Vaccine failure, Rabies immunoglobulin.

Introduction:

Rabies is a 100 percent fatal but 100 percent preventable disease. Intra Dermal Rabies vaccination (IDRV) is a World Health Organization (WHO) approved cost effective method of treatment for animal bite cases and the Updated Thai Red Cross (TRC) regimen of IDRV method is being widely used in the world for treating category II and III animal bite cases.[2,3] Odisha was the 2nd state in India to implement the IDRV and MKCG Medical College Hospital, Berhampur was the 1st to introduce intra dermal rabies vaccination in the year 2007 in Odisha.[4] On an average 80-100 patients are being administered IDRV for Category II & III animal bite cases daily in the Anti-Rabies Clinic (ARC) of MKCG Medical College Hospital, Berhampur. But in the periphery, Primary Health Centres (PHCs) and Community Health Centres (CHCs) of the state, Rabies Immunoglobulin (RIG) is scarce or even not in supply. Therefore patients from those areas are being referred to ARC of MKCG Medical College Hospital for Rabies Immunoglobulin (RIG) administration.

Case/patient Profile

A 11year old boy was bitten by a stray dog on 14.11.2014 over right great toe which was a provoked bite and was treated at District Headquarter Hospital (DHH) Phulbani on the same day. Though it was a category III dog bite, they administered tetanus toxoid vaccine (TT) and Anti Rabies Vaccine i.e. Injection Indirab (purified verocell rabies vaccine, PVRV, manufactured by Bharat Biotech International Limited, Hyderabad and diluted with 1ml of diluent) by intra dermal route on 14.11.2014[5], but without Rabies Immunoglobulin (RIG) administration. The patient was administered Day 3 IDRV on 17.11.2014 and Day 7 IDRV on 21.11.2014 as per schedule at DHH Phulbani. The father of the patient informed to the Medical Officer of DHH Phulbani on 21.11.2014 that the same stray dog had died on 15.11.2014. The DHH Medical Officer referred the patient to MKCG Medical college hospital, Berhampur for considering about Rabies immunoglobulin therapy and mentioning about it in the prescription. The patient reported to the ARC of MKCG Medical College hospital on 22.11.2014.

The parent of the patient was counselled about the necessity of RIG infiltration at the site of bite within first seven days of Vaccine administration which was not done. Again the patient was counselled about the necessity of estimating the antibody titre i.e. RVNA (Rabies Virus Neutralising Antibody). The father of the

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patient agreed to conduct the test at SRL Diagnostics, Mumbai. Mean time he was also cautioned to complete the last dose of IDRV at DHH Phulbani on 12.12.2014 which he completed also.

Sample collection and its result

Blood sample was collected for estimating antibody titre (RVNA) on 22.12.2014 at Berhampur and sent to SRL Diagnostics Mumbai. The sample was received at Mumbai on 24.12.2014 and the result of the test was reported on 29.12.2014.The method used at SRL Diagnostics was Rabies Virus Antibodies Total Antibody, Serum. The result of antibody titre found to be 0.38 IU/mL which was non-immune according to biological reference interval, (immune> 0.50 IU/mL and non-immune ⩽ 0.50 IU/mL titre of antibodies.)[6]

Treatment offered at ARC MKCG Medical College, Berhampur

The patient was treated with PVRV (inj. VERORAB) manufactured by Sanofi Aventis marketed in India by Zuventus Health Care Ltd, Mumbai by Essen regimen through intra muscular (IM) route on days 0-3-7-14-28 along with Human Rabies Immunoglobulin (HRIG) i.e. inj. BERIRAB-P (marketed by Bharat Serums and Vaccines ltd, Mumbai in India) as 20 IU/kg. The calculated dose of HRIG was 4.7 ml (35kg× 20IU/kg= 700IU). Out of the total calculated dose, only 0.7ml could be infiltrated locally over right great toe and rest 4ml was administered over thigh by IM route. The patient was followed up for 6 months and was found to be healthy and free from rabies.

Discussion

Hence it was clearly indicated that the vaccine Indirab (diluted with 1ml of diluent) which was given by IDRV on schedule dates in four doses failed to achieve the required antibody titre (> 0.50 IU/mL) for the protection of individual against rabies. So there may be faulty technical procedure adopted for vaccination i.e. Intra dermal route or failure of cold chain maintenance of the reconstituted vaccine. The potency of the vaccine used at DHH Phulbani is questionable as documented from the result obtained from SRL diagnostics, Mumbai, which indicates that this was a clear cut case of vaccine failure in producing the protective antibody i.e. >0.50 IU/mL.[6] There are many studies where vaccine failure have been documented only in immune-compromised cases like a case report reported by Terapong Tantawichien et al[7] where IDRV fails in a patient with HIV+ve with low CD4 count. But here the patient was not immune compromised.

Conclusion

As adequate protective antibody could not be achieved with use of only ARV through intra dermal route (IDRV), it is high time to consider use of RIG for all category III animal bite at even the District Head Quarter Hospitals. More emphasis should be given for creating awareness among the medical officers for use of RIG within 7 days of initiation of vaccination for all category III animal bite cases and should be oriented to refer to higher centres in case of unavailability of RIG. The study showed that use of RIG especially HRIG along with IDRV is essential to treat Category III animal bite in Children. Therefore the authors recommend the use of HRIG with IDRV for treatment of Category III animal bite cases in children.

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