



## Letter to the Editor

**Evidence supports ribavirin use in Crimean-Congo hemorrhagic fever**

The Perspective “Ribavirin is not effective against Crimean-Congo hemorrhagic fever: observations from the Turkish experience” by Ceylan et al.,<sup>1</sup> published in this Journal, reflected the ‘against’ side of a debate performed in ‘for and against’, or ‘pro et contra’ style that took place in Istanbul in May 2012. The debate concerned the use of ribavirin in Crimean-Congo hemorrhagic fever (CCHF). I was coaching the pro-ribavirin group. From my observations, at the end of the talk, a consensus was reached on the use of ribavirin in post-exposure prophylaxis (PEP), such as after a needle-stick injury of a healthcare worker (HCW). As a result, the question arose: If we use ribavirin for PEP, then why not give it for treatment? I will explain the evidence.

Many studies have previously shown the beneficial effects of ribavirin, despite the lack of power, and the benefit has also been shown in a recent powerful study.<sup>2</sup>

The authors of the Perspective claimed that ribavirin therapy has not been shown to decrease the case-fatality rate (CFR) in Turkey. The published evidence is against this claim.<sup>2–6</sup> Further, some of the studies cited by the authors in their references list are in favor of the use of ribavirin, including those published by our group.<sup>7,8</sup> One study against ribavirin was severely biased, and moreover some of the authors of that biased study were not in agreement with what was written – an editorial has already been published.<sup>9</sup>

Performing a randomized clinical trial (RCT) to examine the role of ribavirin in CCHF is in contravention to the Declaration of Helsinki.<sup>10</sup> Despite this fact, an RCT has been performed.<sup>11</sup> This RCT was biased, because it included late cases. Ribavirin may not be beneficial at the late stage of the disease.<sup>2</sup> Further, the sample size was not calculated.

In another biased study referred to by the authors, oral ribavirin was not given to CCHF patients and a CFR of 5% was reported.<sup>12</sup> However, in another study carried out in a similar setting, the CFR was 2.9% with the use of early ribavirin.<sup>3</sup> The 5% fatality rate cannot be accepted as normal.

Although the authors mentioned the renal and hepatic side effects of ribavirin in the biased study,<sup>9</sup> they did not report the number of patients who experienced these side effects.

In summary, ribavirin has been found to be effective in the treatment of CCHF<sup>2</sup> and as post-exposure prophylaxis,<sup>4</sup> and should be given as early as possible.<sup>2–4</sup> If the physicians who are against

the use of ribavirin were to be infected with the CCHF virus (which I sincerely hope never occurs), would they reject ribavirin treatment? Then, remember the Hippocratic Oath: *primum non nocere*. So, why not give this treatment to the patients?

*Conflict of interest:* No conflict of interest to declare.

**References**

- Ceylan B, Calica A, Ak O, Akkoyunlu Y, Turhan V. Ribavirin is not effective against Crimean-Congo hemorrhagic fever: observations from the Turkish experience. *Int J Infect Dis* 2013;**17**:e799–801.
- Dokuzoguz B, Celikbas AK, Gok SE, Baykam N, Eroglu MN, Ergonul O. Severity scoring index for Crimean-Congo hemorrhagic fever and the impact of ribavirin and corticosteroids on fatality. *Clin Infect Dis* 2013;**57**:1270–4.
- Ozbey SB, Kader C, Erbay A, Ergonul O. Early use of ribavirin is beneficial in Crimean-Congo hemorrhagic fever. *Vector Borne Zoonotic Dis* 2014;**14**:300–2.
- Celikbas AK, Dokuzoguz B, Baykam N, Gok SE, Eroglu MN, Midilli K, et al. Crimean-Congo hemorrhagic fever among health care workers, Turkey. *Emerg Infect Dis* 2014;**20**:477–9.
- Ergonul O. Treatment of Crimean-Congo hemorrhagic fever. *Antiviral Res* 2008;**78**:125–31.
- Ergonul O, Celikbas A, Dokuzoguz B, Eren S, Baykam N, Esener H. Characteristics of patients with Crimean-Congo hemorrhagic fever in a recent outbreak in Turkey and impact of oral ribavirin therapy. *Clin Infect Dis* 2004;**39**:284–7.
- Tasdelen Fisgin N, Ergonul O, Doganci L, Tulek N. The role of ribavirin in the therapy of Crimean-Congo hemorrhagic fever: early use is promising. *Eur J Clin Microbiol Infect Dis* 2009;**28**:929–33.
- Ozkurt Z, Kiki I, Erol S, Erdem F, Yilmaz N, Parlak M, et al. Crimean-Congo hemorrhagic fever in Eastern Turkey: clinical features, risk factors and efficacy of ribavirin therapy. *J Infect* 2006;**52**:207–15.
- Ergonul O. DEBATE (see Elaldi N et al., Efficacy of oral ribavirin treatment in Crimean-Congo haemorrhagic fever: a quasi-experimental study from Turkey. *Journal of Infection* 2009; **58**: 238–244): biases and misinterpretation in the assessment of the efficacy of oral ribavirin in the treatment of Crimean-Congo hemorrhagic fever. *J Infect* 2009; **59**:284–6; author reply 286–9.
- Arda B, Aciduman A, Johnston JC. A randomised controlled trial of ribavirin in Crimean Congo haemorrhagic fever: ethical considerations. *J Med Ethics* 2012;**38**:117–20.
- Koksal I, Yilmaz G, Aksoy F, Aydin H, Yavuz I, Iskender S, et al. The efficacy of ribavirin in the treatment of Crimean-Congo hemorrhagic fever in Eastern Black Sea region in Turkey. *J Clin Virol* 2010;**47**:65–8.
- Duygu F, Kaya T, Baysan P. Re-evaluation of 400 Crimean-Congo hemorrhagic fever cases in an endemic area: is ribavirin treatment suitable? *Vector Borne Zoonotic Dis* 2012;**12**:812–6.

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