

Pre-Exposure and Post-Exposure Prophylaxis of Crimean-Congo Hemorrhagic Fever

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Context: Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne viral disease with a mortality rate of 30% to 80% and reported from more than 30 countries in Asia, Africa, South-Eastern Europe, and the Middle East. It is a zoonotic viral disease and an important health problem. In endemic areas, livestock handlers, livestock market workers, skin processors, veterinary staff, farmers, and healthcare personnel are at risk. Clinical manifestations are non-specific. Diagnosis is based on clinical manifestations, epidemiologic factors, and laboratory tests. Here, we reviewed the routes of transmission, pre-exposure, and post-exposure prophylaxis to help the public health authorities for decreasing rate of the disease in the community.

Evidence Acquisition: Medical databases (PubMed, Scopus, and Embase) were searched from June 1985 to June 2014. Keywords, including CCHF, epidemiology, transmission, control, prophylaxis, and prevention routes were searched.

Results: CCHF is widely distributed in many countries of the world, including our country, Iran which is an endemic region. Infection has a wide distribution that correlates with a global distribution of *Hyalomma* tick (the vector responsible for viral transmission). Preventive measures are very important in lowering the incidence rate. Post-exposure prophylaxis should be considered for people exposed to CCHF virus, such as those who have mucous membrane contact or a percutaneous injury in contact with the secretions or blood of infected animal or patients.

Conclusions: CCHF is a fatal viral disease. Therefore, pre-exposure and post-exposure prophylaxis should be considered to decrease the infection rate. All strategies should be centralized on raising surveillance using standardized case finding and proper case management, reduction of infection in animals, and increasing laboratory capacity in at risk regions for CCHF.

Keywords: Prevention; Transmission; Chemoprevention

1. Context

Crimean-Congo hemorrhagic fever virus (CCHFV) is an infection with a major public health concern. CCHFV could have high mortality rates and could be transmitted from infected animal and human to human (1-3). It has displayed a wide geographical spread during the recent decade. Climatic, and environmental changes which correlates with a global distribution of *Hyalomma* tick as well as the people travels provide opportunities for emerging of infection to spread to previously unaffected regions (1, 4, 5). CCHFV is considered to be one of the major emerging infections that threats spreading to and within other countries. Every year, more than 1000 human cases of CCHF are reported from Balkan countries (6). *Hyalomma* ticks as a vector favor dry and tropical climates and dry soil vegetations, and are plenty in the countries near the Mediterranean Sea where many animals live and may act as CCHFV hosts (6).

As a public health concern, prevention of infection at the community level seems to be more important than

the individual level. Therefore, the analysis of the current information and data plays a basic role to minimize its epidemic potential by decreasing the infection risk factors (6-8). As all vector-borne diseases, environmental factors, and human behaviors are very critical for the constitution and keeping of CCHF endemicity within an area. Humans may change the risk of CCHFV transmission through the changes in land use, their activities, and livestock movement. On the other hand, increasing awareness may affect the incidence of CCHF infection (6, 7). This review will assist decision-makers and public health authorities in understanding risk factors and deciding on effective counteractions.

2. Evidence Acquisition

Online medical databases (PubMed, Scopus, and Embase) were searched from June 1985 to June 2014. Keywords, including CCHF, epidemiology and control, prophylaxis, and prevention routes were searched.

3. Results

3.1. Transmission

CCHF is endemic in many countries in Africa, Asia, Eastern Europe, and since 1999, cases or outbreaks have been reported from Iran, Pakistan, Turkey, Kosovo, Albania, Bulgaria, Greece, South Africa, and in the Southern Federal Districts of Russia (9-14). CCHF virus usually spreads between asymptomatic animals (many species of mammals such as sheep, cow, camel, and goat) and ticks in an enzootic cycle. This virus has been observed in many species of ticks, including in the family of Ixodidae which is known as hard ticks (15-17). Among Ticks, *Hyalomma marginatum* is an important vector for transmission of infection to human. Transovarial and venereal transmission occur among this genus (15-18). Many species of small mammals (such as rats, hedgehogs, and hares) can transmit CCHFV to ticks when they are viremic. With a few exceptions (ostriches), birds seem to be immune to this infection (15, 16). However, they may act as mechanical vectors by transporting infected ticks to other areas or even other countries. Therefore, Migratory birds can spread the virus between very distant geographic areas. Humans can be infected incidentally by the bite of an infected arthropod, direct contact with blood or body secretions of the infected human or viremic livestock, or by aerosol generated from an infected human or rodents in the community (1, 4, 5). Livestock handlers, skin processors, veterinary staff, livestock market workers, farmers, and other personnel employed in jobs requiring some contact with infected animals and animal products are also at high risk for CCHF. Horizontal transmission of CCHFV from a mother to her child has also been reported (19). Nosocomial transmission has been reported from Pakistan, Iran, South Africa, the UAE, and Iraq (20). Risk of nosocomial transmission can be minimized by the suitable infection-control proceedings, careful management of the infected patients, and sometimes, providing prophylactic treatment to healthcare staff after they are exposed to the infection (15-17).

3.2. Control Strategies

Control of ticks is not a realistic goal, and all strategies should be centralized on raising surveillance using standardized case definition, case finding, proper case management, reduction of infection in animal, increasing laboratory capacity within already endemic areas, and the regions where are at risk for CCHF spread. The general population and healthcare workers should be aware of prophylactic measures and modify their risk for infection. Public media can play a major role in education of the people.

3.3. Pre-Exposure Prophylaxis

A public interest regarding CCHF and enough infor-

mation is required to control and prevent the infection. Therefore, we need to know what we must do. There are some important steps that should be taken as follows (20-22):

- 1) Vector control, including surveillance of naturally-occurring vector populations and their suitability for transmission. Measures to avoid tick bites like using tick repellents, and systematic examination of clothing and skin for ticks are the most common ways for prevention. Clothing should be worn to prevent tick attachment, including long pants confined into the boots and long-sleeved shirts;

- 2) Improved case finding using better diagnostic tools and increasing laboratory capacity;

- 3) Control of infection in animals by using acaricides and sprays on domestic animals to control ticks, particularly before their slaughtering or exporting to another region;

- 4) Public awareness campaigns; people should know two points.

In meat, virus is usually inactivated by post-slaughter acidification. But, they should store meat at 4 °C in refrigerator for 24 hours. It is also killed by cooking (56 °C for 30 minutes). Unpasteurized milk should not be consumed.

Laboratory staff must follow a high level of biosafety precautions and a negative-pressure respiratory isolation should be measured, particularly in case of coughing, vomiting, or other activities, which produce the large droplet aerosols. Strict universal precautions are also necessary to prevent nosocomial infections (20-22). People entering the patient's room should wear gloves, gowns, and surgical masks and those approaching with-in one meter should have an eye protection and a mask to prevent contact with blood or other infected body fluids (21, 22). Experience with vaccines against CCHF virus is limited, and the vaccine is not available in many countries because of its method of preparation. An inactivated suckling mouse brain-derived vaccine is used in Bulgaria for protection against CCHF (23).

3.4. Post-Exposure Prophylaxis

Post-exposure prophylaxis should be considered especially for persons exposed to CCHFV, for example, during a bioterrorist attack. All known high-risk people who have mucous membrane contact like kissing or sexual contact or have a percutaneous injury in contact with the infectious fluids, or blood should receive chemoprophylaxis (21, 23, 24). This precaution also applies to those with close contacts such as living with the patients, process laboratory specimens, or healthcare personnel who manage such patients before initiation of standard precautions. The people with close contact should be placed under medical surveillance and instructed to record their temperatures twice daily. If a temperature of 38.3 °C or higher develops, a blood sample should be taken and treatment with ribavirin should be initiated promptly as

probable case of CCHF when other clinical manifestation are observed (20). Oral ribavirin, 200 mg twice daily, for 5 days is recommended for post-exposure prophylaxis (20, 21, 25).

4. Conclusions

CCHF is a fatal viral disease. Therefore, pre-exposure and post-exposure prophylaxis should be considered to decrease the rate of infection. Vector control is an important problem, but public awareness campaigns and public media can help people to increase their knowledge and prevent the spread of the infection. The strategy of technology transfer to train the healthcare staff is required.

Authors' Contributions

Batool Sharifi-Mood and Maliheh Metanat wrote the paper. Each two authors had equal role in design, and manuscript writing.

References

- Mardani M, Keshtkar-Jahromi M, Ataie B, Adibi P. Crimean-Congo hemorrhagic fever virus as a nosocomial pathogen in Iran. *Am J Trop Med Hyg.* 2009;**81**(4):675-8.
- Pirkani SG, Jomezai EK, Ilyas M. Crimean-Congo hemorrhagic fever (CCHF) in blochistan. *Prof Med J.* 2006;**13**:464-7.
- Lacy MD, Smego RA. Viral hemorrhagic fevers. *Adv Pediatr Infect Dis.* 1996;**12**:21-53.
- Metanat M, Sharifi Mood B, Salehi M, Alavi Naini R. Clinical outcomes in Crimean-Congo hemorrhagic fever: A five-years experience in the treatment of patients in oral Ribavirin. *Int J Virol.* 2006;**2**(1):21-4.
- Sharifi-Mood B, Metanat M, Ghorbani-Vaghei A, Fayyaz-Jahani F, Akrami E. The outcome of patients with Crimean-Congo hemorrhagic fever in Zahedan, southeast of Iran: a comparative study. *Arch Iran Med.* 2009;**12**(2):151-3.
- Mertens M, Schmidt K, Ozkul A, Groschup MH. The impact of Crimean-Congo hemorrhagic fever virus on public health. *Antiviral Res.* 2013;**98**(2):248-60.
- Hoogstraal H. The epidemiology of tick-borne Crimean-Congo hemorrhagic fever in Asia, Europe, and Africa. *J Med Entomol.* 1979;**15**(4):307-417.
- Heyman P, Cochez C, Hoffhuis A, van der Giessen J, Sprong H, Porter SR, et al. A clear and present danger: tick-borne diseases in Europe.

- Expert Rev Anti Infect Ther.* 2010;**8**(1):33-50.
- Ahmeti S, Raka L. Crimean-Congo haemorrhagic fever in Kosova : a fatal case report. *Virology.* 2006;**3**:35.
- Papa A, Bino S, Llagami A, Brahimaj B, Papadimitriou E, Pavlidou V, et al. Crimean-Congo hemorrhagic fever in Albania, 2001. *Eur J Clin Microbiol Infect Dis.* 2002;**21**(8):603-6.
- Kunchev A, Kojouharova M. Probable cases of Crimean-Congo haemorrhagic fever in Bulgaria: a preliminary report. *Euro Surveill.* 2008;**13**(17).
- Papa A, Maltezou HC, Tsiodras S, Dalla VG, Papadimitriou T, Pierroutsakos I, et al. A case of Crimean-Congo haemorrhagic fever in Greece, June 2008. *Euro Surveill.* 2008;**13**(33).
- Butenko AM, Korganova GG. *Crimean-Congo Hemorrhagic Fever in Russia and Other Countries of the Former Soviet Union.* Ergonul O, Whitehouse C editors. Dordrecht: Springer; 2007.
- Yilmaz GR, Buzgan T, Torunoglu MA, Safran A, Irmak H, Com S, et al. A preliminary report on Crimean-Congo haemorrhagic fever in Turkey, March - June 2008. *Euro Surveill.* 2008;**13**(33).
- Mardani M, Keshtkar-Jahromi M. Crimean-Congo hemorrhagic fever. *Arch Iran Med.* 2007;**10**(2):204-14.
- Alavi-Naini R, Moghtaderi A, Koohpayeh HR, Sharifi-Mood B, Naderi M, Metanat M, et al. Crimean-Congo hemorrhagic fever in Southeast of Iran. *J Infect.* 2006;**52**(5):378-82.
- Sharifi-Mood B, Mardani M, Keshtkar-Jahromi M, Rahnavardi M, Hatami H, Metanat M. Clinical and epidemiologic features of Crimean-Congo hemorrhagic fever among children and adolescents from southeastern Iran. *Pediatr Infect Dis J.* 2008;**27**(6):561-3.
- Crimean-Congo Hemorrhagic Fever.* Available from: www.cfsph.iastate.edu/Factsheets/.../crimean_congo_hemorrhagic_fever.
- Fisher-Hoch SP, Khan JA, Rehman S, Mirza S, Khurshid M, McCormick JB. Crimean Congo-haemorrhagic fever treated with oral ribavirin. *Lancet.* 1995;**346**(8973):472-5.
- Mardani M, Pourkaveh B. Crimean-Congo Hemorrhagic Fever. *Iran J Clin Infect Dis.* 2012;**7**(1):36-42.
- Mardani M, Namazee N. Close contact precautions could prevent an outbreak of crimean-congo hemorrhagic Fever: a case series report from southern part of tehran. *Int J Prev Med.* 2013;**4**(6):715-9.
- 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**(2):284-7.
- Papa A, Papadimitriou E, Christova I. The Bulgarian vaccine Crimean-Congo haemorrhagic fever virus strain. *Scand J Infect Dis.* 2011;**43**(3):225-9.
- Mardani M, Rahnavardi M, Sharifi-Mood B. Current treatment of Crimean-Congo hemorrhagic fever in children. *Expert Rev Anti Infect Ther.* 2010;**8**(8):911-8.
- Sharifi Mood B, Alavi-Naini R, Metanat M, Rakhshani F. Ribavirin: an effective drug for treatment of children with Crimean Congo hemorrhagic fever: a seven years experience. *Pak J Biolo Sci.* 2006;**9**(8):1598-600.