Caring for patients with rabies in developing countries - the neglected importance of palliative care.
Arnaud Tarantola, Yoann Cabrol, Bangalore Jayakrishnappa Mahendra, Sotheary In, Hubert Barennes, Hervé Bourhy, Yiksing Peng, Sowath Ly, Philippe Buchy

To cite this version:

HAL Id: pasteur-01429841
https://hal-pasteur.archives-ouvertes.fr/pasteur-01429841
Submitted on 9 Jan 2017

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution 4.0 International License
Caring for rabies patients in developing countries - the neglected importance of palliative care

Arnaud Tarantola¹,²; Yoann Crabol¹; Bangalore Jayakrishnappa Mahendra³; Sotheary In¹,²; Hubert Barennes¹; Hervé Bourhy⁴; Yiksing Peng¹,²; Sowath Ly¹; Philippe Buchy⁵

1. Epidemiology and Public Health Unit, Institut Pasteur du Cambodge, Phnom Penh, Cambodia
2. Rabies Prevention Center, Institut Pasteur du Cambodge, Phnom Penh, Cambodia
3. Kodagu Institute of Medical Sciences, Madikeri, India
4. WHO Collaborating Centre for Reference and Research on Rabies, Institut Pasteur, Paris, France
5. Virology Unit, Institut Pasteur du Cambodge, Phnom Penh, Cambodia
6. GlaxoSmithKline, Vaccines Value & Health Sciences, 150 Beach Road, Singapore

Contact:
Arnaud Tarantola, MD, Msc
Head, Epidemiology and Public Health Unit
Institut Pasteur du Cambodge
5, Bvd. Monivong
BP 983 - Phnom Penh
Royaume du Cambodge
Mobile: +855 (0) 12 333 650
Fax: +855 (0) 23 725 606

Email: atarantola@pasteur-kh.org
Ten years after “Management of rabies in humans” – a developing country perspective

Key points

Human rabies cases occur in rural developing settings where clinicians lack training and medication. Even in resource-poor settings and using essential drugs, there is much healthcare workers can do to help patients and families at no risk to themselves.

Key words

Rabies ; treatment ; palliative care; diazepam; midazolam; hydrophobia; developing countries

Abstract

Although limited publications address clinical management of symptomatic rabies patients in intensive care units, the overwhelming majority of human rabies cases occur in the rural setting of developing countries where healthcare workers are few, lack training and drugs. Based on our experience, we suggest how clinicians in resource-limited settings can make best use of essential drugs to provide assistance to rabies patients and their families, at no risk to themselves. Comprehensive and compassionate patient management of furious rabies should aim to alleviate thirst, anxiety and epileptic fits using infusions, diazepam or midazolam and antipyretic drugs via intravenous or intrarectal routes. Although the patient is dying, respiratory failure must be avoided especially if the family, after being informed, wish to take the patient home alive for funereal rites to be observed. Healthcare staff should be trained and clinical guidelines should be updated to include palliative care for rabies in endemic countries.
In 2003, Jackson AC. et al. wrote a comprehensive and well-cited article on the management of human rabies, duly reminding us of its dismal outcome, even in intensive care units of resource-rich countries. As the authors then clearly stated, most human rabies cases notified worldwide occur in developing countries where rabies remains a major and probably underestimated public health issue, even emerging in some heretofore unaffected territories. Over a decade later, little has changed in terms of clinical management of human rabies.

Not all persons who are bitten by a rabid animal become infected with rabies and human patients have – in extremely rare instances - survived rabies, mostly in the New World. This is not the case with confirmed cases of human rabies acquired from dogs in the Old World, which overwhelmingly have a lethal outcome: only two reported cases have survived rabies in India, the country with the highest burden, but both had gross neurological sequelae.

Rabies cases occur mostly in rural settings of developing countries. Few of the many dog bite victims in countries such as Cambodia have access to timely and appropriate post-exposure prophylaxis (PEP). Worldwide, there are an estimated 59,000 human rabies cases (and deaths) attributed to rabies each year.

To date, there is no effective and validated etiological treatment available for rabies once the symptoms have set in and clinicians remain seemingly powerless. This is particularly the case in the rural developing setting where little or no intensive care is available or remains beyond geographical or financial reach. What then can we do to aid rabies patients - especially in rural areas - of developing countries?
Health care workers (HCW) in developing countries confronted with human cases of suspected or confirmed rabies are not entirely helpless and their role remains essential. We wish to remind readers of the specificities of managing rabies cases in the developing setting.

Diagnosis remains a priority when rabies PEP has been undertaken and failed. Other people potentially exposed to the same animal and those among the relatives and the healthcare workers who would require PEP must quickly be identified. In approximately 20% of cases, a "paralytic" presentation resembling Guillain-Barré syndrome will require little intervention on the part of the clinical team. In most (80%) of cases, human rabies, febrile or otherwise, will have a “furious” rabies presentation. Although the patient will most likely die, prompt, effective and holistic compassionate clinical management can alleviate suffering for the patients and their families. This can be performed even with extremely limited equipment and drugs. If possible, the patient should be managed in a quiet and darkened room. Patient privacy and dignity must be preserved. Management of furious cases with hydrophobia and several days of fever, however, will require prompt and determined intervention, which must first and foremost alleviate the sensation of thirst, which in our experience can be of mythical proportions. This can be done through infusion of 5% glucose solutions to compensate loss of water or isotonic (0.9% NaCl) saline solution to compensate water and sodium loss, being careful to immobilize the limb with a splint to prevent needle displacement.

Subcutaneous or intraperitoneal infusion are a useful alternative. Rather than restraint, spastic signs and anxiety can be alleviated with diazepam which will also provide myorelaxant, anticonvulsivant and sedative effects. Diazepam is an affordable drug and is widely available as a part of WHO’s Model List of Essential Medicines. It can be administered intravenously (IV) or intramuscularly or intrarectally (IR) (0.1-0.3 mg/kg IV over 3-5 minutes in children or 0.5 mg/kg intrarectally ; 10 mg IV or IR in adults). This can be repeated every 1 - 4 hours and can be continued over 24 hours using IV infusion (3-10
mg/kg if needed, guided by symptomatology, taking care to avoid respiratory depression. The intrarectal route can be used at the same doses for maintenance therapy if the infusion cannot be maintained or if the patient is taken home by the informed family. Clinicians - and families - should be aware of the risks of respiratory depression and aspiration. An effective alternative, midazolam is included in WHO's List of Essential Medicine. Following a bolus (depending on required level of sedation), midazolam can be administered at a dose of 1 mg every 10 minutes by the intravenous route, taking care to reduce doses in dehydrated/hypovolemic patients. Intramuscular or subcutaneous routes are also possible. Lorazepam is another option, if available, which can also be administered subcutaneously.

Treating fever by sponging may not be tolerated by a "furious" rabies patient, but alternating or combined ibuprofen and paracetamol (also called acetaminophen) by non-oral routes (intravenous, injectable or intrarectal) in patients with hydrophobia may provide some relief by somewhat abating fever if it is present. Unfortunately, these drugs are often not available in injectable form in the developing setting and intrarectal paracetamol/acetaminophen does not effectively provide analgesia in the short-term.

Physical restraint is often used by health care teams who fear that rabid patients may harm them or themselves. It may be useful to prevent infusion displacement or self-harm, but should be used sparingly as it stimulates agitated patients. Restraints may be loosened as soon as patients become sedated/more calm. After prompt albeit limited medical intervention has offered whatever relief it can, local beliefs and economic constraints must be taken into account, in agreement with the patient if possible and the family. In Cambodia, for instance, the patient is usually sent home, preferably alive so that religious rites can be administered and the family not be burdened with the added cost of returning home with a cadaver, which is usually much more costly than with even a moribund patient. Planning for transport may
lead to preferring non-intravenous administration routes.

In developing countries - as probably elsewhere - HCW are fearful of contracting rabies during care. Furthermore, whatever available health care is usually delivered in the first few days or hours by family members potentially exposed to body fluids and without personal protective equipment. Although the risk of transmission from human to human is considered nil, their concerns must be addressed and they must be offered PEP (targeting Category II) following exposure to a human rabies case. This will help ensure they continue to provide the best available care to suspected rabies patients.

The situation of many developing countries is well illustrated by that of Cambodia, a highly enzootic country where only three PEP centers are freely accessible to the public. Much work is needed on the part of the authorities to make PEP accessible after a potentially infective dog bite in developing countries. A network of bite management centers must be developed in rural areas while management of dog populations and systematic immunization of dogs must be promoted countrywide. As clinical guidelines do not include rabies management, much training and communication is also needed. The place of palliative care in the management of rabies patients must be addressed in national and international guidelines. This would help HCW in developing settings realize that - even if the rabies patient will die - they can dramatically alleviate the suffering of rabies patients and their families, at no risk to themselves.

Acknowledgements

We thank Drs. Cécile Aubron and Olivier Huet for their advice and editorial help.

Declaration of competing interests

No competing interests. Philippe Buchy is an employee of GSK Vaccines.


29. **WHO | Midazolam (Inclusion) -- Adults and Children. WHO.**

   http://www.who.int/selection_medicines/committees/expert/18/applications/Midazolam/en/


40. **Clinical Practice Guidelines for Paediatric.;** 2013. ttp://www.webcitation.org/6LpefKr0M.