Ribavirin for Lassa Fever Postexposure Prophylaxis

To the Editor: Lassa fever is an acute, viral, hemorrhagic illness endemic to West Africa. Intravenous ribavirin drastically reduces deaths from Lassa fever (/). During outbreaks, oral ribavirin is often considered for postexposure prophylaxis (PEP), but no systematically collected data exist for this indication of drug use (/–5). We therefore conducted a retrospective follow-up study to examine adherence and adverse effects associated with oral ribavirin given as PEP during an outbreak of Lassa fever in Sierra Leone in 2004 (/6). During this outbreak, family members and some healthcare workers who had direct contact with patients did not use personal protective equipment and were subsequently prescribed oral ribavirin as PEP (200 mg capsules; Schering-Plough Corporation, Kenilworth, NJ, USA).

Approximately 3 months after the possible exposures, we surveyed 23 (92%) of 25 persons known to have been prescribed ribavirin PEP. Respondents were asked about demographics, medical history, details of possible exposure to Lassa virus (LASV), dosage and duration of ribavirin prescribed and taken, and use of concomitant medications. When possible, serum was obtained and tested by ELISA for LASV-specific immunoglobulin (Ig) M and IgG (7).

The mean age of the 23 respondents was 38 years (range 23–73 years); 14 (61%) were male, 17 (74%) had been exposed at home (during bathing, cleaning, and feeding of family members with Lassa fever), and 6 (26%) had had in-hospital contact with blood and bodily fluids. No needle-stick injuries were reported.

All respondents had begun taking oral ribavirin within 2 days after exposure. The drug was prescribed at a mean dose of 800 mg 1×/d (most often as 400 mg 2×/d) for 10 days; however, respondents reported actually taking 400–1,200 mg/d. Only 10 (43%) completed the full 10 days of therapy; mean duration of therapy was 8 days (range 1–14 days). No correlation was found between the prescribed daily dose of ribavirin and the likelihood of completing therapy (p = 0.60).

Therapy was completed by 6 (38%) of the 16 (70%) respondents who reported having experienced minor adverse effects and by 4 (57%) of the 7 who reported not having experienced adverse effects (Figure). Many respondents reported having had symptoms even before beginning ribavirin, suggesting at least a partial psychosomatic or other etiology. No correlation was found between likelihood of adverse effects and age (p = 0.18), sex (p = 0.16), or place of exposure (p = 0.63). Six (26%) respondents reported having preexisting health conditions (gastric ulcers, n = 3; gastrointestinal reflux disease, n = 2; hypertension, n = 1), and 15 (65%) took medications in addition to ribavirin during the postexposure period.

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period, including paracetamol, folic acid, multivitamins, iron, antacids, antimalarial drugs, antimicrobial drugs, and nonsteroidal anti-inflammatory drugs.

Minor adverse effects from oral ribavirin PEP, either biologic or psychosomatic, were frequently noted and decreased adherence. Many of the same adverse effects have been reported (8). Because interviews in our study were conducted months after medication had been taken, recall bias may have occurred. However, 11 (85%) of the 13 respondents who reported not completing therapy could show the interviewer their leftover ribavirin capsules, thus validating their reports. The observational nature of our study prevented us from establishing a causal association between taking ribavirin and the reported adverse effects. Other factors, especially the anxiety often associated with possible LASV exposure, likely contributed to the noted symptoms.

Although we cannot exclude the possibility of asymptomatic infection, we found no evidence of secondary transmission of LASV among the respondents. One person reported having fever and malaise after exposure, but test results for LASV were negative. Only 8 (35%) persons consented to follow-up laboratory testing, probably because most did not think it was necessary because of lack of symptoms; all 8 were LASV IgM negative. The duration of IgM after LASV infection has not been well characterized, and antibodies could have cleared in the 3 months between exposure and testing (7). Another possibility is that swift administration of ribavirin blunted the antibody response. Although not studied in humans, total Ig titers in LASV-infected, ribavirin-treated monkeys eventually reached titers similar to those in untreated monkeys (9). Three persons were LASV IgG positive, indicating past exposure. All 3 had other risk factors for infection in addition to their recent exposure, including residence in a Lassa fever–hyperendemic area (all 3) and occupation as healthcare workers (2 of 3).

The limitations inherent in our study are its small sample size and retrospective, uncontrolled design. Considering the relatively low secondary attack rate, the restriction of LASV endemicity to remote areas of West Africa, and the infrequency of high-risk exposures, controlled trials for ribavirin PEP in Lassa fever will probably never be possible. Experiences in the field must therefore be used to inform future decisions with regard to use of ribavirin for this indication. Use of oral ribavirin PEP for Lassa fever is likely to be challenging because of poor adherence and adverse effects.

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References

Transmission of Ovine Herpesvirus 2 from Asymptomatic Boars to Sows

To the Editor: Malignant catarrhal fever (MCF) is an often lethal viral disease of susceptible biungulates from the Bovidae, Cervidae, and Suidae subfamilies. MCF in pigs has been associated with direct or indirect contact with sheep, which are the main reservoir of ovine herpesvirus 2 (OvHV-2) (1). A recent report detected infected but asymptomatic swine in the absence of known exposure to sheep or goats (2). Porcine MCF is difficult to diagnose because of its nonspecific clinical signs and sporadic nature; however, an outbreak involving 41 swine has been described (3). Pigs are terminal hosts and are not believed to spread the virus. Here we describe OvHV-2 DNA in the blood and semen of asymptomatic boars and from the brain of symptomatic sows and gilts with MCF that was probably transmitted by artificial insemination.

The MCF cases occurred on two 3-site commercial farms with 2,700 and 1,670 sows in 2 different counties in southwestern Brazil. No MCF losses previously had been recorded in the region, and the animals had no known direct or indirect contact with sheep. The 2 farms had high biosecurity. The first case was recorded in September 2004, and the number of cases increased in July 2006. Twenty-eight sows and gilts, 20 of them pregnant and at >25 days’ gestation, died during January 2007–March 2008, when the last case was observed.

Clinical features in sows and gilts were depression followed by abortion, fever (41°C), and anorexia. After the onset of clinical signs, neurologic symptoms developed such as ataxia, tremors, convulsions, and aggressive behavior. Animals that survived longer showed forelimb paralysis, stood in a dog-sit position, and gnawed with abundant salivation on pen bars.

Specimens from randomly selected dead sows and gilts from the outbreaks during 2004–2008 were obtained for histopathologic examination, immunofluorescence testing for rabies virus, viral and bacterial isolation, and PCR. No bacterial or viral growth was detected, and direct immunofluorescence for rabies virus was negative. Microscopic examination showed high-grade nonpurulent meningoencephalitis characterized by lymphocytic cuffings with vasculitis in the brain hemisphere, the brainstem, the spinal cord, and, to a lesser extent, the cerebellum. Multifocal areas of edema, fibrinoid necrosis, and lymphocytic infiltration also were observed (Figure). OvHV-2 DNA was detected by using a specific PCR (4) in 5 of 7 paraffinized sections of the brainstem (5). To analyze the possible presence of other porcine lymphotropic herpesviruses in samples that reacted positively for OvHV-2, a nested PCR with degenerate primers (6,7) was applied. None of the OvHV-2–positive samples reacted positively for porcine lymphotropic herpesviruses. To confirm that the virus was a member of the MCFV group, we purified 1 amplicon and submitted it for automated sequencing. This nucleotide sequence was deposited in GenBank under accession no. HQ223415, and it showed 99% identity with previously deposited OvHV-2 sequences.

To find possible carriers of the virus, blood samples were collected from 9 pregnant sows, 10 nonpregnant sows, and 30 breeding boars and analyzed for OvHV-2 DNA. Samples from 3 boars were positive. Nasal swabs and semen samples were collected from these infected boars to investigate the potential mode of OvHV-2 transmission, and OvHV-2 DNA was detected only in semen samples. Two of the 3 semen samples had >350 copies/2 μg of total DNA, suggesting that these...