Consensus on the clinical use of in-line filtration during intravenous infusions
Current evidence and recommendations for future research

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Disclosure

• Nothing to disclose
Introduction

• The majority of hospitalized patients get some form of intravenous (IV) infusion
• There is a need to further reduce VAD related complications
• In-line filtration has been proposed for many decades
• Indications for in-line filters has been scarce
Introduction

• WoCoVA together with GAVeCeLT started a project to come to **international consensus** on the use of in-line filters
Methods

• Literature search PubMed and Cochrane library Sept 2018, updates in March and July 2019
• Panel of experts on vascular access with focus on in-line filtration
• Peer reviewers to comment the final document
Methods

3 topics for this consensus

1. ‘Evidence about possible harmful effects of inert particles in intravenous infusions’ (group 1)
2. ‘Potential benefits of in-line filters in reducing peripheral phlebitis’ (group 2)
3. ‘Potential benefits of in-line filters in reducing systemic inflammation/infection’ (group 3)
Questions group 1

• Effects of inert particles
  1. Which are the types and dimensions of the particles potentially related to harmful clinical effects?
  2. Is there any evidence of harmful clinical effects due to particles?
  3. Which kind of filters are available for clinical use and which kind of particles are they expected to stop?
  4. Which basic research is currently warranted for further investigation in this area?
Questions Group 2

• Peripheral phlebitis
  1. Please provide an acceptable definition for peripheral catheter-related ‘phlebitis’
  2. Which are the commonly accepted causes of phlebitis?
  3. Is there evidence that phlebitis might be related to particles?
  4. Is there evidence that the clinical use of filters might reduce this risk?
  5. Which clinical research is warranted for further investigation in this area?
Questions Group 3

• Systemic infections

  1. Please provide acceptable definitions for sepsis - systemic infection - SIRS - septic shock
  2. Which is the currently accepted pathogenesis of the pathophysiologic effects of systemic infection?
  3. Is there any evidence that particles might be involved in this pathogenesis?
  4. Is there evidence that the clinical use of filters might reduce systemic infection or systemic inflammatory response? And in which kind of patients?
  5. Which clinical research is warranted for further investigation in this area?
1. Which are the types and dimensions of the particles potentially related to harmful clinical effects?

- 5% of the particles in IV drug solutions are > 50 micron and visible
- >50% between 5 and 15 micron and sub-visible (Oie et al 2005; Lehr et al 2002; Schafer et al 2008)
- All particles >10 micron may potentially cause obstruction; 10-12 micron particles stay lodged in pulmonary capillaries
- 3-6 micron particles are lodged in spleen and hepatic lymph nodes for prolonged periods
- 1 micron particles are lodged in the liver (Perez et al 2016)
Intrinsic / Extrinsic

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<td></td>
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Which are the types and dimensions of the particles potentially related to harmful clinical effects?

Perez et al, 2016
2. Is there any evidence of harmful clinical effects due to particles?

- Single clinical case reports, report great variety of pathological conditions due to local tissue damage (particularly in the lung)

3. Which kind of filters are available for clinical use and which kind of particles are they expected to stop?
   • Commercially available filters with different pore sizes; filters with pore size of 0.2 micron will stop majority of particles,
     – 1.2 micron will stop lipids,
     – >8 or 15 micron are probably unable to stop harmful particles
• Hospitals have reported that in-line filters interfere with therapy delivery because the block and the filter must be removed or replaced to continue therapy delivery.

• The filter is doing precisely what it was put there to do; to prevent the infusion of particles and to warn the user that their practice is unsafe.

  – Recommended max use
    • 24 hours (Polyethersulphone)
    • 96 hours (polyamide)

Patrick Ball, 2013

PALL Medical
Results Group 1 cont.

4. Which basic research is currently warranted for further investigation in this area?

- Randomized controlled clinical trials comparing IV administration with and without inline filtration
An acceptable definition for Peripheral Catheter-Related ‘Phlebitis’. (PCRP):

Inflammation of the vein, which may be mechanical, chemical or bacterial in origin, is based on a variable spectrum of symptoms, the most frequent of which are erythema/redness, local pain, edema/swelling, warmth and palpable venous cord (Arias-Fernandez et al. 2017)
Which are the commonly accepted causes of phlebitis?

- Chemical (irritation of the vein wall by solutions)
- Bacterial (contamination, either extraluminal or intraluminal)
- Mechanical (trauma by inappropriate securement of the catheter)

Is there evidence that phlebitis might be related to particles?

Scientific evidence is still missing, but it has been postulated that inert particles, drug precipitates, endotoxin, bacteria, etc. may be involved in damage of the venous endothelium.
4. Is there evidence that the clinical use of filters might reduce this risk?
   • A few well-designed randomized study suggest that in-line filters may concur in reducing the risk of PIVC-related phlebitis

5. Which clinical research is warranted for further investigation in this area?
   • Further randomized clinical trials
Results Group 3

1. Please provide acceptable definitions for sepsis - systemic infection - SIRS - septic shock
   Relevant here: Systemic Inflammatory Response Syndrome (SIRS) may occur in absence of sepsis, as a non-bacterial related inflammatory response.

2. Which is the currently accepted pathogenesis of the pathophysiologic effects of systemic infection?
   The pathogenesis is still largely unclear, though it appears that bacterial invasion may start a systemic inflammatory response

3. Is there any evidence that particles might be involved in this pathogenesis?
   No clear and direct evidence
4. Is there evidence that the clinical use of filters might reduce systemic infection or systemic inflammatory response?

- The available clinical evidence suggest that inline filters may play a role in reducing systemic complications

4b) In which kind of patients?

- In the pediatric and neonatal populations
5. Which clinical research is warranted for further investigation in this area?

• More clinical studies are needed.
  – Proper identification of the patient population (neonates vs. children)
  – Type of treatment (PN solutions vs non-nutritional IV therapies)
  – Definition of the primary endpoint (organ failure; SIRS; systemic infection; mortality; etc.).

Large randomized controlled trials in the neonatal population are recommended, as it is this population that may hugely benefit from the use of in-line filtration.
Preliminary Conclusion

• In-line filtration with 0.2 and 1.2 μm filters could reduce systemic inflammation and maybe morbidity in critically ill patients and improve patient safety.

• Further prospective randomised studies are needed to strengthen these outcomes.
Timeline

• Comments of panel members and recent updates will be processed
• Final version goes to peer reviewers
• Final conclusions will be written after comments of the peer reviewers
• Article will be published before the 6th WoCoVA in Athens
# People involved in this project

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<th>Expert group</th>
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Thank you

- Further information
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Questions?