

Inactivation of Middle East respiratory syndrome-coronavirus in human plasma using amotosalen and ultraviolet A light

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BACKGROUND: Middle East respiratory syndrome-coronavirus (MERS-CoV) is a novel zoonotic pathogen. Although the potential for MERS-CoV transmission through blood transfusion is not clear, MERS-CoV was recognized as a pathogen of concern for the safety of the blood supply especially after its detection in whole blood, serum, and plasma of infected individuals. Here we investigated the efficacy of amotosalen and ultraviolet A light (UVA) to inactivate MERS-CoV in fresh-frozen plasma (FFP).

STUDY DESIGN AND METHODS: Pooled FFP units were spiked with a recent clinical MERS-CoV isolate. Infectious and genomic viral titers were determined in plasma before and after inactivation with amotosalen/UVA treatment by plaque assay and reverse transcription-quantitative polymerase chain reaction, respectively. In addition, residual replicating or live virus after inactivation was examined by passaging in the permissive Vero E6 cells.

RESULTS: The mean MERS-CoV infectious titer in pretreatment samples was 4.67 ± 0.25 log plaque-forming units (pfu)/mL, which was reduced to undetectable levels after inactivation with amotosalen/UVA demonstrating a mean log reduction of more than 4.67 ± 0.25 pfu/mL. Furthermore, inoculation of inactivated plasma on Vero E6 cells did not result in any cytopathic effect (CPE) even after 7 days of incubation and three consecutive passages, nor the detection of MERS RNA compared to pretreatment samples which showed complete CPE within 2 to 3 days postinoculation and log viral RNA titer ranging from 9.48 to 10.22 copies/mL in all three passages.

CONCLUSION: Our data show that amotosalen/UVA treatment is a potent and effective way to inactivate MERS-CoV infectious particles in FFP to undetectable levels and to minimize the risk of any possible transfusion-related MERS-CoV transmission.

Transfusion of blood components saves millions of lives by controlling bleeding due to accidents, surgeries, or other disease complications. However, transmission of pathogens is one of the biggest risks of transfusion of labile blood components. Therefore, a key mission of blood transfusion services is to provide safe blood and blood products. Screening of blood products has reduced the spread of known blood-borne pathogens such as hepatitis B and C viruses (HBV and HCV), human immunodeficiency virus (HIV), and human T-lymphotropic virus (HTLV).^{1,2} However, other known or

ABBREVIATIONS: CPE = cytopathic effect; IBS = INTERCEPT Blood System; MERS-CoV = Middle East respiratory syndrome-coronavirus; pfu = plaque-forming units; RT-qPCR = reverse transcription-quantitative polymerase chain reaction; SARS-CoV = severe acute respiratory syndrome-coronavirus.

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