Reviewer's report

Title: Polyphenols of CAMELLIA SINENESIS decrease mortality, hepatic injury and generation of cytokines and reactive oxygen and nitrogen species after hemorrhage/resuscitation in rats

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Reviewer: Gavin E Arteel

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General Comments

BMC Complementary and Alternative Medicine by Lehnert et al., “Polyphenols of Camellia sinenesis decrease mortality, hepatic injury and generation of cytokines and reactive oxygen and nitrogen species after hemorrhage/resuscitation in rats.” The purpose of the this study was to determine if green tea polyphenols will protect against mortality and liver damage caused by hemorrhage/resuscitation. The authors showed that green tea polyphenols protected against death in a lethal version of the model and protected against liver injury in a milder version of the model. This protective effect correlated with a blunting of proinflammatory cytokine expression (TNF, IL-6 and IL-1) and decreased indices of oxidative and nitrosative stress.

The findings are generally interesting and the work is sound. However, there is little mechanistic insight into exactly how the green tea polyphenols mediate this protective effect. Furthermore, the authors state that such extracts could be a useful therapy for clinical situations that the paradigm models. However, the authors gave the green tea polyphenols prior to the hemorrhagic event, which limits this proof-of-concept. The authors are encouraged to investigate deeper into the mechanism and/or determine the effect of green tea polyphenols administered after the hemorrhage. Specific suggestions for both approaches are detailed below.

Major Revisions

Whereas polyphenols clearly have antioxidant effects in vivo, whether or not this is due to direct scavenging of free radicals is unclear. Alternatively, the polyphenols may blunt the production of intrinsically-derived ROS/RNS. Indeed the authors have previously shown that NADPH oxidase deficient mice are protected against liver damage in this model. Furthermore, others have shown that iNOS is hepatotoxic in this model system. The authors should therefore determine the effect of green tea polyphenols on NOX activation and iNOS expression.

No information is given regarding the source, purity and polyphenolic content of the polyphenols used in this study. Given major batch-to-batch variations in the preparations of these extracts, this information is important.
Figure 4. Quantitation of the HNE signal for the Shams is missing from the histogram.

As mentioned above, it would be very useful to determine green tea extract can be protective in a rescue-type situation (i.e., after hemorrhage, but before resuscitation). This would strengthen very much the claims of the authors of this approach having clinical relevance.

Discretionary Revisions
Endothelial cells are likely damaged in this model. It would be interesting to determine the effect of H/R and green tea polyphenols on plasma hyaluronic acid, which should increase during endothelial dysfunction.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests