

Evaluation of intradermal vaccination at the anti rabies vaccination OPD

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ABSTRACT

Rabies is a virtually 100% fatal acute viral encephalitis caused by an RNA virus belonging to family Rhabdoviridae and genus *Lyssavirus*. The virus can infect all warm blooded animals. The disease is transmitted to humans by the bite, lick or scratch of an infected animal. More than 99% of all human rabies deaths occur in the developing world. It is preventable with timely and proper usage of modern immunobiologicals (vaccines and immunoglobulins). Once exposure occurs, modern prophylaxis entails immediate wound care, local infiltration of rabies immune globulin and parenteral administration of modern cell culture vaccines in multiple doses. The annual medicinal (vaccines and other drugs) cost for animal bite treatment is Rs. 2 billion approximately (2004). The objective of the present study is to evaluate the performance of the Intradermal (ID) route vis a vis the Intramuscular (IM) route in our clinical setting the Antirabies Vaccination (ARV) OPD, Sir J.J. Hospital, Mumbai. A total of 1460 patients were administered the Antirabies vaccine by the Intradermal route over the 1 year period as compared to 1075 patients who were administered the Antirabies vaccine by the Intramuscular route in the previous year. 1230 (84.2) of the patients who were administered the vaccine by the ID route completed the schedule and 230 (15.8%) partially completed the schedule. Four hundred thirty two (40%) of the patients who were administered the vaccine by the Intramuscular route completed the schedule and 643 (59.8%) partially completed the schedule. The vaccine cost for ID was Rs. 2,80,600. The vaccine cost for the intramuscular (IM) assuming 84% compliance was estimated as Rs. 15, 64, 000. Assuming 40% compliance the cost was estimated as Rs. 7, 82, 230. Thus a saving of Rs. 5, 01, 630 to Rs. 12, 83, 400 was effected. In our setting, the Intradermal regime was cost effective and increased patient adherence and enrolment. It has now been routinely adopted at the clinic.

Keywords: Rabies, intradermal vaccination, cost effective

INTRODUCTION

Rabies is a virtually 100% fatal acute viral encephalitis caused by an RNA virus belonging to family Rhabdoviridae and genus *Lyssavirus*. The virus can infect all warm blooded animals. The disease is transmitted to humans by the bite, lick or scratch of an infected animal. More than 99% of all human rabies deaths occur in the developing world. The disease has not been brought under control in most of the affected countries.¹

An estimated 55,000 persons die of rabies globally every year of which 31,000 are from the Asian continent. In India, the Annual Incidence of Human Rabies is 20,000 Cases. The frequency of human rabies deaths is 1 case every 30 minutes (1/2 hour) approximately. The principal animal reservoir is dog (96.3%). The Animal bite incidence rate (per 1000 population) is 17.4 and this translates to a whopping 17.4 million bites every year. The frequency of animal bites in India is 1 every 2 seconds and the annual man-days lost due to animal bite is 38 million. It is preventable with timely and proper usage of modern immunobiologicals (vaccines

and immunoglobulins).² Once exposure occurs, modern prophylaxis entails immediate wound care, local infiltration of rabies immune globulin and parenteral administration of modern cell culture vaccines in multiple doses. Pre-exposure vaccination should occur in selected population groups at risk of occupational exposure.³

Government of India has banned the production and use of Nervous Tissue Vaccine (NTV) in December, 2004 which was the vaccine widely used in the public sector. With the stoppage of NTV, the availability and affordability of modern Cell Culture Vaccine became a major issue with many States.⁴

The annual medicinal (vaccines and other drugs) cost for animal bite treatment is Rs. 2 billion approximately.²

Intradermal regimens: The intradermal regimens are of particular interest in areas where rabies vaccines are in short supply or available but inaccessible, in view of their price, to people at risk of contracting rabies.⁵ With the recommendations of WHO, National experts

and ICMR study on the use of intradermal vaccines, National Regulatory Authority has permitted the use of this economical and efficacious route in India in 2006.⁵⁻⁷ Chhabra *et al* (NICD) demonstrated that PCECV is safe and highly immunogenic in Indian subjects when administered intradermally as 0.1 mL/site using the "2-2-0-1-1" post-exposure regimen.⁸

Sufficient clinical evidence was presented indicating that a single dose of vaccine given on day 90 of the original Thai Red Cross regimen ("2-2-0-1-1" regimen) can be replaced if two doses of vaccine are given on day 28 ("2-2-0-2" regimen).^{9,10} The Thai Red Cross regimen considerably lowers the cost of vaccination as the total volume of vaccine required is much less than that needed for intramuscular regimens.⁷

The WHO recommends that this route of administration is one of the ways to ensure the provision of effective treatment to the large number of bite victims at an affordable cost.⁸ The anti-rabies vaccines currently approved for use in India through ID route are Rabipur (PCECV), Verorab (PVRV), Abhayrab (PVRV) and Pasteur Institute of India, Coonoor (PVRV).⁹

Our clinical setting was the Antirabies Vaccination (ARV) clinic in a tertiary government hospital in Mumbai, Maharashtra. The Purified Chick Embryo Cell Vaccine (Rabipur TM) supplied by the hospital on rate contract costed Rs. 230 per vial. The cost was a major concern as a patient enrolled in the OPD would require 5 vials to complete the Essen's regime. After the DCGI clearance to Intradermal vaccination, it was initiated in the Antirabies Vaccination (ARV) OPD on the 1st of July 2008.¹¹ All the patients enrolled in the OPD from the 1st of July 2008 were administered the vaccine using the Intradermal route.

Objective of the study: To evaluate the performance of the Intradermal(ID) route vis a vis the Intramuscular (IM) route in our clinical setting in terms of adherence and cost

MATERIALS AND METHODS

Setting: Antirabies Vaccination OPD, Sir J.J. Hospital, Mumbai

Study Period: 1st July 2008 - 30th June 2009 for the Intradermal (ID) route

1 year data (2007 - 2008): For the Intramuscular (Essen's) regime

Vaccine used: Purified Chick Embryo Cell Vaccine (RabipurTM) supplied by the hospital on rate contract

2 site Intradermal schedule (2-2-0-2) : As per Drugs

Controller General of India (DCGI) (Annexure-2), the schedule recommended for IDRV is the updated Thai red cross schedule.¹¹ One dose of 0.1 ml vaccine at each of the two sites was given on days 0,3, 7 and 28.¹² The most common site was the deltoid.

Essen's regime: One dose 1 ml intramuscular (deltoid) on day 0,3, 7, 14 and 28.¹⁰

Data was analysed using the Stata SE 10.1 software. Pearson's Chi square test (2 sided p values), Odds Ratio's and 95% Confidence Intervals (Exact) were calculated.

RESULTS

A total of 1460 patients were administered the Antirabies vaccine by the Intradermal route over the 1 year period as compared to 1075 patients who were administered the Antirabies vaccine by the Intramuscular route in the previous year (Table-1). One thousand two hundred thirty (84.2) of the patients who were administered the vaccine by the ID route completed the schedule and 230 (15.8%) partially completed the schedule. 432 (40%) of the patients who were administered the vaccine by the Intramuscular route completed the schedule and 643 (59.8%) partially completed the schedule (Fig. 1). OR (95%CI) = 7.96 (6.61 - 9.59) χ^2 = 532.3, d.f. = 1, $p < 0.0001$ (VHS)

Table-1: Patient enrolment ID vs IM regime

Route	Completed Schedule	Partially Completed Scheduled	Total
ID (2008 - 2009)	1230 (84.2)	230 (15.8)	1460
IM (2007 - 2008)	432 (40.2)	643 (59.8)	1075
Total	1662 (65.6)	873 (34.4)	2535

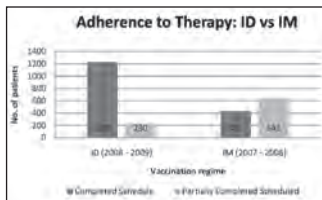


Fig. 1. Adherence to therapy

OR (95%CI) = 7.96 (6.61 - 9.59) χ^2 = 532.3, d.f. = 1, $p < 0.0001$ (VHS)

The PCECV Rate Contract at Sir J.J. Hospital was Rs.

230/ Vial. A total of 1220 vials were used. The vaccine cost for ID was Rs. 2,80,600. The vaccine cost for the intramuscular (IM) assuming 84% compliance was estimated as Rs. 15, 64, 000. Assuming 40% compliance the cost was estimated as Rs. 7, 82, 230. Thus a saving of Rs. 5, 01, 630 to Rs. 12, 83, 400 was effected (Fig. 2). 1230 patients received 4 doses each (Fig. 3). A total no. of 1220 vials were used during the study period and the total no. of doses administered were 5482. Thus per vial, 4.49 doses were administered. The vaccine wastage was 10.13%.

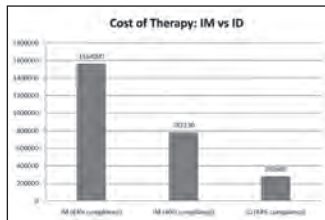


Fig. 2. Cost of therapy (in Indian Currency)

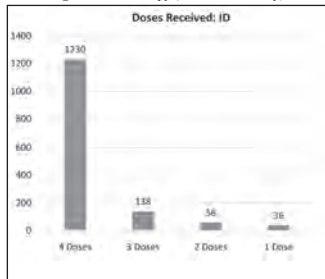


Fig. 3. Number of doses received during the study period

DISCUSSION

Patients attending the clinic and ARV used has increased over the years, adding financial burden to the institute. The main issue with the previous Essen (IM) regime was the cost of the vaccine resulting in supply issues. To address these issues, where vaccine and money are in short supply, ID route seemed ideal in terms of economic benefits, safety and efficacy. The introduction of Intradermal vaccination at the ARV Clinic was associated with a very significant rise in patient compliance. We were also able to enroll more patients after initiating the

intradermal regime. The vaccine wastage was minimal (10.13%).

It has reduced the cost of vaccination by about 82% (assuming 84% compliance). This makes it an attractive option for middle and low level income countries like ours.¹³ With commitment and effort, an ideal IDRV vaccine clinic can be set-up. ID administration requires some amount of technical skills which may be imparted by training interns and staff nurses.¹⁴ We have trained 196 interns in this time period. In our setting, the Intradermal regime was cost effective and increased patient adherence and enrolment. It has now been routinely adopted at the clinic.

Sudarshan *et al*¹⁵ carried out a comparative study of IDRV, Sempole vaccination and modern vaccines by intramuscular route based on the available studies and prevailing cost factors and estimated that IDRV would cost nearly one third of the intramuscular Essen regimen.

Rahim *et al*¹⁶ did a retrospective analysis of case records of a three-year period (2006-2008). All cases who have been treated with intramuscular ARV (both partial and complete) for a period of three years (2006-2008) in the preventive clinic of Calicut Medical College were included in the study. The cost of ARV for three years was calculated and compared with intradermal regimen (modified Thai schedule). The benefit in terms of expenditure to the Government was calculated if ID regimen had been used in all these cases. They estimated that the ID regimen reduces the cost of vaccination by about 70-80%. This concurs with our findings.

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