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胆总管结石并胆道感染患者胆汁中致病菌的分布及耐药性分析*

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摘要 目的:了解胆总管结石并胆道感染患者胆汁中致病菌的分布以及耐药性的情况,为临床中胆总管结石并胆道感染患者的诊治提供参考。**方法:**选取2012年1月至2012年12月期间被我院收治的胆总管结石并胆道感染患者内镜逆行胰胆管造影术(ERCP)抽取胆汁标本150例,对其进行细菌培养和药敏试验,观察和分析细菌分布情况和耐药性情况。**结果:**①细菌培养阳性的例数为123例(阳性检出率82.0%),其中,革兰氏阴性菌39例(31.71%),主要为大肠埃希菌23例(18.70%);革兰氏阳性菌64例(52.03%),主要是粪肠球菌22例(17.89%)和甲型溶血性链球菌10例(8.13%);真菌(白假丝酵母菌)20例(16.26%)。②患者胆汁中的细菌主要敏感的药物有美罗培南、亚胺培南、万古霉素、庆大霉素、头孢吡肟和阿米卡星等。**结论:**胆总管结石并胆道感染患者胆汁中病原菌分布出现了新的变化,临床中应根据患者胆汁药敏试验结果选择有效的治疗方法和抗菌药物。

关键词:胆管结石并胆道感染;胆汁;ERCP;病原菌;药敏试验

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Biliary Pathogenic Bacteria Distribution and Drug Resistance Analysis in Patients with Common Bile Duct Stones Combined Biliary Tract Infection*

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ABSTRACT Objective: To study the situation of biliary infection distribution and drug resistance of pathogenic bacteria in patients bile with common bile duct stones and biliary tract infection and to provide a reference for the clinical diagnosis and treatment in patients with common bile duct stones combined biliary tract infection. **Methods:** 150 cases of bile specimens extracted via endoscopic retrograde pancreatic angiography (ERCP) from patients with common bile duct stones combined biliary tract infection during the period of January 2012 to December 2012 in our hospital were selected, the bacterial distribution and drug resistance were observed and analyzed. **Results:** ① There were 123 germiculture positive cases (positive detection rate 82.0%). Among them, gram negative bacteria were detected in 39 cases (31.71%), 23 cases of which were e. coli (18.70%); Gram positive bacteria were detected in 64 cases (52.03%), mainly consisted of 22 cases of dung enterococcus (17.89%) and 10 cases of alpha hemolytic streptococcus (8.13%); White fungus (candida) were detected in 20 cases (16.26%). ② The main sensitive drugs to biliary bacteria were Meropenem, Imipenem, Vancomycin, Gentamicin, Cefepime and Amy card magnitude. **Conclusion:** Bacteria distribution in patients with common bile duct stones combined biliary tract infection present changes. Effective treatment and antibacterial drugs can be utilized in clinic according to patients biliary drug susceptibility test results.

Key words: Bile duct stones combined biliary infection; Bile; ERCP; Pathogenic bacteria; Drug sensitive test

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前言

胆总管结石伴胆道感染是消化内科和肝胆外科常见的和多发的感染性疾病^[1,2]。正常情况下胆汁中并没有细菌繁殖,但当肿瘤、炎症、寄生虫、结石等因素引起胆道梗阻,胆汁排泄不畅时,肠道中的细菌就会经十二指肠乳头逆行侵入胆道系统,胆汁中的细菌异常生长,从而引起胆道感染^[3]。有研究表明,胆道感染严重时,可引起机体菌血症与脓毒血症,病死率高达10.0%,是肝胆外科围手术期致命性的并发症^[4]。胆道感染的诊断一经确立,应立即进行抗生素治疗。由于胆道感染胆汁中的

致病菌的分布情况在不同时期、不同地域存在一定的差异。近年来,随着抗生素的广泛应用,各地医师使用抗生素的习惯不同,致病菌种类也在不断发生的变化,各地区或同地区不同时期的胆道感染通常具有的自身的致病微生物学分布和药物敏感性特点具有差异性。因此,如何合理选择抗生素成为治疗的重点^[5,6]。对感染患者诊治初期,临床医师通常根据经验使用抗生素,而此经验则来源于既往患者的胆汁细菌培养和药敏试验分析。所以,及时了解近期本地区患者胆汁标本的病原微生物学分布及对抗菌药物敏感性的情况,对选择合理抗生素非常重要。本研究对150例胆总管结石伴胆道感染患者内镜逆行胰胆

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管造影术(ERCP)抽取胆汁标本,进行细菌培养和药敏试验,观察和分析细菌分布情况和药物敏感性情况,旨在为临床用药提供可靠依据,提高经验用药的准确性。

1 资料与方法

1.1 一般资料

选取 2012 年 1 月至 2012 年 12 月期间被我院收治的胆总管结石并胆道感染患者内镜逆行胰胆管造影术(ERCP)^[7]抽取胆汁标本 150 例,其中男性 79 例,女性 71 例;年龄 20~80 岁,平均年龄(43.2±6.8)岁。所有患者入院时均出现发热、畏寒、黄疸或程度不同的上腹疼痛,症状严重者可出现神志改变,甚至是感染性休克。患者术前均经腹部 CT、B 超或 MRCP 确诊为胆总管结石,术中经 ERCP 证实诊断。

1.2 胆汁的收集与处理

采用富士 ED530 型电子十二指肠镜行 ERCP,当用严格消毒的导管经十二指肠乳头插入胆道,在注射造影剂前,用一次性无菌注射器抽吸 5 mL 胆汁,立即注入已备好的无菌试管内,

并于 2 h 内接种,置于 35℃ 温箱中,孵育 18-24 h,进行细菌培养及药物敏感性试验。采用法国梅里埃半自动微生物鉴定仪进行细菌鉴定。

1.3 病原菌分离鉴定与药敏试验

分离鉴定按《全国临床检验操作规程》进行,药物敏感试验为 Kirby-Bauer 扩散法试验。对质控菌株(金黄色葡萄球菌(ATCC25923),大肠埃希氏菌(ATCC25922),铜绿假单胞菌(ATCC27853))进行跟踪质控。判定标准参考美国临床实验室国家标准化委员会(NCCLS)公布的标准。

2 结果

2.1 胆总管结石并胆道感染患者胆汁标本细菌分离培养情况

将 150 例患者的胆汁标本送检,细菌培养阳性的例数为 123 例即阳性检出率为 82.0%,其中,革兰阴性菌 39 例,占 31.71%,大肠埃希菌 23 例(18.70%);革兰阳性菌 64 例,占 52.03%,粪肠球菌 22 例(17.89%),甲型溶血性链球菌 10 例(8.13%);真菌 20 例,占 16.26%。具体分布情况见表 1。

表 1 123 株细菌菌株的分布结果 [n(%)]
Table 1 The distribution of 123 strains of bacteria [n(%)]

菌属 Bacterial genus	细菌种类 Bacterial species	例数 Cases	构成比(%) Constituent ratio(%)
G- [39(31.71%)]	大肠埃希菌 <i>Escherichia coli</i>	23	18.70
	肺炎型肺炎克雷伯菌 <i>Pneumonic Klebsiella pneumoniae</i>	5	4.07
	布氏柠檬酸杆菌 <i>Pulmonary Citrobacter braakii</i>	3	2.44
	产酸克雷伯氏菌 <i>Klebsiella oxytoca</i>	2	1.63
	皮氏罗尔斯顿菌 <i>Petri Rawls meal bacteria</i>	2	1.63
	鲍曼氏不动杆菌 <i>Bauman's Acinetobacter</i>	1	0.81
	人苍白杆菌 <i>Ochrobactrum anthropi</i>	1	0.81
	铜绿假单胞菌 <i>Pseudomonas aeruginosa</i>		
	粪肠球菌 <i>Enterococcus faecalis</i>	22	17.89
	甲型溶血性链球菌 <i>Hemolytic streptococcus</i>	10	8.13
	表皮葡萄球菌 <i>Staphylococcus epidermidis</i>	6	4.88
	口腔链球菌 <i>Oral streptococci</i>	5	4.07
	鸪鸡肠球菌 <i>Enterococcus gallinarum</i>	4	3.25
	副血链球菌 <i>Streptococcus parasanguis</i>	3	2.44
G+ [64(52.03%)]	科氏葡萄球菌 <i>Staphylococcus cohnii</i>	3	2.44
	铅黄肠球菌 <i>Enterococcus casseliflavus</i>	3	2.44
	腾黄微球菌 <i>Huang Micrococcus</i>	2	1.63
	金黄色葡萄球菌 <i>Staphylococcus aureus</i>	2	1.63
	鸟肠球菌 <i>Enterococcus avium</i>	1	0.81
	西宫皮肤球菌 <i>Nishinomiya skinaureus</i>	1	0.81
	牛链球菌 <i>Streptococcus bovis</i>	1	0.81
	咽峡炎链球菌 <i>Streptococcus anginosus</i>	1	0.81
	白假丝酵母菌 <i>Candida albicans</i>	20	16.26
真菌 Fungus [20(16.26%)]			
合计 Total		123	100.00

2.2 胆总管结石并胆道感染患者胆汁标本药物敏感性情况

本研究患者胆汁药敏试验结果显示,对美罗培南和亚胺培南的敏感性最高,药敏阳性例数 63 例,敏感阳性率均为 51.22%;其次,万古霉素、庆大霉素、头孢吡肟和阿米卡星的敏

感例数均在 40 例以上;对左氧氟沙星、哌拉西林/他唑巴坦、头孢哌酮/舒巴坦、利奈唑胺、奎奴普丁和环丙沙星等药物的敏感性也很高。见表 2。

表 2 抗生素对胆汁细菌敏感性结果 [n(%)]

Table 2 The antibioticsensitivity of bacteria in bile[n(%)]

抗生素 Antibiotics	药敏阳性(%) Drug sensitivity of positive(%)	抗生素 Antibiotics	药敏阳性(%) Drug sensitivity of positive(%)
美罗培南 Meropenem	63(51.22)	环丙沙星 Ciprofloxacin	35(28.46)
亚胺培南 Imipenem	63(51.22)	妥布霉素 Tobramycin	21(17.07)
万古霉素 Vancomycin	48(39.02)	头孢曲松 Ceftriaxone	15(12.20)
庆大霉素 Gentamicin	47(38.21)	头孢他啶 Ceftazidime	13(10.57)
头孢吡肟 Cefepime	45(36.59)	替考拉宁 Teicoplanin	12(9.76)
阿米卡星 Amikacin	45(36.59)	青霉素 Penicillin	11(8.94)
左氧氟沙星 Levofloxacin	38(30.89)	克林霉素 Clindamycin	9(7.32)
哌拉西林 / 他唑巴坦 Piperacillin / tazobactam	38(30.89)	氯霉素 Chloramphenicol	8(6.50)
头孢哌酮 / 舒巴坦 Cefoperazone/ sulbactam	38(30.89)	头孢噻肟 Cefotaxime	6(4.88)
利奈唑胺 Linezolid	37(30.08)	复方新诺明 Cotrimoxazole	5(4.07)
奎奴普丁 Quinupristin	36(29.27)	红霉素 Erythromycin	5(4.07)

3 讨论

胆结石与胆道感染的发生有着密切关系,两者相互作用、互为因果^[8-11]。各种原因直接或间接地引起胆道系统形成结石后,可引起胆道梗阻、胆汁淤积,使胆囊内压力的增高,进而使胆囊黏膜受损并促进炎症介质的释放,引起胆囊炎症^[12-14]。与此同时,来自肠道的条件致病菌会逆行侵入或经血行、淋巴系统进入胆道及胆囊,造成胆道系统感染。而胆道感染后,可以进一步致使胆泥的增多,胆汁粘稠、弹道阻塞,易于胆石的形成^[15]。胆总管结石并胆道感染若得不到及时有效的治疗,有可能会危及生命,因此,病原菌的检测对胆总管结石并胆道感染患者的治疗具有非常重要的临床价值^[16]。本文选取我院 2012 年 6 月至 2013 年 6 月期间 150 例胆总管结石并胆道感染患者的胆汁标本进行细菌培养和药敏试验。

本组研究发现,150 例患者胆汁标本细菌检出 123 例,阳性检出率为 82.0%。胆汁细菌感染革兰氏阴性菌以大肠埃希菌最多;革兰氏阳性菌以粪肠球菌和甲型溶血性链球菌居多;真菌以白假丝酵母菌最多。胆道感染的致病菌分布说明其致病菌大多来自于肠道细菌的逆行感染,种类与肠道细菌的几乎一样。而此研究中主要的致病菌种类(大肠埃希菌、粪肠球菌和白假丝酵母菌)与不同年代和地区的报道差异较大,分析其原因,除与所选的患者不同和胆汁采集和培养技术等有一定关系外,也可能与抗生素的使用不当和滥用,耐药菌谱的不断变迁有关。随着内镜技术的迅速发展^[17],大多数胆总管结石并胆道感染患者的治疗不需要手术治疗,可在内镜下切乳头括约肌取石,此法创伤小、恢复快、安全经济等优点,使内镜逆行胰胆管造影术(ERCP)成为良好的治疗方法^[18,19]。在对内镜治疗的患者,经导管抽取部分胆汁进行细菌培养和药敏试验,在结果返回之前,根据临床经验选用抗生素。本研究的统计结果显示,大多数胆道细菌对美罗培南、亚胺培南、万古霉素、庆大霉素、头孢吡肟和阿米卡星等药物敏感,这与以往研究有些许差异^[20]。

综上所述,根据本组研究胆汁的细菌分布情况和药物敏感

性情况,胆汁中的菌群和药物敏感性发生了变化,胆总管结石并胆道感染患者的治疗应当根据当地的最近病原学检测资料对经验性抗生素选用进行调整以及更新,为临床中合理使用抗生素,指导有效治疗,促进患者康复提供科学依据。

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