

THE IMPACT OF BILIARY DRAINAGE MODE ON BACTERIOBILIA OCCURRENCE IN PATIENTS WITH HILAR MALIGNANT OBSTRUCTION

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The *purpose* of this study was comparative assessment of the frequency of bacterial colonization of the bile in patients with hilar malignant biliary obstruction after the palliative biliary decompression using different methodological approaches.

Methods. 50 patients with proximal mechanical jaundice of tumor origin aged of ~62 years (25 males and 25 females), who were on steady-state treatment in Main military clinical hospital (Kyiv, Ukraine) were recruited in this prospective study. All patients underwent cholangiostomy using percutaneous transhepatic (PTBD) and external-internal suprapapillary (EISBD) approaches. Bile specimens were taken right after the biliary drainage. Identification of bacterial isolates was performed using standard cultural and biochemical methods.

Results. The incidence of cholangitis was almost twice lower in EISBD group ($n = 26$) than in PTBD group ($n = 24$): 25.6% vs 49.1%. The rates of bacteriobilia did not differ significantly in patients from different groups: 23.1% in EISBD group and 25.0% in PTBD group. However, the frequency of biliary bacterial colonization coupled with cholangitis was also 2 times lower in EISBD group in comparison with patients underwent PTBD: 7.7% vs 16.7%. *Escherichia coli* predominated in bile specimens from patients with bacteriobilia associated with cholangitis in both groups.

Conclusions. The use of EISBD for palliative biliary decompression in patients with proximal mechanical jaundice of tumor origin is associated with lower risk of bacterial colonization of the bile as compared to PTBD approach, and as a result with less risk of the development of infectious complications.

Key words: hilar malignant biliary obstruction, biliary decompression methodology, bacteriobilia.

Palliation of jaundice is therapeutic purpose in majority patients with malignant hilar obstruction [1]. Malignant obstruction to outflow of bile predisposes to bacteriobilia, in part as a result of high frequency of the use of biliary interventions and immunocompromised state in these patients [2, 3]. Biliary tree is usually the aseptic system. Obstruction in biliary tree magnifies ductal pressure, causes biliary stasis and multiplication of bacteria (bacteriobilia), and, as a result, the development of cholangitis. There are three main pathways of the infection of bile system: ascending from ampulla, hematogenous, and

lymphatic. Numerous experimental studies evidences that malignant biliary obstruction impairs already compromised local and systemic innate immunity due to metabolic exhausting of phagocytic cells, that in turn facilitates further bacterial translocation and can adversely affect the clinical outcome [4]. Biliary decompression methodology is one of the common factors crucially affecting bacteriobilia occurrence. The purpose of this study was comparative assessment of the frequency of bacterial colonization of the bile in patients with hilar malignant biliary obstruction after the palliative biliary

decompression using different methodological approaches.

Materials and Methods

50 patients with proximal mechanical jaundice of tumor origin aged of ~62 years (25 males and 25 females), who were on steady-state treatment in Main military clinical hospital (Kyiv, Ukraine) were recruited in this prospective study. After providing informed consent, all patients underwent cholangiostomy under ultrasound and X-ray control using percutaneous transhepatic (PTBD) and external-internal suprapapillary (EISBD) approaches. Bile specimens were taken right after the biliary drainage. Identification of bacterial isolates was performed using standard cultural and biochemical methods according to EUCAST. The clinical diagnosis of cholangitis was established on the basis of the following criteria: body temperature above 38.5 °C, white blood cell count > 10×10⁹/L, and neutrophil granulocytes percentage > 70. Statistical processing of the obtained data was performed using the IBMSPSS Statistics 22 package. Descriptive statistics were carried out. The normality of the distribution of variables was assessed using the Shapiro-Wilk test.

Results and Discussion

The incidence of cholangitis was almost 2 folds lower in EISBD group ($n = 26$) than in PTBD group ($n = 24$): 25.6% vs 49.1%. The rates of bacteriobilia did not differ significantly in patients from different groups: 23.1% in EISBD group and 25.0% in PTBD group. However, the frequency of biliary bacterial colonization coupled with cholangitis was also 2 times lower in EISBD group in comparison with patients underwent PTBD: 7.7% vs 16.7%. *Escherichia coli* predominated in bile specimens from patients

with bacteriobilia associated with cholangitis in both groups. *Klebsiella* spp. was also isolated from infected bile specimens from both groups. *Enterococcus* spp. was isolated in patients from PTBD group but not from EISBD group (Table).

All isolated bacteria were sensitive to ceftriaxone. Regular sanitation of the drainage along with the appointment of ceftriaxone allowed to eliminate the clinical manifestations of cholangitis and achieve bile sterility within 5–6 days in both groups.

In this study we observed advantages of EISBD approach for the biliary decompression in patients with hilar malignant biliary obstruction in context of the occurrence of bacteriobilia and cholangitis. One of the shortcomings of PTBD approach is the loss of bile. It is well known that bile acids and cholates participate in maintaining intestinal barrier integrity and commensal microbiota balance. The lack of cholates leads to an imbalance of intestinal microbiota with a predominance of gram-negative bacteria, increases intestinal permeability, and as a result bacterial translocation and endotoxemia followed by the development of septic complications and renal dysfunction [5]. In addition, disturbances in bile outflow are associated with metabolic disorders of Kupffer cells [6, 7], that might be one of the reasons for increased risk of bacteriobilia.

Conclusion

We believe, that one of the reasons of moderately lower rates of bacteriobilia in patients from EISBD group is the nature of external and internal drainage, which can be of at least two types: those that come into contact with the contents of the duodenum, i.e. pass through Vater's nipple, and those that do not come into contact with it and are located subpapillary. This is a very important fact, because, as was mentioned above, among

Table. Microorganisms in bile specimens of patients with malignant biliary obstruction and concomitant cholangitis who underwent different approaches for biliary decompression

Biliary decompression approach	<i>Escherichia coli</i>		<i>Enterobacter</i> spp.		<i>Klebsiella</i> spp.	
	The number of infected specimens	%	The number of infected specimens	%	The number of infected specimens	%
PTBD ($n = 4$)	2	66.7	1	25	1	25
EISBD ($n = 3$)	2	50.0	0	0	1	33.5

the pathways of drainage infection: antegrade (from the outside), retrograde (from the intestinal flora) and hematogenous, the most important one is retrograde, and in the case of EISBD, this way of infection is excluded.

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REFERENCES

1. Pan H., Liang Z., Yin T. S., Xie Y., Li D. W. Hepato-biliary-enteric stent drainage as palliative treatment for proximal malignant obstructive jaundice. *Med Oncol.* 2014, 31(3), 853. <https://doi.org/10.1007/s12032-014-0853-3>
2. Narkhede R., Desai G., Pande P. Bacteriobilia in Hepato-Pancreato-Biliary Surgery: an Enemy or a Friend in Disguise? *Indian J. Surg.* 2019, v. 81, 479–484. <https://doi.org/10.1007/s12262-019-01933-0>
3. Loeuillard E., Conboy C. B., Gores G. J., Rizvi S. Immunobiology of cholangiocarcinoma. *JHEP Rep.* 2019, 1(4), 297–311. <https://doi.org/10.1016/j.jhepr.2019.06.003>
4. Lan T., Qian S., Tang C., Gao J. Role of Immune Cells in Biliary Repair. *Front Immunol.* 2022, v. 13, 866040. <https://doi.org/10.3389/fimmu.2022.866040>
5. Vagholkar K. Obstructive jaundice: understanding the pathophysiology. *International Journal of Surgery and Medicine.* 2020, 6(4), 26–31. <https://doi.org/10.5455/ijsm.2020-07-061-jaundice>
6. Sano T., Ajiki T., Takeyama Y., Kuroda Y. Internal biliary drainage improves decreased number of gut mucosal T lymphocyte and MAdCAM-1 expression in jaundiced rats. *Surgery.* 2004, 136(3), 693–699. <https://doi.org/10.1016/j.surg.2004.02.001>
7. Yan M., Hou L., Cai Y., Wang H., Ma Y., Geng Q., Jiang W., Tang W. Effects of Intestinal FXR-Related Molecules on Intestinal Mucosal Barriers in Biliary Tract Obstruction. *Front Pharmacol.* 2022, 13, 906452. <https://doi.org/10.3389/fphar.2022.906452>