

## The use of N-acetylcysteine to prevent hepatic dysfunction during laparoscopic surgery

Sir,

We read with interest the study, “The effects of N-acetylcysteine (NAC) on hepatic function during isoflurane anaesthesia for laparoscopic surgery patients” by Beyaz *et al.*<sup>[1]</sup> We have few concerns with the study that need to be clarified to make the study more informative.

Hepatic function may be affected by various reasons, including duration of surgery, the patient anaesthetic exposure of volatile agent (Minimum alveolar concentration-hours), the creation of pneumoperitoneum, degree of intrabdominal pressure (during laparoscopy) and the fluid management including blood loss. All these factors can contribute to a difference in the hepatic function rather than the isoflurane itself, as emphasized by the authors. Therefore, these parameters need to be mentioned and compared in the two groups.

Also, the authors concluded that isoflurane with NAC has a lesser effect on liver function as compared with isoflurane alone, but the tables represent increased glutathione S-transferase (GST), prolonged prothrombin time (PT) and International normalized ratio in the isoflurane–NAC group as compared with the isoflurane group, which needs to be clarified. It has been emphasized that the therapeutic doses of NAC cause abnormal haemostatic activity, and this needs to be considered when the haemostatic function is assessed as a predictor for hepatic injury.<sup>[2]</sup> Also, the role of NAC on PT is controversial, but a recent study regarding use of NAC in cardiac surgery mentioned that the use of NAC has no effect on PT, platelet count, blood loss or the need for blood transfusion. It appears that, in the present study, there should be other factors that led to altered coagulation profile rather than NAC itself, which needs to be analysed.<sup>[3]</sup>

The pain itself is responsible for secretion of many endogenous substances that may affect the hepatic function by decreasing the hepatic blood flow. Please clarify the avoidance of opioids or any other analgesia technique for pain management.

The effect of hypercarbia may have an impact on hepatic perfusion; therefore, details of this including duration of carboperitoneum, total flow of carbon dioxide and blood carbon dioxide levels, may be more informative. It has been studied in animals that mild hypercapnia causes depression of hepatic function in spite of increase in portal vein and hepatic artery blood flow.<sup>[4]</sup> Also, elevated intra-abdominal pressures (both in terms of level and duration) due to gas insufflations for laparoscopy results in regional flow changes, including liver, and thus may affect the hepatic function.<sup>[5]</sup> On the other hand, gasless laparoscopic procedures have been shown to preserve hepatic functions.<sup>[6]</sup> Thus, it becomes prudent to compare the level of carbon dioxide and intra-abdominal pressure in the two groups as different types of surgical procedures were included for the study.

GST is a sensitive and specific marker for hepatocellular damage. GST has a short half-life of ~1 h; therefore, it reflects hepatocellular damage more rapidly as compared with other liver enzymes. In the authors' study, GST level was significantly increased in the NAC group, indicating increased hepatocellular damage in the NAC group. Then, the authors' conclusion that "liver functions were well preserved with the administration of NAC during anaesthesia with isoflurane" needs to be justified.

The hepatic functions are significantly more impaired after laparoscopic cholecystectomy in elderly patients as compared with younger patients.<sup>[7]</sup> Therefore, it becomes prudent to mention the demographic profile of the patients to relate the changes on hepatic functions. The sample size calculation for a primary outcome variable has not been mentioned in the article. Without the sample size, the significance of outcome cannot be interpreted scientifically. Also, it will be more informative if exact *P* values for various comparisons may be mentioned. In the statistical analysis, the authors mention that the parameters without normal distribution were evaluated with the Mann-Whitney U-test, but the data represented only shows mean±SD. Please clarify which parameters were not normally distributed and the level of skewness.

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