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SCIENTIFIC PAPER

IN-LINE FILTER AND ENDOTOXIN RETENTION

WHY TO USE INFUSION FILTERS?

Filters are available as single add-on devices or as in-line components as an integral part of the administration set. They are used during infusion of intravenous solutions to prevent the administration of particles, air, micro-organisms, or endotoxin. *[Phillips et al. 2014]*

BACTERIAL SPECTRUM AND CAUSE OF ENDOTOXIN CONTAMINATION

Sepsis is a multi-factorial process that involves an uncontrolled inflammatory response by the host cells. As a consequence, sepsis is a major cause of morbidity and mortality. Both gram-negative and gram-positive bacteria play a major role in causing sepsis. Most commonly isolated pathogenic bacteria have been gram-positive, although gram-negative organisms have recently become more common. *[Riesner et al. 2017, Erfani et al. 2016, Kuenzli et al. 2014, Kaase 2012]* Currently, the most commonly isolated causative organisms are gram-negative bacteria and the data are based on epidemiological studies. *[Erfani et al. 2016]*

This increase in gram-negative bacteria has been accompanied by an increased risk of endotoxin load. *[Rockel & Hartung 2012]*

Endotoxin is a complex aggregate of acidic lipopolysaccharides and consists of an innermost core of hydrophobic fatty acid groups and a central and outermost region composed of hydrophilic polysaccharides. Endotoxin is continuously shed from the outer membrane of viable gram-negative bacteria and is released when the bacterial cell dies. Endotoxins have serious effects on the inflammatory and coagulation system. The presence of endotoxins in blood can provoke septic shock if there is a pronounced immune response. Moreover, endotoxins interact with the vascular endothelium and stimulate the complement and blood coagulation pathways. [*Harm et al. 2016, Bononi et al. 2008]*

There is a trend of increasing endotoxin-like activity with an increasing duration of infusion. It is known that endotoxin-like activity is not detected in filtrate eluted from contaminated filter sets during the initial 24 hrs of infusion. Levels above baseline values are significantly detectable after 24 hours. *[Holmes et al. 1980]* Only filters that retain endotoxins can safely be used for more than 24 hours. *[Richards & Grassby 1994]*

ENDOTOXIN RETENTION WITH POSITIVELY CHARGED FILTER MEMBRANES

While intact bacteria can be captured using a 0.2 µm filter, the retention of endotoxins is more challenging. Endotoxin is negatively charged at pH above 2. Therefore, bacterial endotoxins from infusion solutions can only be removed with positively charged filter membranes that electrostatically attract or retain endotoxins. *[Bononi et al. 2008, Bethune et al. 2001, Gerba & Hou 1985, Levin 1982]* Several clinical studies evaluated in-line filters for endotoxin retention and concluded that positively charged membrane filter can retain endotoxin over 96 hours. *[Bononi et al. 2008, Bethune et al. 2001, Barnett & Cosslett 1996]* Bononi et al. performed endotoxin measurements on the filtrates from positively charged filters and indicated that the amounts of endotoxin which had passed through the filters during the infusion experiment time were less than 0.03 EU/ml for 96 hours. *[Bononi et al. 2008]*

Conclusion

Only filters that retain endotoxins can safely be used for more than 24 hours. Positively charged filter membranes have been introduced on the market to protect patients from inadvertent microbial and associated endotoxin contamination. Several clinical studies showed that only filters equipped with a positively charged membrane were able to retain the endotoxin. A change interval of 96 hours is recommended due to the fact that positively charged membrane load may be exhausted after 96 hours.
A non-charged-filter (inclusive filter needle and straw) does not have an endotoxin retentive function and may be used for a maximum of 24 hours since gram-negative-based endotoxin activity is already detectable after 24 hours.

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