Biliary Drainage and Inflammatory Environment in Patients with Malignant Obstructive Jaundice

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Malignant disease of the extrahepatic distal or proximal biliary tract is the most prevalent cause of obstructive jaundice. Obstructive jaundice itself is associated with a proinflammatory state, resulting from portal and systemic endotoxemia.The exposure to endotoxemia and bacterial translocation leads to an uncontrolled induction of the inflammatory cascade.[1] Previous studies seemed to agree that the level of proinflammatory cytokines, including tumor necrosis factor (TNF) alpha and interleukin 6 (IL-6), will increase in the presence of biliary obstruction.[1,2,3] Concordant findings were shown in Sabarudin's study, evaluating 40 patients with malignant obstructive jaundice, which were later treated by palliative biliary drainage.[2]

However, a recent study demonstrated that patients with malignant obstructive jaundice had reduced capacity to generate proinflammatory cytokine responses to endotoxin to a greater extent compared with healthy controls and those with benign obstructions (IL-6: 3,442 compared with 6,157 pg/mL, p = 0,002). This phenomenon of endotoxin tolerance subjects to the lower clearance capacity of Kuppfer cells, thus exposing immune cells to higher and longer exposure of infectious agents, particularly lipopolysaccharides.Another study had similar in vitro condition for TNF alpha.[4]

Frequently the tumors are unresectable at diagnosis and only palliative treatment is possible to improve patients' quality of life.[5] Although it is still debatable, biliary drainage is still proven to be a beneficial way to intervene by both relieving jaundice and restoring immune functions. Biliary drainage procedures, either by means of endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic biliary drainage (PTBD), are almost exclusively associated with beneficial results: improved liver function and nutritional status, reduction of systemic endotoxemia, and therefore an improved immune response.[1] As many as 34 subjects in Sabarudin's study underwent ERCP, meanwhile the rest underwent PTBD for treating either cholangiocarcinoma (n = 22; 55%), ampulla vateri tumour (n = 10; 25%), or pancreatic tumour (n = 8; 20%).[2]

Sabarudin found that there was a significant difference of TNF-alpha before and after biliary drainage, especially for ERCP (4,87 to 8,93 pg/mL), but it was not found in 6 patients treated with PTBD (5,48 to 5,10 pg/mL). IL-6 level was not significantly different for both study groups (7,39 to 7,97 pg/mL for TNF and 8,49 to 8,02 pg/mL for IL-6).[2] Following biliary drainage with ERCP, Kimmings, et al. previously did not find any significant alteration for TNF (21,7 vs. 18,4 pg/mL, p =0,2) and IL-6 (4,2 vs. 6,1 pg/mL, p = 0,9) three weeks after the procedure.[6] Contradictive result was found by Chowdhury, et al, in which IL-6 secretion from monocytes was shown to undergo a rise from the level of 2,488 to 3,250 pg/mL, p = 0,01.[4] No significant changes in TNF (34 vs. 42 vs. 27 pg/mL, p = 0,052) and IL-6 (20 vs. 31 vs. 17,9 pg/mL, p = 0,094) level was recorded following PTBD in 53 patients with malignant obstructive jaundice on the fifth hour and fifth day after the procedure. It was believed that the short-term activation of inflammation by PTBD may not create a significant change in cytokine. Furthermore, subgroup analysis showed that IL-6 level on fifth day after procedure in patients alive 30 days after PTBD differed significantly with those who died 30 days after PTBD (15,0 vs. 128,8 pg/mL, p = 0,011).[7]

These significant findings may reflect the restored cytokine secretory responses, but at the same time also possesses the risk of periprocedural infection.[4] Nevertheless, it must be noted that a negative side-effect of biliary drainage is the associated complications of the procedure itself.Every trauma in the procedure performed may give an influence for the inflammation cascade environment, rendering the result to biases.[1] Also, it is quite interesting to find out if similar findings will occur on larger number of patients, as well as in the setting of patients without exposure of analgesics or antibiotics, which are known to influence both cytokine release and systemic inflammatory response syndrome

(SIRS) occurence.[8]

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