

## Original article

# Evidence on Efficacy of Two Routes of Vaccine Administration for Post Exposure Prophylaxis in Rabies Prevention – A Meta Analysis

Sara Varghese, Rajamohan Pillai, Muraleedharan Nair, Thomas Mathew, Regi Jose

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## Abstract:

Rabies, a major public health problem is important in that it is 100% fatal and 100% vaccine preventable if timely & appropriate post exposure prophylaxis is provided with modern cell culture vaccines. Though there are many studies proving the efficacy of cell culture antirabies vaccines, many have been done in different setting and some have relatively small sample size. A meta analysis was done with a view to bring about a more precise estimate and to study the dispersion of effect if present.

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## Introduction

Rabies is an enzootic viral disease wide spread throughout the world. It causes fatal encephalomyelitis in virtually all warm blooded animals including man. Though fatal, it is a vaccine preventable zoonosis. India has the highest incidence of rabies related deaths-20,000 per year. An estimated 20,000 persons die of hydrophobia every year in this country and approximately 500,000 undergo post-exposure prophylaxis. The present management includes providing post exposure prophylaxis with modern cell culture vaccines intramuscularly. Kerala is now in a transitional stage of providing the vaccine from the standard practice of Intramuscular to the newer technique of providing it through the intradermal route.

Though there are many studies proving the efficacy and effectiveness of modern cell culture vaccines, they show variation in effect size as they are done in different setting and have relatively small sample size. It is in this context that a Meta analysis was planned, to obtain a pooled estimate with maximum precision.

## Objective

To do a Meta analysis of clinical trials done on efficacy of Intramuscular versus Intradermal route of administration of Antirabies Cell Culture vaccines.

## Method Meta Analysis

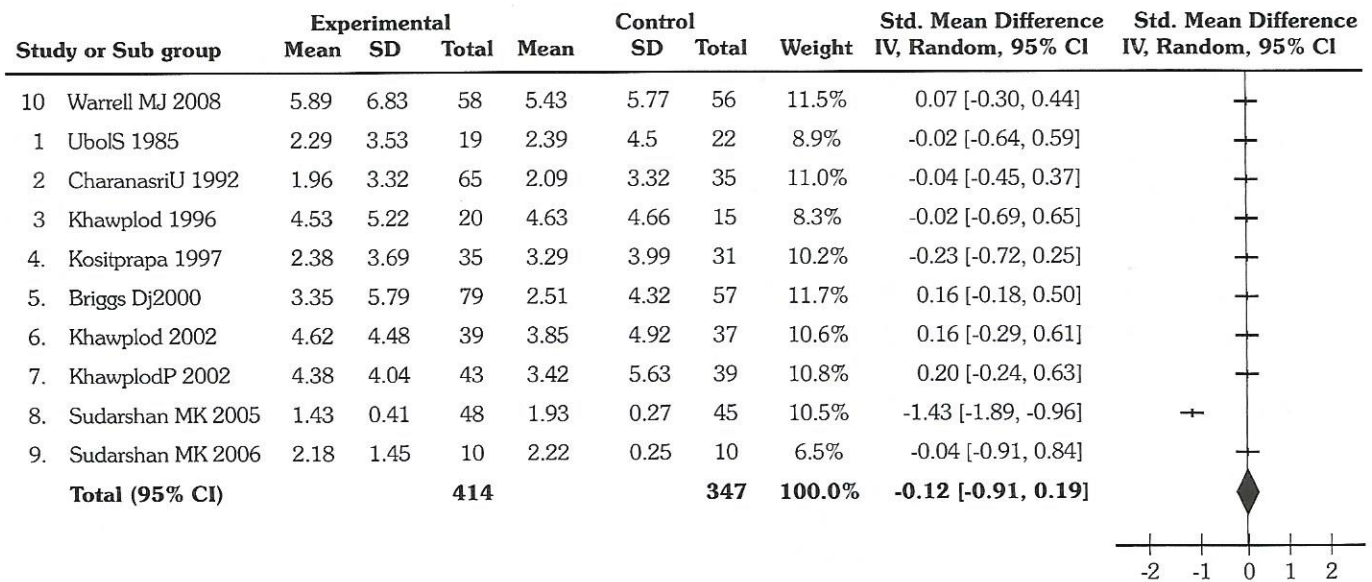
The quantitative analysis of selected studies was done using the software Rev Man of Cochrane collaboration. Step wise description of the tasks that were performed when statistical methods are used to combine data : (i) Deciding whether to combine data and defining what to combine, (ii) Evaluating the statistical heterogeneity of data, (iii) Estimating a common effect, (iv) Exploring and explaining heterogeneity, (v) Assessing the potential for bias, and (vi) Presenting the results.

A thorough search was done using different means for studies based on fixed selection criteria. A total of 133 studies were identified of which ten studies were finally included after applying the inclusion criteria. The levels of evidence of these studies were assessed using guidelines by Sackett and colleagues. The methodological quality was done using the software. As there was wide variation in the outcome measure, the log values of these were taken and entered in the table provided in Rev Man and the result was computed as the Forest Plot.

The cost incurred by patients on post exposure prophylaxis by the intramuscular and the intradermal routes were assessed by interviewing a sample of 368 persons attending three first referral units and the cost was compared between the groups.

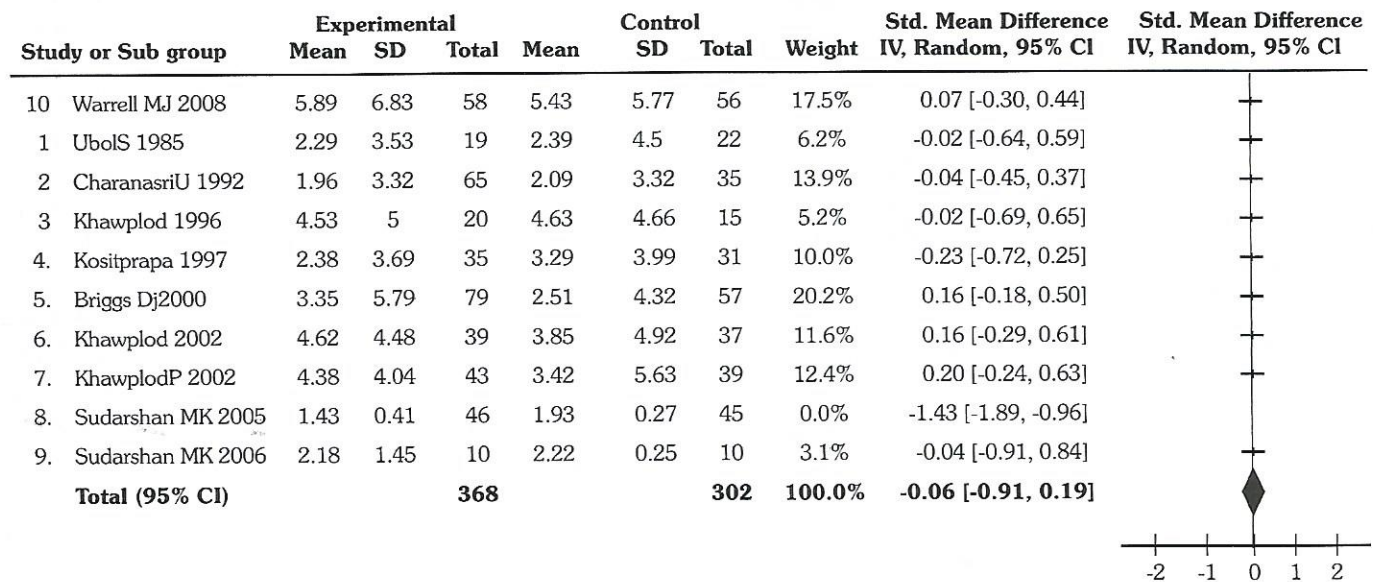
## Results

Meta analysis reports its results in a graphical plot called Forest Plot. It shows the summary effect size of individual studies and also pooled effect estimate of all studies included. The point estimate of each study is represented in the forest plot as a square or box. The horizontal line extending from the sides of the box represent the confidence interval. The vertical line represents line of no effect. Heterogeneity between the studies was also tested during the process. Ten studies were included for the analysis. One study showed considerable heterogeneity and when this was removed the heterogeneity was reduced to zero. Since the confidence interval of all except one study crosses the vertical line, there is no difference in the immunogenicity of cell culture vaccines when administered through either route, except the 8<sup>th</sup> study which favors the intrdermal route of administration. The funnel plot showed no publication bias.



Heterogeneity,  $Tau^2 = 0.18$ ,  $Ch^2 = 38.22$ ,  $df = 9$  { $P < 0.0001$ },  $I^2 = 76\%$   
 Test for over all effect  $Z = 0.75$  ( $P = 0.45$ )

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Heterogeneity,  $Tau^2 = 0.00$ ,  $Ch^2 = 2.71$ ,  $df = 8$  ( $P < 0.95$ ),  $I^2 = 0\%$   
 Test for over all effect  $Z = 0.71$  ( $P = 0.48$ )

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**Conclusion**

This Meta analysis shows that there is no difference in the immunogenicity of Cell Culture vaccines when administered through either the intramuscular or the intradermal route. A comparison of the costs incurred was also done, which showed that there was an excess cost of rupees nine hundred and fifty eight incurred by those who had the vaccine through the intramuscular route. To conclude, the Intradermal route of administration of modern Cell Culture Vaccines are efficacious and

economical alternative to the Intramuscular route of administration of the vaccines.

**Policy Implications**

As the modern cell culture vaccines used for post exposure prophylaxis in rabies is seen to be equally efficacious, when administered through either the intramuscular or intradermal routes and since there is a cost saving of nearly Rs.1000/- for those on the intradermal route, the decision taken by the government is most appropriate.