Author's response to reviews

Title: Effects of abdominal hot compresses on indocyanine green elimination - a randomized cross over study in healthy subjects

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Author's response to reviews: see over
To the Editor of
BMC Gastroenterology

MS 5695821712240386, "Effects of abdominal hot compresses on indocyanine green elimination – a randomized cross over study in healthy subjects”

Dear Editor,

thank you for considering our manuscript for publication in BMC Gastroenterology and for the opportunity to outline our work in more detail according to the recommendations of the reviewers. In the following you find the point-by-point response to the concerns of the reviewers. Please do not hesitate to contact me in case of any further questions.

With kind regards,

Dr. Roman Huber
(for the authors)
Response to Reviewer Samir Sakka

1. Results of liver specific enzyme tests were added in a new table (table 1)

2. Height and weight of the participants were presented in table 1

3. Unfortunately there is no simple adequate reference technique for ICG-PDR. ICG-PDR has been validated in comparison to other liver function tests (e.g. Bromosulphthalein-(Bromsulphalein) test) and in complex animal studies measuring directly the liver blood flow. Doppler- and colour–duplex ultrasound has been used by our group in pre-studies. Limitations in measuring liver blood flow during application of hot compresses were:
   a. highly artificial conditions (loud noise of the duplex machine, probands have to stop breathing during measurement and therefore can’t relax)
   b. problems to reproducibly identify and measure intrahepatic liver arteries in healthy subjects (even if performed from specialists). Variability of measurements was very high.
   c. hepatic artery and portal vein cannot be measured simultaneously
   d. measurements (contact of the probe to the skin) had to be performed through a whole in the hot compress which might have influenced the effect of the compress

Portal vein flow did not change systematically during these pre-study experiments. We decided to use ICG-PDR because it is a global test of liver blood flow. If results would have been positive, a next step would have been to evaluate portal and arterial flow separately.

4. Variability of ICG-half life in double experiments with healthy volunteers was ±3.9% (Brühl et al. 1971). This information was added in the discussion

5. ICG half life was additionally presented as k-value (%/min) in table 2 (former table 1)

6. Results of our experiments with Doppler and Colour-Duplex ultrasound have been added in the discussion
Response to Reviewer Daniel de Backer

1. The discussion about the limitation of ICG-PDR to discriminate between liver blood flow and liver function was added in the discussion section. Because markers of liver disease (aminotransferase levels, bilirubin) were completely normal in all analyzed subjects, the assumption that an increase in hepatic blood flow may have been missed due to deterioration of liver function can be excluded.

2. ICG-PDR has shown to be sensitive to detect an increase of liver blood flow in healthy subjects during the circadian rhythm (Lemmer and Nold 1991, see Ref. 21) or medication (Nifedipin, Burggraaf et al. 1998, see Ref. 13). Therefore it can be concluded, that PDR can further increase when blood flow is further increased.

3. Aminotransferase levels and serum bilirubin were investigated only before the study (exclusion criteria). One subject had an elevated bilirubin (1.8 mg/dl) before the study and was erroneously included. The abnormal bilirubin was realized before the second investigation and the subject had been excluded. The sentence reads now: “One subject who had erroneously be included with a bilirubin of 1.8 mg/dl had to be excluded from the analysis.”

4. It was addressed in the discussion that our results do not rule out a potential beneficial effect of hot compresses in patients with liver disease.