SPECIAL ARTICLE

The World Health Organization recommendations on rabies prophylaxis, 2018: What India should do?

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1. Preamble

Globally about 59,000 human rabies deaths are known to occur annually of which about 20,000 (one third) is from India alone. Recently in 2015, WHO declared the global goal of achieving dog mediated human rabies free world by 2030 to which India is also committed to. Till 2004 the nerve tissue (Sheep brain/ Semple) vaccine (NTV) formed the mainstay of rabies vaccination and the use of rabies immunoglobulin (RIG) was very low (2%) in the country. Following the stoppage of production of NTV in 2004, there was an immediate shift to cell culture vaccine (CCV) by intramuscular route (IM) that led to sudden scarcity of rabies vaccine in the country. Consequently, in 2006 the Government of India introduced the cost and vaccine saving intra-dermal rabies vaccination (IDRV) and simultaneously there was an increased production of CCVs both in the public and private sectors. Also the indigenous production of the Equine RIGs was started in the private sector. Though there was a good demand for rabies vaccine, the demand for RIGs was very poor due to professional apathy and public ignorance.

Recently in 2017 the Serum Institute of India, Pune has launched its indigenously produced and the world's first human rabies monoclonal antibody (R'Mab)

2. Current scenario

The current annual production of rabies vaccine (about four main brands – Rabipur, Abhayrab, Vaxirab-N & Indirab and other/ co-brands like Zoonovac-V, BeRab, XP-Rab, etc) in the country is about 30 million doses (2015-16); ERIG 1.5 million vials and R'Mab about 2 lakh vials since its launch in September, 2017 (personal communication). Occasionally a small and variable quantity of rabies vaccine is imported from China. The human RIG is imported and its quantity & availability are varied.

The rabies post-exposure prophylaxis (PEP) is by IM route in the private sector and in the government sector it is mostly by intra-dermal (ID) route in the bigger institutions and IM route in the smaller institutions. As rabies vaccine is procured by the state governments its availability is very varied among the different states.

Overall, in a recent WHO-APCRI survey of seven states, the vaccine availability was found "good" in the states of Gujarat, Kerala and Himachal Pradesh; "satisfactory" in Madhya Pradesh & Bihar and "bad" in Manipur. Though the use of RIG has improved from 2% in 2003 to 16% in 2017 but still in many instances it is being wrongly injected by IM route (34%). (APCRI, 2018)

The schedules of vaccination approved currently for use in India for post-exposure prophylaxis (PEP) are the five dose Essen regimen by IM route -one dose each injected on days 0-3-7-14-28, i.e. 1-1-1-1-1 ; updated Thai Red Cross Society (TRCS) by ID route , one dose of 0.1mL vaccine injected at two sites on days 0-3-7-28, i.e. 2-2-2-0-2 ; for pre-exposure prophylaxis (PrEP) – one vial of vaccine by IM route or 0.1mL of vaccine by ID route injected on days 0-7-21 or 28. (Government of India, 2015)

3. The WHO recommendations, 2018 on rabies prophylaxis (WHO, 2018, a)

3.1. The vaccine regimens: The following regimens are approved for use.

Regimen (post-exposure/PEP) and (pre-exposure, PrEP) regimen	Duration of course	No. of injection sites per clinic visit (days 0,3,7,14,21-28)
WHO – recommended intradermal regimen (PEP)		
1 week, two sites	7days	2-2-2-0-0
WHO-recommended intramuscular regimens (PEP)		
2 weeks	14-28 days	1-1-1-1-0
3 weeks	21 days	2-0-1-0-1
WHO –recommended intradermal regimen (PrEP)		
Two visits	7 days	2-0-2-0-0
WHO –recommended intramuscular regimen (PrEP)		
Two visits	7days	1-0-1-0-0

3.2. Use of rabies immunoglobulins

Infiltrate as much as possible into the wound; the remainder of the calculated dose of RIG does not need to be injected IM at a distance from the wound but can be fractionated in smaller, individual syringes to be used for other patients, aseptic retention given. If RIG is not available, thorough, prompt wound washing, together with immediate administration of the first vaccine dose, followed by a complete course of rabies vaccine, is highly effective in preventing rabies. Vaccines should never be withheld, regardless of the availability of RIG.

If a limited amount of RIG is available, RIG allocation should be prioritized for exposed patients based on the following criteria: Multiple bites, deep wounds, bites to highly innervated parts of the body (such as head, neck and hands), severe immunodeficiency, the biting animal is a confirmed or probable rabies case, and bites, scratches or exposures of mucous membranes caused by a bat.

If available, the use of MAb products instead of RIG is encouraged (WHO, 2018, b).

4. What India should do now?

India is heavily burdened with the problem of human rabies mortality despite producing good amounts of rabiesvaccine and ERIG/R'Mab and even exporting them. India has a federal structure, health is a subject under the domain of the states and as a result currently rabies biologicals are procured directly by the state governments from thevaccine producers using the state budget and consequentlythere is very little role for the central government.

The above recommendations of WHO need to be reviewed for its adoption/acceptance for implementation in the country by a national expert consultation and this is due at NCDC, Delhi on 8th January, 2019.Following a scarcity of rabies vaccines(&RIG) locally, Himachal Pradesh has gone a step ahead and already implemented the recent WHO recommendations. The new recommendations of the WHO for PEP has shortened the regimens from four weeks / 5 doses to three to four weeks / 4 doses (IM regimen) and from four weeks / 4 doses to one week / 3 doses(ID regimen). This is based on the clinical evidence of a single study from Cambodia, in a small population, using one vaccine (0.5mL, PVRV) that has limited reach out globally. In India, this vaccine is no more in use and besides four main other brands of vaccine are widely in use.

As rabies is practically 100% fatal, it is important that any reduction in the dosage/regimen of this life saving vaccine must be based on clinical evidence that is generated locally. Incidentally, prior to launching of the IDRV in the country in 2006, a national multicentric feasibility study was conducted in 2004-2005 by National Institute of Epidemiology, Indian Council of Medical Research, Chennai, using the locally available vaccines. Hence, even this

time it is important that local evidence is generated before effecting any shortening of the PEP regimens. This will also meet the regulatory requirements of the Drug Controller General of India, New Delhi for change of label/ package inserts of the rabies vaccines.

The new change in the procedure/practice of use of RIG giving it only locally/infiltrating into the wounds without any systemic injection (of the quantity left over after injecting all wounds) is based on the evidence generated by a centre in Shimla, HP, India and this too needs approval of national expert consultation .

Since human R'Mab, produced indigenously by Serum Institute of India is available, its use instead of RIG as recommended by WHO also needs to be finalized by the national expert consultation.

Lastly, APCRI must play a strong scientific advisory and advocacy role in this endeavour at the national level to ensure that effective regimen/s of rabies PEP are formulated to prevent human rabies deaths in the country.

References:

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