Table 3. The number and percentage (%) of seroconversions as per titer levell on days 14 and 28 in the PVRV pre- and post exposure ID regimen groups (Group 1 and 2).

RFFIT titers in UI/mL	Pre-exposure group		Post-exposure group	
	Day 14	Day 28	Day 14	Day 28
	N=60	N=60	N=60	N=60
0.5 - 0.99	4(6.7%)	3(5.0%)	1(1.7%)	1(1.7%)
1 - 30.99	56(93.3%)	54(90.0%)	59(98.3%)	57(95.0%)
31 - 60.99				1(1.7%)
61 and up		3(5.0%)		1(1.7%)

Note : No subject had detectable antibodies on Day 0.

Table 4. The geometric mean concentration (GMC, in IU/mL) and 95% confidence intervals (95% CI) in the PVRV pre-and post exposure ID regimen groups.

Ab Assay points	Pre-exposure group			Post-exposure group		
	Number of subjects	GMC	95% CI	Number of subjects	GMC	95% CI
Day 14	60	3.30	2.63-3.90	60	3.73	3.11-4.47
Day 28	60	4.37	3.68-6.12	60	4.82	3.90-5.97

Discussion

The occurrences of the mild local (redness and itchiness) and systemic (fever or body temperature rise) reactions in some of the subjects were considered as common sequels to any standard immunization regimens using current types of vaccines. The greater number of subjects that were observed to have developed redness at the site of vaccination in Group 1 compared with Group 2 was attributed to mere chance variation. Although, regardless of the cause, such mild redness (even with swelling) and mild itchiness at the site of injection is known to typically occur with most routine vaccinations including those for rabies [9]. These reactions are usually mild and are self-limiting.

The GMC values for both groups on days 14 and 28 were noted to have reached high levels. Notably, the GMC values in Group 1 were at levels close to the GMC values obtained in Group 2, even though the post-exposure subjects received additional vaccine doses with an additional vaccination on day 3. This seems to signify that even a single 0.1 mL ID dose of the vaccine administered at three points (days 0, 7 and 28) instead of four (plus a day 3) is sufficiently immunogenic. However, it is to be noted that six subjects in Group 1 had titers below 1 IU/mL on day 14 and two with titers at just above the cut-off value (0.5 IU/mL) on day 28, whereas in Group 2 there were only two subjects (one each on day 14 and 28) with titers below 1 IU/mL. Nevertheless, all these titers signified adequate seroconversions, so a conclusion on comparative merits could not be drawn. Overall, both groups gained reasonable titer levels on day 14, which signify a desirable rate of antibody development within two weeks of initiating immunization. The distributions of the subjects as per titer levels appear to be similar for both groups, except for a few outlying subjects, which accounted for the differences in the 95% Cis. Thus, both groups seem to have generally demonstrated adequate antibody responses with upsurges in GMCs from day 14 to day 28. However, day 7 and beyond day 28 titers were not determined in this study, which could otherwise further reveal relevant information on the rates and extents of seroconversions. As this study did not aim to determine the relative advantage of the (2-2-2-0-2) post-exposure ID regimen over the pre-exposure regimen, which requires fewer vaccine doses. This matter is set aside for further evaluation in the future.

The 20% dropout rate was believed to have had a minimal impact on the overall outcome of the study as the reasons given for withdrawal from the study were not related to occurrences of adverse reactions or to inadequate antibody responses. Based on the clinical observations and serologic assay results, it can be concluded that Abhayrab is a safe and immunogenic vaccine that could elicit the required, and even very high, antibody responses, if given intradermally to animal-bite patients. This study is in agreement with the report and recommendation of WHO stating that modern cell-culture rabies vaccines are well tolerated, safe and can be administered intradermally to people of all ages [8]. The conclusion is in line with the findings in a previous study conducted by the Indian Council of Medical

Research involving four different human rabies vaccines administered to subjects employing the intradermal regimen. Those results revealed that out of the four vaccines studied, only three, including Abhayrab, were suitable for use in intradermal rabies vaccination in India, with Abhayrab eliciting 100% seroconversion rates on days 14, 28 and 90, and the highest geometric mean antibody titers (GMT) on days 28 and 90 [10]. For more than 20 years, the ID route has been routinely and effectively used for other rabies vaccines [11-13], and recently for some other important human vaccines [14-18]. The use of the ID route, coupled with the use of a relatively affordable vaccine product, leads to significant savings in the total amount of vaccines required for a full pre- or post-exposure vaccination series, thereby enormously reducing the cost of active immunization for the benefit of the public.

In conclusion, Abhayrab is a safe and immunogenic rabies vaccine when administered intradermally. As this study involved healthy volunteer subjects, a follow-on study involving category III dog bite patients is being planned with both the test vaccine and a rabies immunoglobulin (RIG) being administered to the patients to determine the effect of RIG on the active antibody stimulation expected from the vaccine.

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