

## Original Article

## A Cross Sectional Study- Intradermal Versus Intramuscular Anti Rabies Prophylaxis

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### ABSTRACT

**Background:** Rabies is a disease caused by an RNA virus belonging to the Lyssa virus genus and capable of infecting all mammals. Rabies occurs in more than 150 countries and territories. In India, 20,000 human deaths occur due to rabies each year. Our study was conducted to highlight the economic advantages and compliance of using Intra Dermal (ID) regimen (Updated Thai Regimen) over Intra Muscular (IM) regimen (Essen Regimen).

**Objectives:** To assess compliance and cost benefits of ID regimen (Updated Thai Regimen) over IM regimen.

**Study design:** Hospital record based Cross sectional descriptive study.

**Methodology:** Patients who attended anti rabies vaccination OPD from 1 April, 2010 to 31 March, 2011 for IM regimen (Essen Regimen) and from 1 April, 2011 to 31 March, 2012 for ID regimen (Updated Thai Regimen) were included in study. Data was analyzed by using Epi-info 7 software.

**Result:** Class II exposure was most prevalent i.e. 72.02% in 2010-11 and 71.07% in 2011-12. In both regimen compliance of treatment was more in males compare to females. Compliance of treatment was more in Update Thai regimen (ID) as compared to Essen regimen, which is statistically significant. Also intradermal regimen found to be cost beneficial over intramuscular regimen.

**Conclusion:** Use of Intradermal regimen should be promoted over Intramuscular regimen as study shows Intradermal is more compliant and cost benefit.

**Key words:** Intradermal, Anti rabies prophylaxis, Dog-bite, Anti rabies vaccine (ARV), Compliance

### INTRODUCTION

Rabies is a disease entrenched in history, dating back to ancient Egypt. Caused by an RNA virus belonging to the *Lyssavirus* genus, rabies is capable of infecting all mammals. Rabies is primarily a disease of terrestrial and airborne mammals, including dogs, wolves, foxes, coyotes, jackals, cats, bobcats, lions, mongooses, skunks, badgers, bats, monkeys and humans [1]. The dog has been, and still is, the main reservoir of rabies in India. Other animals, such as monkeys, jackals, horses, cattle and rodents, seem to bite incidentally on provocation, and the fear of rabies leads the victim to seek post-exposure prophylaxis. The number of cases involving monkey bites has been increasing in the last few years. Monkeys are susceptible to rabies, and their bites necessitate post exposure prophylaxis [2].

Rabies occurs in more than 150 countries and territories [3]. With the expectation of some areas in the South Pacific, rabies persists as a major Public Health hazard in many countries across the world [4]. It is estimated that the South East Asia Region accounts for approximately 60% of human deaths due to rabies in the world [5]. Data available from 14 developing countries of Africa, Asia, South and Central America report a dog/inhabitant ratio of between 150/1,00,000 to 200/1,00,000 [6]. Stray dogs are mainly responsible for 99% of human infection [7]. In India, Some studies have estimated that there are as high as 17 million animal bites per annum and 20,000 human deaths occur due to rabies each year. Based on vaccine utilization, approximately 3 million people receive post-exposure treatment in our country.

Rabies is 100% fatal, at the same time 100% preventable if managed appropriately and timely. Anti-Rabies treatment is based on local wound care and administration of appropriate Rabies biological as Rabies Immunoglobulin and Vaccines.

Previously in India, nervous tissue vaccines (NTV) were used mostly. But with the advent of modern cell culture vaccines, which are highly potent and safe, the post-exposure vaccination for rabies underwent a dramatic change with almost painless injections, much reduced doses over the deltoid region and negligible side effects. But higher cost of intramuscular administration of Cell culture vaccine (CCV) is a limiting factor for its wider use [7].

To overcome this problem, WHO has recommended use of efficacious, safe and feasible intra-dermal (ID) route of inoculation of CCVs. Clinical trials conducted in India have proved intra-dermal route to be safe, efficacious and feasible for use in the country [7]. Our study was conducted to highlights the economic advantages and compliance of using ID regimen (Updated Thai Regimen) over IM regimen (Essen Regimen).

## MATERIALS & METHODS

This was hospital record based descriptive study, conducted on patients having animal bite and attended anti rabies vaccination clinic at Dr VMGMC & Hospital, Solapur. All patients who attended anti rabies vaccination OPD from 1 April, 2010 to 31 March, 2011 for IM regimen (Essen Regimen) [7] and from 1 April, 2011 to 31 March, 2012 for ID regimen (Updated Thai Regimen) [7] were included in study. Before start of study permission from the ethical committee was taken.

This hospital had implemented ID regimen for Anti-rabies vaccination from 1<sup>st</sup> April 2011, before that hospital were using IM regimen. So to compare cost effectiveness and compliance of ID regimen with IM regimen, data was collected for 2 year duration, 1 year before and 1 year after starting ID regimen from patients. Data was analyzed by using Epi-info 7 software and appropriate test of significant was applied wherever required.

## RESULTS

Total number of new registered animal bite cases was 14,935 in two year. Of this, 7796 animal bite cases

were registered during 2010-11 and 7166 during 2011-2012.

**Table 1: Distribution of patients according to Class of exposure**

Category of bite	During IM Regimen (2010-11)	During ID Regimen (2011-12)
<b>Category I</b>	0268 (02.31%)	0190 (02.65%)
<b>Category II</b>	5545 (72.02%)	5053 (71.07%)
<b>Category III</b>	1983 (25.67%)	1923 (27.99%)
<b>Total</b>	7796 (100%)	7166 (100%)

Table shows distribution of patients as per the WHO classification of animal bite wound and their administration of vaccination. In the present study, both year class II exposure was most prevalent i.e. 72.02% in 2010-11 and 71.07% in 2011-12 followed by class III exposure i.e. 25.67% in 2010-11 and 27.99% in 2011-12. (Table-1)

**Table 2: Total estimated expenditure on anti rabies treatment for both regimens**

	Intramuscular Regimen (2010-11)	Intradermal Regimen (2011-12)
<b>No. of patients requiring ARV</b>	7528	7071
<b>Total ARV required (in ml.)</b>	37640	5656.8
<b>Total cost (INR)</b>	1,12,92,000	16,97,040

(All calculation based in 1ml ARV vaccine e.g. Raipur, price=300INR)

In year 2010-11 total 7528 patients needed ARV doses. According to intra muscular regimen (Essen regimen) required 5 full doses to complete post exposure prophylaxis schedule per patient. Total cost of all doses was 1,12,92,000 INR (considering one ARV vial for 300 INR ).

**Table 3: Dose wise compliance of treatment for ID and IM regimen**

Received dose	IM (%)	ID (%)
<b>Only 1<sup>st</sup> dose (0)</b>	403 (05.35)	0353 (04.99)
<b>1<sup>st</sup> &amp; 2<sup>nd</sup> (0,3)</b>	446 (05.92)	0456 (06.45)
<b>1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, (0,3,7)</b>	932 (12.38)	1809 (25.58)
<b>1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> &amp; 4<sup>th</sup> (0, 3, 7, 14)</b>	2074 (27.55)	-----
<b>1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> 5<sup>th</sup> (0, 3, 7, 14, 28)</b>	3673 (48.79)	4453 (62.97)*
<b>Total</b>	7528 (100)	7071(100)

(\*For Intradermal regimen 14<sup>th</sup> day's dose is not in schedule)

In year 2011-12 total 7071 patients needed ARV doses. According to intra dermal regimen (update Thai regimen). Each patient need 0.2 cc X 4 doses and total dose required 0.8 ml for complete vaccination of one patient needs. So total cost of treatment of all patients was 16,97,040 INR. Thus for whole year total cost of treatment is reduce by 91,70,700 INR (Table 3).

Table 3 is showing pattern of drop out patients from Rabies prophylaxis. Drop out was maximum after fourth dose in IM regimen while it was maximum after third dose in ID regimen.

**Table 4: Compliance of treatment according to sex of patients**

Regimen	Sex	Completed (%)	Not completed (%)	Total (%)
<b>IM (2010-11)</b>	Male	2537 (49.98)	2539 (50.02)	5076 (100)
	Female	1136 (46.33)	1316 (53.67)	2452 (100)
	<b>Total</b>	3673 (48.79)	3855 (51.21)	7528 (100)
$(\chi^2=8.82, df=1, p<0.002, \text{highly significant})$				
<b>ID (2011-12)</b>	Male	3012 (65.52)	1585 (34.48)	4597 (100)
	Female	1441 (58.25)	1033 (41.75)	2474 (100)
	<b>Total</b>	4453 (62.97)	2618 (37.03)	7071 (100)
$(\chi^2=36.511, df=1, p<0.0000001, \text{highly significant})$				

It was observed that, in both regimen compliance of treatment was more in males compare to females. Compliance (completeness) of treatment in male was 49.98% in IM regimen and 65.52% in ID regimen (table 4). Difference between compliance of treatment and sex of patient's is found to be statistically significant in both regimens.

**Table 5: Comparison of compliance ID vs IM vaccination schedule**

Schedule	Completed	Not completed	Total
<b>IM (2010-11)</b>	3673 (48.79%)	3855 (51.21%)	7528 (100)
<b>ID (2011-12)</b>	4453 (62.97%)	2618 (37.03%)	7071 (100%)

$(\chi^2=297.2, d.f.=1, p<0.0000001, \text{highly significant})$

For IM regimen, Out of 7528 subjects, 3673 (48.79%) completed treatment and remaining 3855 (51.21%) not received complete treatment while for ID regimen,

Out of 7071 subjects, 4453 (48.79%) received completed treatment and remaining 2618 (37.03%) not received complete treatment (Table 5).

Compliance of treatment was more in Update Thai regimen (ID) as compared to Essen regimen (IM); this difference is found to be statistically highly significant.  $(\chi^2=297.2, df=1, p<0.0000001, CI=95\% \text{ highly significant})$

## DISCUSSION

Rabies is 100% fatal disease and after development of rabies there is no treatment for it. Only method to prevent rabies is anti rabies prophylaxis. For the prevention of rabies presently two type of vaccine regimen are in practiced in India. In both regimen cell culture vaccine is used. In India, IDRv was recommended for use in the government sector in 2006. Compliance to post-exposure vaccination is crucial to achieve optimum level of antibody titers. The present study was planned to assess the compliance of 4 dose Intra-dermal regimen (updated Thai regimen) over 5 dose intramuscular regimen (Essen regimen). It was observed that compliance was more in Intra-dermal regimen as compare to intramuscular regimen and it was found to be statistically significant. While administering the standard IM regimen, one of the major concerns is the requirement of repeated clinic visits by the patients which increases the cost of travel, more time spent and leading to lot of inconvenience. Probably these causes reduce the compliance of the patients to intramuscular regimen which may prove fatal in definite rabid exposures. A study conducted by Rohi KR, Mankeshwar R.(2014) [8] observed that compliance was more in Intradermal (65.3%) vaccination schedule as compared to intramuscular (40.2%) vaccination schedule. Similar finding was also demonstrated in studies conducted by Khawplod P, Wilde H et al (2006) [9] at Thailand that the compliance for the Intradermal regimen was high as compare to Intradermal regimen. Compliance of treatment was more in male compare to females for both regimens; it shows that irrespective of regimen compliance was more in male, probably due to- male has more outdoor activity, less house hold activity and ignorance to female health etc. So, more intense counseling of female patient and her family members about vaccination and follow up can be important strategy to improve compliance. Apart from compliance, Intradermal regimen found Cost Benefit over Intramuscular regimen (1500 INR in Intramuscular Vs 300 INR in Intradermal) cost of

treatment approximately reduces by 80% of intramuscular regimen. A study conducted by Rohi K R, Mankeshwar R (2014) [8] conducted study on 2051 patients, found that Intradermal regimen is more cost beneficial than Intramuscular (Essen) regimen. Present study showed that, 25.67% & 27.99% patients belongs to category III and 72.02% and 71.07% belongs to category II during year 2010-11 & 2011-12 respectively. Pattern of distribution was found similar during both year. N.J. Gogtay et al (2014) [10] found that maximum patients belonged to category II (78.3%) followed by category III (21.7%). Contrast to our study, Shah Venu, et al (2012) [11] found that 67.8% were belonged category III followed by 19% to category I and 13.2% to category II exposure. Study shows that as prophylaxis treatment precede dropout rate increased, so counseling part and follow up is very important to avoid dropouts. As incomplete treatment offer no immunity against rabies so given doses become useless if patient is non-compliant to treatment.

## CONCLUSION

With the availability of safe and potent tissue culture vaccines, prophylaxis of rabies is possible by immediate and appropriate post exposure treatment. Use of Intradermal regimen should be promoted over Intramuscular regimen as study shows Intradermal is more compliant and cost benefit. Proper counseling and follow up system should be developed to increase compliance and to avoid drop out. Counseling part should be more targeted toward women as they have less compliance toward treatment.

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