Angiopoietin-1 mimetic restores microcirculatory perfusion disturbances and microvascular leakage during haemorrhagic shock

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Introduction

Microcirculatory dysfunction is associated with multiple organ failure and unfavourable patient outcome. Although crystalloids are effective in restoring macrohaemodynamics during haemorrhagic shock (HS), microcirculatory dysfunction often persists. Therapeutic targeting of the angiopoietin/Tie2 system might preserve microvascular integrity. Therefore, we investigated the effects of an angiopoietin-1 mimetic (Ang1mim) on microcirculatory perfusion and microvascular leakage during HS.

Methods

Rats underwent HS or sham surgery receiving Ang1mim or PBS. HS was induced by blood withdrawal to achieve a mean arterial pressure (MAP) of 30 mmHg for one hour, followed by resuscitation with crystalloids and blood until baseline MAP was reached.

- microcirculatory perfusion measurement in cremaster using intravital microscopy
- microvascular leakage by Evans blue dye extravasation

Results

Characteristics

Figure 1: Decreased blood pressure (left) and base excess (right) in rats during shock and resuscitation compared to sham rats

Microvascular leakage

Figure 3: Increased microvascular leakage after shock and fluid resuscitation in kidney and lung, which could be reduced after treatment with an Ang1mim

Less resuscitation volume required

Figure 4: Less resuscitation volume is required in the rats treated with an angiopoietin-1 mimetic

Microcirculatory perfusion disturbances

Figure 2: Shock disturbed microcirculatory perfusion, which could not be restored by fluid resuscitation. Ang1mim was able to restore microcirculatory perfusion during fluid resuscitation

Increased circulating Angiopoietin-2

Figure 5: Shock increased Angiopoietin-2 protein in plasma, which could not be restored by fluid resuscitation, but decreased after Ang1mim treatment

Conclusion

Administration of an angiopoietin-1 mimetic restores microcirculatory perfusion during haemorrhagic shock and reduced requirement of fluid resuscitation, possibly due to less microvascular leakage.