Insecticide treatment of cattle to kill sand flies and combat leishmaniasis

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Bihari villagers live and work in close proximity to their livestock. Credit: David Poché

With an estimated 500,000 human infections and 50,000 deaths annually, visceral leishmaniasis (VL) is the second most prevalent parasitic killer, behind malaria. *Leishmania* parasites are transmitted through the bite of phlebotomine sand flies. A study published in *PLOS Neglected Tropical Diseases* makes the case that fighting the insects by treating cattle with the long-lasting insecticide, fipronil, could substantially reduce VL in areas where people and cattle live in close proximity.

Two-thirds of VL cases occur on the Indian subcontinent, and 90% of the Indian VL cases are reported in the densely populated and impoverished state of Bihar. Female sand flies there primarily bite humans and cattle (mostly at night), and after sand fly eggs hatch, the larvae feed on organic matter, the most abundant source being cow patties. At present, control of sand flies in India involves indoor residual spraying with pyrethroid insecticides, but Bihari villagers regularly sleep outdoors during the hot summer months.

Fipronil is an insecticide with a long half-life. The insecticide remains in the system of animals for several weeks to several months, dependent on the concentration administered. Fipronil does not harm mammals at low concentrations, but when fed to cattle at low concentrations in drug form, can kill adult blood-feeding sand flies and sand fly larvae that feed on the cattle feces. Fipronil-based sand fly control could therefore last for several months following a single treatment—and complement the practice of indoor spraying.

David Poché, from Texas A&M University in College Station, USA, and colleagues set out to explore the insecticide's potential to control sand flies. The researchers developed a mathematical model that describes the effects of fipronil-induced mortality on a sand fly population within a village in Bihar. They describe the model and evaluate its performance based on known parameters. Then they use the model to simulate

fipronil-based control schemes with different treatment timing and frequency, and compare their effect on reductions in sand fly populations during spring and summer (June, July, and August are the period of peak human exposure).

Single annual treatments applied in March, May, June, or July noticeably reduced the population peaks that occurred over the 30 to 60 days following treatment, but populations recovered relatively quickly. Treatments applied 3 times per year at 2-month intervals were most effective when initiated in March, reducing the population peaks in April through August by roughly 90% relative compared with no treatment. Treatments applied 6 times per year at 2-month intervals were most effective when initiated in January, reducing population peaks in June through August by over 95%. Monthly treatments resulted in eradication of the sand fly population within 2 years.

Overall, the simulation results suggest that the success of fipronil treatment depends not only on the frequency of applications but also on the timing relative to the sand fly lifecycle. Maintaining high drug levels in cattle feces during the period of high larval abundance seems particularly important.

As the researchers discuss, "while more frequent applications obviously are more efficacious, they also are more expensive and more difficult logistically. Thus, the ability to assess not only efficacy of treatment schemes per se but also their cost-effectiveness and their logistical feasibility is of paramount importance". In this context, they mention an estimated cost of $1 per cow per treatment, as well as the fact that milk production per cow is estimated to increase by $0.50 per day, thus offering an incentive to villagers to treat their animals.

Further evaluation of sand fly control through the use of fipronil-based drugs in cattle, the researchers say, ideally would involve a field trial in

Bihar. Such a trial could provide data on the actual proportion of adult sand flies that obtain their blood meal from cattle and the proportion of eggs laid in organic matter containing cattle feces; numbers that are currently unknown and therefore force the researchers to make assumptions that cause uncertainty in the model predictions.

Suggesting that their model could be adapted to settings where donkeys, dogs, rabbits, or rodents are the main animal targets of blood-thirsty sand flies, the researchers hope that it "will prove useful in the a priori evaluation of the potential role of treatment schemes involving the use of fipronil-based drugs in the control of leishmaniasis on the Indian Subcontinent and beyond".

More information: Poché DM, Grant WE, Wang H-H (2016) Visceral Leishmaniasis on the Indian Subcontinent: Modelling the Dynamic Relationship between Vector Control Schemes and Vector Life Cycles. *PLoS Negl Trop Dis* 10(8): e0004868. DOI: 10.1371/journal.pntd.0004868