



Understanding Rabies in Indian scenario to defeat it

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ABSTRACT

Rabies is a fatal neuropathogenic disease. Of the estimated 55,000 deaths occurring world-wide attributable to rabies every year, 31,000 of occurs in Asia. In Asia the largest proportion of rabies death occurs in India. Dog bites are the primary source of human rabies in all rabies endemic countries and accounting for 96% of rabies cases in the South East Asia Region. The vision of Association for Prevention and control of Rabies in India is to "Make India Rabies Free by 2020". There is no specific treatment for clinical rabies. Post-Exposure prophylaxis includes local wound care, categorization of animal bite wounds, rabies immunoglobulin and anti-rabies vaccine. The recommended strategies for eradication of rabies in India include educating public about post exposure vaccination, addition of pre exposure rabies vaccination to routine childhood immunization schedule, making rabies a notified disease, vaccination of dogs and animal birth control programs.

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Introduction

Rabies is a zoonotic disease, in India it is recognised since Vedic period (1500- 500 BC) and described in Atharvaveda, where Yama, God of death is depicted to be attended by two dogs as his constant companions, the emissaries of death¹. Rabies is a fatal neuropathogenic disease caused by rabies virus, that is an enveloped RNA virus of Lyssa virus genus, Rhabdoviridae family². Rabies is primarily a disease of terrestrial and airborne mammals including dog, wolf, fox, coyote, jackal, cat, bobcat, lion, mongoose, skunk, badger, bat, monkey and human^{3, 4}. Bites or scratches introduce virus laden saliva from the rabid animal to the host. Nevertheless rare human cases have been transmitted by aerosols in laboratory accidents and in a cave containing millions of bats and also by transplantation of tissues and organs^{2, 5, 6}. The average incubation period is 1-3 months but may range from fewer than 7 days to 6 years⁷. It depends on several factors such as bite site, virus quantity in the saliva, kind of and depth of the bite wound and virulence of the virus⁸. This review was done to analyse the current strategies in achieving the Rabies free India. Information was collected from PubMed, Google Scholar and the WHO database using the key words Rabies, dog bite and animal bite. A manual search of the literature was conducted in the B.B. Dikshit library and National Medical library, New Delhi.

Burden:

Of the estimated 55,000 deaths occurring world-wide attributable to rabies every year, 31,000 of occurs in Asia⁹. In Asia the largest proportion of rabies death occurs in India¹⁰. In addition globally another 3 billion people are at risk in over 100 countries¹¹. Incidence of animal bites is 18 per 1000 population in India¹². It is estimated that there is an animal bite every second and death due to rabies every 30 minutes in India¹³. Surprisingly islands of Andaman and Nicobar and Lakshadweep are rabies free¹⁴. Dog bites are the primary source of human rabies in all rabies endemic countries and accounting for 96% of rabies cases in the South East Asia Region^{15, 16}. According to World Health Organization 40% of victims bitten by rabid animal are younger than 15 years of age^{17, 18}. The annual number

of person days lost is 38 million and cost of post bite treatment pegged at about 25 million US dollars³. The vision of Association for Prevention and control of Rabies in India is to "Make India Rabies Free by 2020"¹⁹.

Clinically, onset of rabies is insidious with a variable asymptomatic period following the incubation period. Prodromal symptoms of rabies are nonspecific and are frequently not recognized by the practicing clinicians. Most of the cases are of classic encephalitic or furious form, while progressive paralytic illness is less often seen. In classic rabies hydrophobia is present in 50 to 80 per cent of cases, while aerophobia and agitation alternating with calmness also occur²⁰⁻²². Local sensory symptoms like paraesthesia and itching also occur in as many as 30% of patients who develop rabies²³. Progression to death through various stages occurs in 100% of the cases. Patients with furious disease die earlier on average compared with those having paralytic form of the disease^{21, 22, 24, 25}. As the clinical features like hydrophobia and hyper salivation occur late and are often of milder nature in paralytic or "dumb" rabies²⁵ they are more challenging to diagnose. Clinical features of different clinical variants of rabies may be related to tropism of the virus, route of spread through nerves, sites of neural involvement, immune response to the infecting agent and possibly other pathological mechanism^{21, 22, 24}.

Current Strategies:

The World Health Organization has recommended classification of animal bite into three categories²⁶. Category I comprises touching or feeding of animals and animal licks on intact skin, no PEP is required if reliable history is available. Category II contact includes nibbling of uncovered skin by the animal and minor scratches or abrasions of the skin without bleeding. It is considered to be minor exposure and management includes local wound care and anti-rabies vaccination for active immunization. Category III contact includes single or multiple transdermal bites or scratches, licks on broken skin by the animal and/or contamination of mucous membrane with saliva.

There is no specific treatment for clinical rabies. Post-Exposure prophylaxis includes local wound care, categorization

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of animal bite wounds, local infiltration of rabies immunoglobulin for passive immunization and anti-rabies vaccine for active immunization. In addition injection tetanus toxoid should also be given to unimmunized individuals. Suitable antibiotic course can also be given to prevent sepsis in appropriate subjects. All bites whether provoked or unprovoked should be treated. Local wound management involves washing with soap under running tap water for at least 15 minutes. By mere washing of wounds and application of antiseptics reduces of the risk of rabies to half²⁵. Suturing of the wound is to be avoided, if unavoidable minimum number of loose sutures should be placed after adequate local treatment along with proper infiltration of rabies immunoglobulin. Cauterization of wound is no longer recommended²⁷.

Rabies vaccine was developed by Louis Pasteur and Émile Roux in year 1885²⁸. As a rule of thumb, live attenuated viral vaccines induce better immunity. But World Health Organization has forbidden the use of live attenuated rabies vaccine in humans due to risk of rabies²⁷. Available vaccines in India for intramuscular administration are Cell Culture Vaccines and Purified Duck Embryo Vaccine. Cell culture vaccines include Human Diploid Cell Vaccine, Purified Chick Embryo Cell Vaccine (PCECV) and Purified Vero Cell Rabies Vaccine (PVRV). Only Purified Vero Cell Rabies Vaccine is produced in public sector in India, rest are produced in private sector¹⁹. Window period of Vaccine is of 7-14 days²⁶. The World Health Organization recommends issue-culture or purified duck-embryo vaccines of potency at least 2.5 IU per single intramuscular immunizing dose should be applied according to the following intramuscular schedules. One dose of the vaccine should be administered on days 0, 3, 7, 14 and 30. All injections must be given into the deltoid region or, in small children, into the anterolateral area of the thigh muscle. Vaccine should never be administered in the gluteal region²⁷. There is no contraindication for post exposure immunization including pregnancy, lactation, HIV, AIDS and other infectious diseases¹⁹. Day 0 dose is to be doubled in patients who seek treatment after 48 hours of animal bite, have extensive bites, immune-deficient, severely malnourish, chronic disease or for whom rabies immunoglobulin is recommended but unavailable.

In order to reduce the cost of post-exposure treatment, the World Health Organization approved intradermal rabies vaccination in year 1992²⁷. In India intra-dermal rabies vaccination was started in 2006 at few sites¹⁹. The World Health Organization recommended the 2-site intradermal method (2-2-2-0-1-1) for use with PVRV and PCECV²⁷. Only three countries, Sri Lanka, Thailand, and Philippines are practicing intra-dermal rabies vaccination as a routine²⁹. As Thailand has longest experience for intra-dermal rabies vaccination, schedule from the Thai Red Cross is approved in India¹⁹. It is mandatory to get DCGI approval for all intradermal vaccines for rabies. These should be stored at a temperature of 2-8 Celsius. Content of these vaccines should be used within eight hours of reconstitution¹⁶. Vaccinated person is considered protective if rabies virus neutralizing antibody titre is greater than or equal to 0.5IU/ml³⁰.

Besides vaccination administration of rabies immunoglobulin is recommended for all category 3 bites, bites of wild animals and category 2 immunodeficient patients. Rabies immunoglobulin is always to be given along with vaccination. Ideally rabies immunoglobulin should be given within 24 hours of vaccination, if not up to 7 days latest. Recent World Health Organization stated that the equine rabies

immunoglobulin could be administration irrespective of skin test. Previously it was recommended that half of rabies immunoglobulin is to be infiltrated into the wound and the other half to be given intramuscular. Presently it is recommended that full dose of rabies immunoglobulin have to be infiltrated in the wound locally³¹.

Globally, the most cost effective strategy for preventing rabies in humans is eliminating rabies in dogs³². In addition control of dog population is done by animal birth control programme (ABC programme). In this the stray dogs are impounded, sterilized and released back in the area for where they were captured³³. To prevent dog bites Centre for Disease Control recommends that before bringing a dog into a household a professional to know the breeds of dogs are best fit for household, aggressive dogs with history of aggression should be avoided in household with children, before buying a dog some time should be spent with it, if infant or toddler is present in the house additional caution is required before bringing a dog into the house³⁴.

Challenges:

In rabies endemic country like India every animal bite should be considered as rabid animal bite and the management should be started immediately. Ignorance, fear of injections and cumbersome repeated visits to the hospital are reportedly the main reasons for the delay in reaching the hospital³⁵. Local wound management of animal bites is an important aspect of treatment but there is poor awareness of the correct practices for local wound management. It is associated with poor socioeconomic status and lower literacy²³. High cost of vaccine and non availability of free vaccine at the primary health facilities is a major hurdle. Moreover high cost of infiltration of immunoglobulin and anti-rabies serum at the site of animal bite declines its use. A multi-centric rabies survey in 2004 found that 79 percent of rabies victims did not receive vaccine treatment in India^{3,36}.

Longer incubation periods might make reaching a diagnosis difficult as the history of bite may not be recalled³⁷. Individuals should be immediately immunized after animal bite. However, those presenting late, even months later after possible rabies exposure need to be evaluated and managed³⁸. As rabies is not a notified disease in India and there is no recognized surveillance system, the number of actual deaths due to rabies may be much higher. Bites by domestic rats, mice, squirrel, hare and rabbit seldom require treatment. Human to human transmission of rabies may occur by organ transplantation and in close contacts of patients with rabies by coming in contact with their secretions. There are numerous myths about rabies in India treatment with herbal extracts, magic or religious practices, washing of wound can cause hydrophobia, dietary restriction, and single dose of vaccine will prevent rabies and others¹⁹.

Conclusion:

The recommended strategies for eradication of rabies in India include educating public about post exposure vaccination, addition of pre exposure rabies vaccination to routine childhood immunization schedule, making rabies a notified disease, vaccination of dogs and animal birth control programs. Patient should be advised not to touch the wound with bare hand, apply anything irritating and rub the site of intradermal injection after the injection is given. Patient should also be advised not to stop the course of immunization in between due to panic by the common side effects of vaccination like itching and pain at the site of injection. They should be counselled that no dietary restriction is needed. The patient should be informed that

deviation from standard management practices may lead to a failure of the schedule of post-exposure prophylaxis and this in turn can increase the risk of subsequent development of rabies. For pet lovers education should be done that infants or young children should not be left alone with the dog, aggressive games like wrestling should not be played with the dog and the dog should be properly socialized and trained. Children should also be taught not to approach unfamiliar dog, not to scream or run from a dog, to remain motionless when approached by unfamiliar dog, not to play with a dog unless supervised by an adult, not to disturb a dog that is sleeping, eating or caring for puppies, not to pet a dog without allowing it to see and sniff them, to roll into a ball and lie still if a dog knocks them.

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