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Factors associated with outcome of liver surgery and hepatocellular carcinoma

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CHAPTER 5

EVIDENCE AGAINST A ROLE OF SEROTONIN IN LIVER REGENERATION IN HUMANS

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We read with great interest the paper by Starlinger and colleagues in which evidence for a role of serotonin in liver regeneration in humans was provided.¹ We would like to report on our findings in a prospective study on serotonin levels in platelet-rich plasma in adult patients undergoing a (extended) right hemi-hepatectomy (n=16) in comparison to levels in patients undergoing a pylorus-preserving pancreaticoduodenectomy (PPPD) (n=10), and healthy controls (n=22). Patient characteristics were published elsewhere.² We drew blood samples after induction of anesthesia, at the end of the surgery, and at postoperative day 1, 3, 5, 7, and 30. In addition, we took blood samples from the portal and from the hepatic vein just prior to the start and just after completion of parenchymal transection in the patients undergoing a hemi-hepatectomy. Serotonin levels in platelet-rich plasma were determined by liquid chromatography-tandem mass spectrometry and levels were corrected for platelet count. The study protocol was approved by the local medical ethical committee and informed consent was obtained from each participant before inclusion in the study.

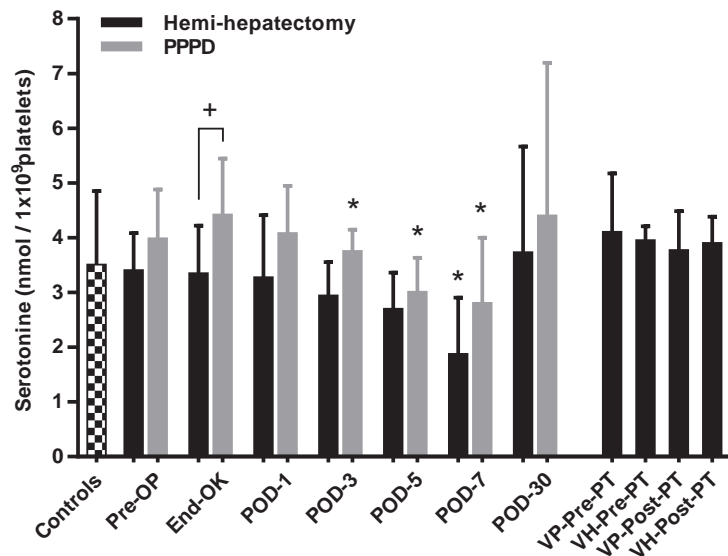


Figure 1: Median serotonin levels in controls, patients undergoing hemihepatectomy, and patients undergoing PPPD. Shown are serotonin levels corrected for platelet count. *P<0.05 compared to the baseline levels of serotonin within the group (Friedman test). +P<0.05 vs controls. End-OK: end of surgery, HV: hepatic vein, PT: parenchyma transection, Pre-OP: Preoperative, POD: postoperative day, VP: vena porta

Serotonin levels at baseline were comparable between patients undergoing hemihepatectomy, patients undergoing PPPD, and healthy subjects (figure 1). In contrast to the Starlinger study, no changes in serotonin were observed in the early post-operative period. Only at postoperative day 5 and 7, serotonin levels clearly decreased, but importantly, the decrease was similar between the hemihepatectomy and PPPD patients. Serotonin content

was identical between samples taken in the afferent and efferent liver veins prior to and after hemihepatectomy indicating that there was no detectable serotonin consumption by the liver directly after hemihepatectomy.

Although the number of patients we studied was smaller compared to the Starlinger study, we studied more time points in a more homogeneous cohort consisting of non-cirrhotic patients undergoing a major hepatectomy, included an appropriate control group, and studied the serotonin gradient over the liver prior to and just after full parenchymal transection. Technical differences between the studies included measurement of serotonin in platelet-rich plasma versus a calculated serum-platelet poor plasma difference as studied by Starlinger. Importantly, we calculated serotonin content per platelet, thereby correcting for consumption of platelets as a result of dilution or consumption. Although we do not dispute that platelets are likely important for liver regeneration in humans,³ our data do not support the notion that platelet serotonin is key in this process.

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