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[Intervention Review]

Ribavirin for treating Crimean Congo haemorrhagic fever

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ABSTRACT

Background

Crimean Congo haemorrhagic fever (CCHF) is a tick-borne disease that occurs in parts of Asia, Europe and Africa. Since 2000 the infection has caused epidemics in Turkey, Iran, Russia, Uganda and Pakistan. Good-quality general supportive medical care helps reduce mortality. There is uncertainty and controversy about treating CCHF with the antiviral drug ribavirin.

Objectives

To assess the effects of ribavirin for treating people with Crimean Congo haemorrhagic fever.

Search methods

We searched the Cochrane Infectious Diseases Group Specialized Register; the Central Register of Controlled Trials (CENTRAL); MEDLINE (PubMed); Embase (OVID); Science Citation Index-Expanded, Social Sciences Citation index, conference proceedings (Web of Science); and CINAHL (EBSCOHost). We also searched the WHO International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov for trials in progress. We conducted all searches up to 16 October 2017. We also contacted experts in the field and obtained further studies from these sources.

Selection criteria

We evaluated studies assessing the use of ribavirin in people with suspected or confirmed Crimean Congo haemorrhagic fever. We included randomised control trials (RCTs); non-randomised studies (NRSs) that included more than 10 participants designed as cohort studies with comparators; and case-control studies.

Data collection and analysis

Two review authors assessed eligibility, risk of bias, and extracted data. For non-randomized studies we used the ROBINS-I tool to assess risk of bias. The main effects analysis included all studies where we judged the risk of bias to be low, moderate or high. We summarized dichotomous outcomes using risk ratios (RRs) and continuous outcomes using mean differences (MDs), and used meta-analyses where appropriate. We carried out a subsidiary appraisal and analysis of studies with critical risk of bias for the primary outcome, as these are often cited to support using ribavirin.

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Main results

For the main effects analysis, five studies met our inclusion criteria: one RCT with 136 participants and four non-randomized studies with 612 participants. We excluded 18 non-randomized studies with critical risk of bias, where none had attempted to control for confounding.

We do not know if ribavirin reduces mortality (1 RCT; RR 1.13, 95% confidence interval (CI) 0.29 to 4.32; 136 participants; very low-certainty evidence; 3 non-randomized studies; RR 0.72, 95% CI 0.41 to 1.28; 549 participants; very low-certainty evidence). We do not know if ribavirin reduces the length of stay in hospital (1 RCT: mean difference (MD) 0.70 days, 95% CI -0.39 to 1.79; 136 participants; and 1 non-randomized study: MD -0.80, 95% CI -2.70 to 1.10; 50 participants; very low-certainty evidence). We do not know if it reduces the risk of patients needing platelet transfusions (1 RCT: RR 1.23, 95% CI 0.77 to 1.96; 136 participants; very low-certainty evidence). For adverse effects (including haemolytic anaemia and a need to discontinue treatment), we do not know whether there is an increased risk with ribavirin in people with CCHF as data are insufficient.

We do not know if adding ribavirin to early supportive care improves outcomes. One non-randomized study assessed mortality in people receiving ribavirin and supportive care within four days or less from symptom onset compared to after four days since symptom onset: mortality was lower in the group receiving early supportive care and ribavirin, but it is not possible to distinguish between the effects of ribavirin and early supportive medical care alone.

In the subsidiary analysis, 18 studies compared people receiving ribavirin with those not receiving ribavirin. All had a critical risk of bias due to confounding, reflected in the mortality point estimates favouring ribavirin.

Authors' conclusions

We do not know if ribavirin is effective for treating Crimean Congo haemorrhagic fever. Non-randomized studies are often cited as evidence of an effect, but the risk of bias in these studies is high.

2 April 2019

Up to date

All studies incorporated from most recent search

Updated review: all eligible published studies found in the last search (16 Oct, 2017) were included

PLAIN LANGUAGE SUMMARY

Ribavirin for treating Crimean Congo haemorrhagic fever

What is the aim of this review?

The aim of this Cochrane review is to find out if ribavirin is an effective treatment for Crimean Congo haemorrhagic fever. Cochrane researchers collected and analysed all relevant studies to answer this question. We found 23 studies. We include five studies in this review that helped answer the question. We analysed the other 18 studies to help describe the limitations of the evidence.

Key messages

There is insufficient reliable evidence to show whether ribavirin is effective in treating Crimean Congo haemorrhagic fever. A randomised clinical trial could help answer this question.

What was studied in the review?

Crimean Congo haemorrhagic fever (CCHF) is an infection spread by tick bites. It has become more common in the last 15 years, particularly in Turkey and parts of Eastern Europe. CCHF can be life threatening. The most important way of caring for people who are seriously unwell with CCHF is to monitor them closely in hospital and give them any fluid or blood products they may need.

Ribavirin is an antiviral drug that some doctors use to treat CCHF. It is widely available and is normally taken by mouth. There is debate over whether ribavirin is needed to treat CCHF; some argue that it is an effective treatment, or helps if given early, whilst others say that it has no effect, in terms of the risk of death, the length of time needed in hospital, and the extent of harm from the drug itself.

Overall, the study designs did not take into account factors other than taking ribavirin that could result in better outcomes in the intervention group, including how ill the patient was when diagnosed, or when good supportive medical care was started. This made any association between ribavirin and lower mortality problematic.

We found five studies that took into account important factors that could confound the risk of dying with whether or not a patient received ribavirin. These include how sick the study participants were, what other care they received, and how long after they became sick they received medical care. All included studies were conducted in Turkey and Iran, and compared people with CCHF who received ribavirin

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and supportive care to those who received supportive care alone. We looked at five different outcomes relating to ribavirin use in CCHF, and found that there is insufficient reliable evidence to determine whether ribavirin is effective.

How up to date is the review?

The review authors searched for studies that had been published up to 16 October 2017.