临床与基础桥接研究
Clinical and Basic Bridging Research

头孢特仑体外抗菌作用研究

Research on the *in vitro* antibacterial effect of cefteram

刘姚姚, 薛 峰, 李 耘

(北京大学 第一医院 临床药理研究所, 北京 100034)

LIU Yao-yao, XUE Feng, LI Yun

(*Institute of Clinical Pharmacology, Peking University First Hospital, Beijing 100034, China*)

摘要: 目的 评价头孢特仑对近3年临床常见分离菌的体外抗菌活性。**方法** 收集临床分离细菌,用标准微量肉汤二倍稀释法测定最低抑菌浓度(MIC)。**结果** 对2021—2023年全国范围内临床分离484株细菌进行了MIC测定。结果显示头孢特仑对除青霉素耐药肺炎链球菌(青霉素MIC≥2 mg·L^{-1})外的其他链球菌属细菌均有很好抗菌活性,MIC_{90}值≤1 mg·L^{-1},细菌敏感率为100.0%,与青霉素相似,略优于头孢泊肟,优于头孢呋辛、头孢克肟、头孢克洛和头孢氨苄。革兰氏阴性菌中,头孢特仑对超广谱β内酰胺酶(ESBLs)阴性大肠埃希菌、肺炎克雷伯菌、奇异变形杆菌以及流感嗜血杆菌,卡他莫拉菌同样具有很好抗菌作用,MIC_{90}值≤2 mg·L^{-1},敏感率为100.0%。其中对流感嗜血杆菌,头孢特仑优于全部对照药;对其他革兰氏阴性菌,与头孢泊肟相似,优于头孢呋辛、头孢克洛和头孢氨苄。对于厌氧菌中消化链球菌属,头孢特仑与头孢呋辛相似,优于其他对照药。**结论** 头孢特仑对国内近年临床分离常见革兰氏阳性、阴性及厌氧菌具有广泛、均衡抗菌作用,对青霉素中介、氨苄西林耐药流感嗜血杆菌保存较好活性,为口服头孢菌素中较好品种。

关键词: 头孢特仑;口服头孢菌素;最低抑菌浓度;体外
DOI: 10.13699/j.cnki.1001-6821.2025.05.010
中图分类号: R978.1 **文献标志码:** A
文章编号: 1001-6821(2025)05-0646-08

Abstract: Objective To evaluate the *in vitro* antibacterial activity of cefteram against common clinically isolated bacteria in the past three years. **Methods** The clinical isolates were collected and the minimal inhibitory concentration (MICs) were determined by the microdilution method. **Results** A total of 484 pathogenic bacteria over the period 2021-2023 were studied. The results show that cefteram has good antibacterial activity against *Streptococcus spp* other than penicillin-resistant *Streptococcus pneumoniae* (MICs of penicillin ≥ 2 mg·L^{-1}), MIC_{90} value of cefteram was less than or equal 1 mg·L^{-1}, and the susceptibility rate was 100.0%, which was similar to penicillin, slightly better than cefpodoxime, better than cefuroxime, cefixime, cefaclor and cefalexin. Against gram-negative bacteria, cefteram also showed better antibacterial activity, especially against β-lactamase (ESBLs) negative *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Haemophilus influenzae*, and *Moraxella catarrhalis*. The MIC_{90} value of cefteram was ≤ 2 mg·L^{-1}, and the susceptibility rate was 100.0%. Especially for *Hemophilus influenzae*, cefteram was better than all comparator agents, were comparable to cefpodoxime, better than cefuroxime, cefaclor and cefalexin. For *Peptostreptococcus spp.*, cefteram was comparable to cefuroxime, better than all compared agents. **Conclusion** Cefteram had a

作者简介: 刘姚姚(1996-),女,学士,主要从事细菌耐药相关方面的研究
通信作者: 李耘,副研究员
Tel:(010)82802440
E-mail:liyun19702@sina.com

wide and balanced antibacterial against clinical isolatied of gram – negative bacteria, gram – positive bacteria and anaerobic bacteria in China in recent years. Cefteram also showed better antibacterial activity, especially against penicillin intermediate and ampicillin – resistant *Hemophilus influenzae*, and is a good variety among oral cephalosporins.

Key words: cefteram; oral cephalosporin; minimal inhibitory concentration; *in vitro*

头孢特仑新戊酯(cefteram pivoxil)为日本富山化学工业株式会社研发的第3代口服头孢菌素,本身并无抗菌活性,口服吸收后经肠管壁酯酶水解释放头孢特仑发挥抗菌作用[1-2]。头孢特仑的作用机制同其他β内酰胺类抗菌药物,通过与青霉素结合蛋白(penicillin binding proteins,PBPs)结合,干扰细胞壁合成而发挥抗菌作用,主要结合位点为PBP3,对广谱酶及部分超广谱β内酰胺酶(extended spectrum β-lactamases,ESBLs)稳定[3]。既往研究显示,头孢特仑对链球菌属、肠杆菌目中多数菌属、嗜血杆菌属、卡他莫拉菌及革兰氏阳性厌氧菌有较好抗菌活性[3-4]。头孢特仑和头孢地尼在呼吸及泌尿系统等方面疗效相似[5],其中头孢特仑降解速度与高温、光照、湿度呈正相关[6]。本研究旨在评价头孢特仑对近年国内临床常见分离菌的体外抗菌作用。

材料与方法

1 材料

药品 头孢特仑,规格:每支500 mg,批号:AE111R,效价:81.6%,深圳华润九新药业有限公司提供;头孢泊肟,规格:每支100 mg,批号:267041,效价:98.75%,购自美国MCE公司;头孢克肟,规格:每支100 mg,批号:130503-202007,效价:88.9%,头孢呋辛,规格:每支100 mg,批号:130493-201706,效价:91.9%,头孢克洛,规格:每支100 mg,批号:130481-202007,效价:94.1%,头孢氨苄,规格:每支200 mg,批号:130408-202212,效价:94.1%,氨苄西林,规格:每支100 mg,批号:130410-201908,效价85.6%,均购自中国食品药品检定研究院;青霉素,规格:每支100 mg,批号:130437-200904,效价:88.8%,克林霉素,规格:每支100 mg,批号:130422-200705,效价:86.0%,均购自中国药品生物制品检定所。

菌株 最低抑菌浓度(minimal inhibitory concentration,MIC)标准质控菌株:肺炎链球菌ATCC49619、大肠埃希菌ATCC25922、流感嗜血杆菌ATCC49247、脆弱拟杆菌ATCC25285;临床分离菌株:484株;革兰氏阳性菌株:208株;革兰氏阴性菌:257株;厌氧菌:消化链球菌属19株。

2 培养基与孵育条件

链球菌为含5%脱纤维马血CAMHB培养基,(35±2)℃孵育20~24 h[7];流感嗜血杆菌为Mueller-Hinton肉汤培养基+5%脱纤维马血+20 mg·L^{-1} β-NAD(MH-F肉汤),(35±1)℃孵育18 h[8];其他需氧、苛氧菌为CAMHB培养基,(35±2)℃孵育16~20 h。厌氧菌为Wilkins-Chalgren Anaerobe Agar厌氧培养基+5%无菌脱纤维羊血,厌氧环境(厌氧罐+厌氧袋Thermo AnaeroGen™ 3.5 L)(36±1)℃孵育48 h[7]。

3 MIC测定

厌氧菌用琼脂二倍稀释法,被试菌悬液用多点接种仪接种,每点接种量为1×10^5 CFU。其他菌种用微量肉汤二倍稀释法,菌液终浓度为5×10^5 CFU·mL^{-1}。抗菌药物测定浓度范围256~0.002 mg·L^{-1}。每株细菌在试验前经过平板转活分纯,以新鲜菌体用于试验。每次试验用标准菌株作为敏感试验质控菌;不含抗菌药物的菌液孔或平皿作为试验菌株生长对照。

4 统计学处理

用Excel软件处理MIC测定结果,计算MIC_{50}、MIC_{90}、MIC_{mode}、MIC_{range}。头孢特仑对需氧菌敏感、耐药率参照文献[9]计算(敏感≤2 mg·L^{-1},耐药≥8 mg·L^{-1})。其他药物按照CLSI 2024折点[7]计算细菌敏感、耐药率。

结 果

1 头孢特仑及对照药对链球菌属MIC结果

头孢特仑对青霉素敏感肺炎链球菌(penicillin susceptible *Streptococcus pneumoniae*,PSSP;青霉素MIC≤0.06 mg·L^{-1})具有很好抗菌作用,MIC值≤0.12 mg·L^{-1},菌株100%敏感(表1)。头孢特仑与青霉素、头孢泊肟、头孢呋辛相似,略优于头孢克肟、头孢克洛和头孢氨苄,优于克林霉素(图1)。对青霉素中介肺炎链球菌,头孢特仑MIC值在

表1 抗菌药物对革兰氏阳性菌最低抑菌浓度(MIC)结果及细菌敏感、耐药率

Table 1 Minimal inhibitory concentration (MIC) values of antibacterial agents against gram-positive bacteria and susceptibility(S) and resistance(R) rates

Strain	Antibiotic	MIC_{50} ($mg \cdot L^{-1}$)	MIC_{90} ($mg \cdot L^{-1}$)	MIC_{mode} ($mg \cdot L^{-1}$)	MIC_{rang} ($mg \cdot L^{-1}$)	S(%)	R(%)
PSSP($n=32$)	Cefteram	0.016	0.06	0.008,0.016	0.004-0.12	100.0	0
	Cefpodoxime	0.03	0.06	0.03	0.008-0.12	100.0	0
	Cefixime	0.12	1	0.12	0.06-2	-	-
	Cefuroxime	0.016	0.12	0.016	0.016-0.25	100.0	0
	Cefaclor	0.25	0.5	0.25	0.12-1	100.0	0
	Cefalexin	2	4	1	1-4	-	-
	Penicillin	0.008	0.016	0.008	0.008-0.06	100.0	0
	Clindamycin	>256	>256	>256	0.12- >256	6.3	90.6
PISP($n=30$)	Cefteram	0.5	1	1	0.06-2	100.0	0
	Cefpodoxime	1	2	1	0.25-4	23.3	40.0
	Cefixime	16	16	16	2-32	-	-
	Cefuroxime	2	4	4	0.25-8	23.3	50.0
	Cefaclor	32	64	64	4-64	0	100.0
	Cefalexin	128	256	128	16-256	-	-
	Penicillin	1	1	1	0.12-1	0	0
	Clindamycin	>256	>256	>256	0.12- >256	3.3	96.7
PRSP($n=44$)	Cefteram	4	8	8	1-8	38.6	43.2
	Cefpodoxime	8	16	8	2-16	0	100.0
	Cefixime	64	64	64	16-64	-	-
	Cefuroxime	16	16	16	4-32	0	100.0
	Cefaclor	128	128	128	32-256	0	100.0
	Cefalexin	>256	>256	>256	128- >256	-	-
	Penicillin	2	2	2	2	0	100.0
	Clindamycin	>256	>256	>256	0.12- >256	6.8	93.2
S. pyogenes($n=33$)	Cefteram	0.008	0.008	0.008	0.004-0.03	100.0	0
	Cefpodoxime	0.016	0.016	0.016	0.008-0.06	100.0*	0
	Cefixime	0.06	0.12	0.06	0.06-0.5	-	-
	Cefuroxime	0.008	0.016	0.008	0.008-0.06	100.0*	0
	Cefaclor	0.06	0.12	0.06	0.06-0.5	100.0*	0
	Cefalexin	0.25	0.5	0.25	0.25-2	100.0*	0
	Penicillin	0.008	0.008	0.008	0.008-0.03	100.0	0
	Clindamycin	>256	>256	>256	0.06- >256	18.2	78.8
S. agalactiae($n=34$)	Cefteram	0.016	0.03	0.016	0.008-0.03	100.0	0
	Cefpodoxime	0.03	0.06	0.03	0.008-0.06	100.0*	0
	Cefixime	0.25	0.25	0.25	0.06-0.25	-	-
	Cefuroxime	0.03	0.03	0.03	0.016-0.03	100.0*	0
	Cefaclor	0.25	0.5	0.25	0.12-0.5	100.0*	0
	Cefalexin	1	2	1	1-2	100.0*	0
	Penicillin	0.03	0.03	0.03	0.016-0.03	100.0	0
	Clindamycin	8	>256	>256	0.03- >256	41.2	58.8
Streptococcus spp. viridans group ($n=35$)	Cefteram	0.06	0.25	0.12	0.004-2	100.0	0
	Cefpodoxime	0.25	1	0.25	0.016-8	-	-
	Cefixime	2	8	2	0.06-32	-	-
	Cefuroxime	0.25	2	0.25	0.016-4	-	-
	Cefaclor	1	16	1	0.06-64	-	-
	Cefalexin	4	32	2	1-256	-	-
	Penicillin	0.03	0.25	0.03	0.008-1	77.1	0
	Clindamycin	128	>256	0.06	0.03- >256	45.7	54.3

*: With reference to CLSI and EUCAST, penicillin is an alternative to cefpodoxime, cefuroxime, cefaclor and cephalexin, i.e., penicillin-susceptible strains are also sensitive to the above drugs; -: No breakpoint; PSSP: Penicillin susceptible *Streptococcus pneumoniae*; PISP: Penicillin intermediate *Streptococcus pneumoniae*; PRSP: Penilin resistant *Streptococcus pneumoniae*; *S. pyogenes*: *Streptococcus pyogenes*; *S. agalactiae*: *Streptococcus agalactiae*.

表 2 抗菌药物对革兰氏阴性菌 MIC 结果及细菌敏感、耐药率(%)

Table 2 MIC values of antibacterial agents against gram – negative bacteria and S and R rates (%)

Strain	Antibiotic	MIC_{50} (mg·L^{-1})	MIC_{90} (mg·L^{-1})	MIC_{mode} (mg·L^{-1})	MIC_{rang} (mg·L^{-1})	S(%)	R(%)
ESBLs negative	Cefteram	0.25	0.5	0.25	0.06 – 1	100.0	0
E. coli (n = 52)	Cefpodoxime	0.5	0.5	0.5	0.12 – 1	100.0	0
	Cefixime	0.5	1	0.25,0.5	0.03 – 1	100.0	0
	Cefuroxime	4	8	4	1 – 16	78.8	0
	Cefaclor	4	16	4	0.5 – 128	71.2	9.6
	Cefalexin	8	16	8	4 – 32	–	–
ESBLs negative	Cefteram	0.12	0.5	0.12	0.016 – 1	100.0	0
K. pneumoniae	Cefpodoxime	0.12	0.25	0.12	0.016 – 2	100.0	0
(n = 50)	Cefixime	0.06	0.12	0.06	0.016 – 0.5	100.0	0
	Cefuroxime	2	4	2	1 – 16	90.0	0
	Cefaclor	0.5	1	0.5	0.25 – 2	100.0	0
	Cefalexin	4	8	4	4 – 8	–	–
ESBLs negative	Cefteram	0.03	0.12	0.03	0.016 – 1	100.0	0
Proteus	Cefpodoxime	0.06	0.06	0.06	0.03 – 0.25	100.0	0
mirabilis (n = 50)	Cefixime	0.008	0.016	0.008	0.004 – 0.03	100.0	0
	Cefuroxime	1	2	1	0.5 – 8	98.0	0
	Cefaclor	2	4	2	0.5 – 8	100.0	0
	Cefalexin	32	64	32	8 – 64	–	–
Ampicillin –	Cefteram	0.016	0.03	0.016,0.03	0.004 – 0.5	100.0	0
susceptible	Cefpodoxime	0.12	0.25	0.06,0.12	0.016 – 0.5	100.0	0
H. influenzae (n = 35)	Cefixime	0.03	0.5	0.03	0.016 – 0.5	100.0	0
	Cefuroxime	0.5	4	0.5	0.25 – 8	97.1	0
	Cefaclor	2	8	1	0.5 – 32	91.4	2.9
	Cefalexin	8	256	8	1 – 256	–	–
	Ampicillin	0.25	1	0.25	0.06 – 1	100.0	0
BLPAR	Cefteram	0.25	1	0.5	0.016 – 1	100.0	0
H. influenzae	Cefpodoxime	1	8	1	0.06 – 16	74.5	25.5 *
(n = 51)	Cefixime	1	4	1	0.03 – 16	74.5	25.5 *
	Cefuroxime	8	64	2	0.5 – 128	49.0	45.1
	Cefaclor	32	128	32	1 – 256	35.3	54.9
	Cefalexin	8	>256	8	2 – >256	–	–
	Ampicillin	128	>256	128	16 – >256	0	100.0
BLNANS	Cefteram	1	2	1	0.03 – 2	100.0	0
H. influenzae	Cefpodoxime	2	16	2	0.12 – 16	78.9	21.1 *
(n = 19)	Cefixime	1	16	0.5	0.03 – 16	63.2	36.8 *
	Cefuroxime	4	128	128	1 – >256	57.9	42.1
	Cefaclor	4	>256	2,4	2 – >256	63.2	31.6
	Cefalexin	8	>256	4	2 – >256	–	–
	Ampicillin	8	>256	2	2 – >256	0	68.4
Moraxella	Cefteram	0.5	1	0.5	0.06 – 2	100.0	0
catarrhalis	Cefpodoxime	0.5	0.5	0.5	0.25 – 1	–	–
(n = 52)	Cefixime	0.12	0.25	0.12	0.03 – 0.5	–	–
	Cefuroxime	1	2	1	0.5 – 4	100.0	0
	Cefaclor	0.5	4	0.5	0.25 – 8	100.0	0
	Cefalexin	2	64	2	1 – 64	–	–

*: Non – susceptibility; –: No breakpoint; *E. coli*: *Escherichia coli*; ESBLs: Extended spectrum β – lactamases; *K. pneumoniae*: *Klebsiella pneumoniae*; *H. influenzae*: *Haemophilus influenzae*; BLPAR: β – lactamase positive ampicillin resistant; BLNANS: β – lactamase negative ampicillin non – susceptible.

0.06 ~ 2 mg·L^{-1} MIC_{50}、MIC_{90}值分别为 0.5 mg·L^{-1}和1 mg·L^{-1},较 PSSP 升高 16 ~ 32 倍,细菌敏感率为 100.0%。所测 β 内酰胺类药物均呈现此特征,MIC_{50}、MIC_{90}值升高 16 ~ 128 倍,菌株对头孢泊肟、头孢呋辛、头孢克洛和青霉素的敏感率分别为 23.3%、23.3%、0 和 0,明显低于头孢特仑(图 2)。对青霉

表3 抗菌药物对厌氧菌MIC结果及细菌敏感、耐药率

Table 3 MIC values of antibacterial agents against anaerobic bacteria and S and R rates

Strain	Antibiotic	MIC_{50} (mg·L^{-1})	MIC_{90} (mg·L^{-1})	MIC_{mode} (mg·L^{-1})	MIC_{rang} (mg·L^{-1})	S(%)	R(%)
Peptostreptococcus spp. (n=19)	Cefteram	0.25	8	0.12	0.06–8	–	–
	Cefpodoxime	0.5	32	0.5	0.12–64	–	–
	Cefixime	8	64	1	0.5–128	–	–
	Cefuroxime	0.25	8	0.12	0.06–16	–	–
	Cefaclor	1	8	0.12	0.06–64	–	–
	Cefalexin	2	64	0.12	0.06–64	–	–
	Clindamycin	0.25	256	0.25	0.06–256	57.9	42.1

素耐药肺炎链球菌,头孢特仑MIC_{50}、MIC_{90}值分别为4和8 mg·L^{-1},细菌敏感率为38.6%。其他β内酰胺类药物MIC_{50}、MIC_{90}值在8~>256 mg·L^{-1},均100%耐药(图3)。克林霉素耐药率始终在90%以上。

头孢特仑对化脓性链球菌和无乳链球菌均具有很好抗菌活性,MIC值≤0.03 mg·L^{-1},细菌100%敏感。除克林霉素外,对照药也均显示较好抗菌作用(图4~5)。草绿组链球菌对青霉素敏感率为77.1%,头孢特仑MIC_{50}、MIC_{90}值分别为0.06和0.25 mg·L^{-1},与青霉素相似,略优于其他头孢菌素类药物(图6)。

2 头孢特仑及对照药对革兰氏阴性菌MIC结果

头孢特仑对ESBLs阴性大肠埃希菌、肺炎克雷伯菌和奇异变形杆菌具有很好抗菌作用(表2),MIC值≤1 mg·L^{-1},MIC_{90}值0.12~0.5 mg·L^{-1},菌株100%敏感,与头孢泊肟、头孢克肟相当,优于头孢呋辛、头孢克洛和头孢氨苄(图7~9)。对氨苄西林敏感的流感嗜血杆菌,头孢特仑MIC值≤0.5 mg·L^{-1},菌株100%敏感,与头孢泊肟相似,略优于头孢克肟和氨苄西林,优于头孢呋辛、头孢克洛和头孢氨苄(图10);对产β内酰胺酶氨苄西林耐药流感嗜血杆菌,头孢特仑与对照药MIC值均有明显上升,头孢特仑MIC_{50}、MIC_{90}值分别为0.25和1 mg·L^{-1},低于对照药4~>256倍,细菌敏感率为100%(图11)。对非产β内酰胺酶氨苄西林耐药流感嗜血杆菌,除头孢克洛和氨苄西林MIC_{50}值较产酶菌下降8~16倍,其他药物MIC值及细菌敏感率与产酶菌相似,头孢特仑100%敏感(图12)。

头孢特仑对卡他莫拉菌MIC值在0.06~2 mg·L^{-1},除头孢氨苄,其他所测头孢菌素也具有很好抗菌作用(图13)。

3 头孢特仑及对照药对厌氧菌MIC结果

头孢特仑对消化链球菌属细菌具有较好抗菌作用(表3),MIC_{50}、MIC_{90}值分别为0.25和8 mg·L^{-1},与头孢呋辛基本一致,优于头孢克洛、头孢泊肟、头孢氨苄,显著优于头孢克肟(图14)。

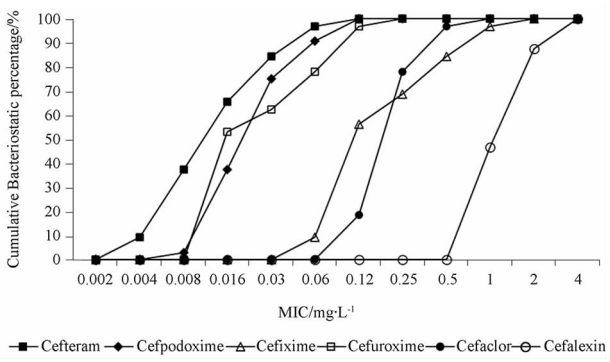

图1 头孢特仑及对照药对32株青霉素敏感(青霉素MIC≤0.06 mg·L^{-1})肺炎链球菌的累积抑菌百分比

Figure 1 Cummulative bacteriostatic percentage of cefteram and compared agents against 32 penicillin susceptible *Streptococcus pneumoniae* (MICs of penicillin ≤ 0.06 mg·L^{-1})

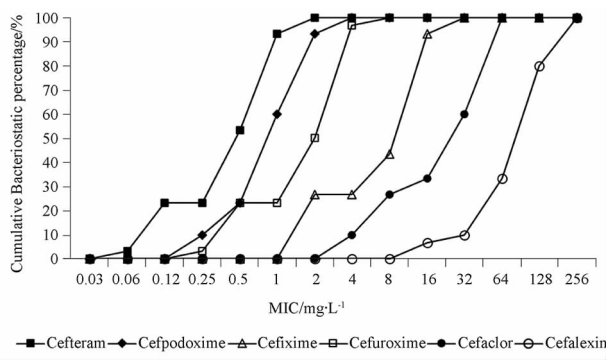

图2 头孢特仑及对照药对30株青霉素中介(青霉素MIC=0.12~1 mg·L^{-1})肺炎链球菌的累积抑菌百分比

Figure 2 Cummulative bacteriostatic percentage of cefteram and compared agents against 30 penicillin intermediate *Streptococcus pneumoniae* (MICs of penicillin = 0.12–1 mg·L^{-1})

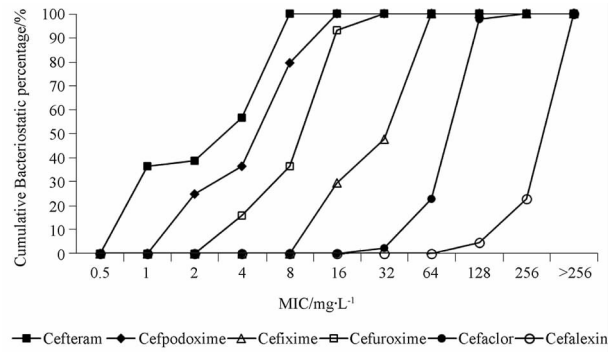

图 3 头孢特仑及对照药对 44 株青霉素耐药(青霉素 MIC ≥ 2 mg · L^{-1})肺炎链球菌的累积抑菌百分比

Figure 3 Cummulative bacteriostatic percentage of cefteram and compared agents against 44 penicillin resistant *Streptococcus pneumoniae* (MICs of penicillin ≥ 2 mg · L^{-1})

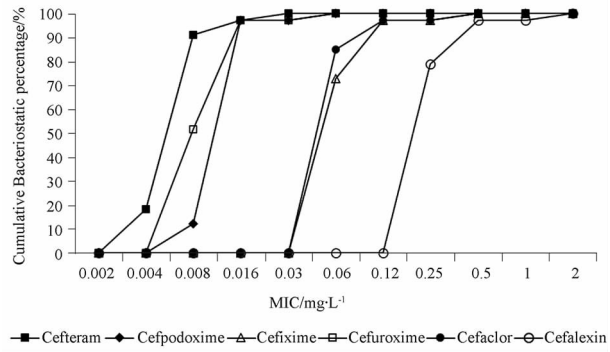

图 4 头孢特仑及对照药对 33 株化脓链球菌的累积抑菌百分比

Figure 4 Cummulative bacteriostatic percentage of cefteram and compared agents against 33 *Streptococcus pyogenic*

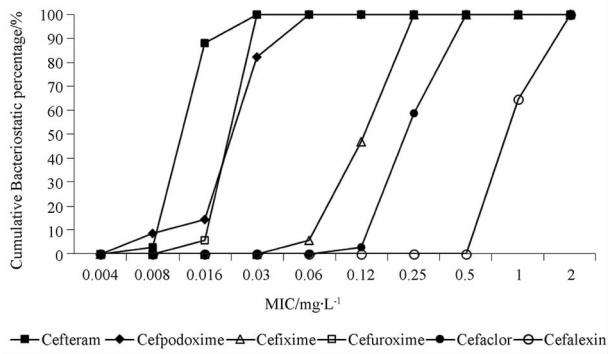

图 5 头孢特仑及对照药对 34 株无乳链球菌的累积抑菌百分比

Figure 5 Cummulative bacteriostatic percentage of cefteram and compared agents against 34 *Streptococcus agalactiae*

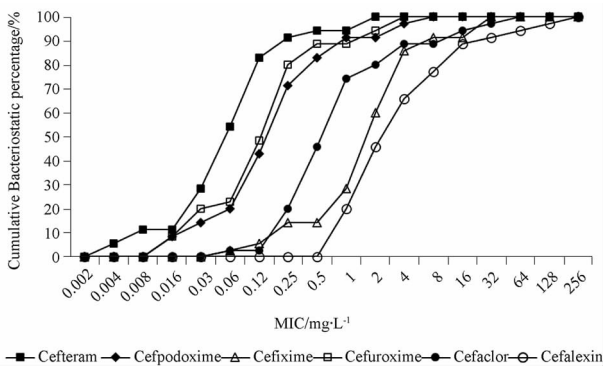

图 6 头孢特仑及对照药对 35 株草绿组链球菌的累积抑菌百分比

Figure 6 Cummulative bacteriostatic percentage of cefteram and compared agents against 35 *Streptococcus spp. viridans*

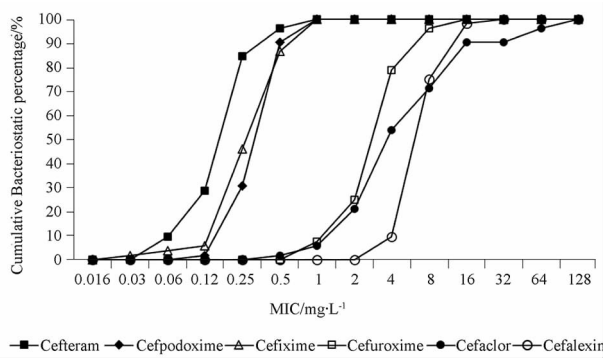

图 7 头孢特仑及对照药对 52 株超广谱 β 内酰胺酶(ESBLs)阴性大肠埃希菌的累积抑菌百分比

Figure 7 Cummulative bacteriostatic percentage of cefteram and compared agents against 52 extended spectrum β – lactamases (ESBLs) negative *Escherichia coli*

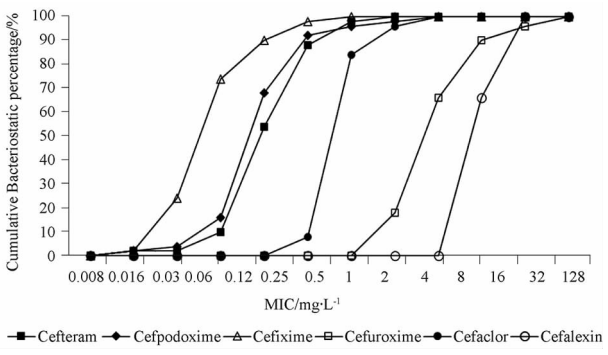

图 8 头孢特仑及对照药对 50 株 ESBLs 阴性肺炎克雷伯菌的累积抑菌百分比

Figure 8 Cummulative bacteriostatic percentage of cefteram and compared agents against 50 ESBLs negative *Klebsiella pneumoniae*

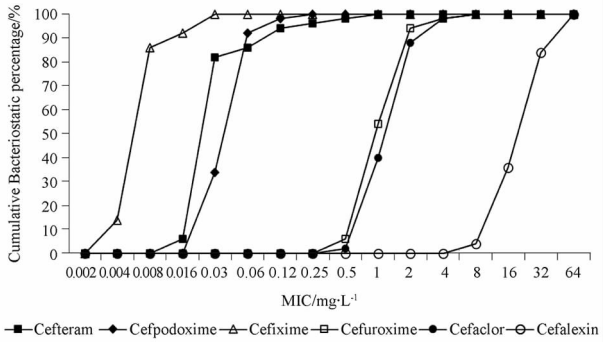

图 9 头孢特仑及对照药对 50 株 ESBLs 阴性奇异变形杆菌的累积抑菌百分比

Figure 9 Cummulative bacteriostatic percentage of cefteram and compared agents against 50 ESBLs negative *Proteus mirabilis*

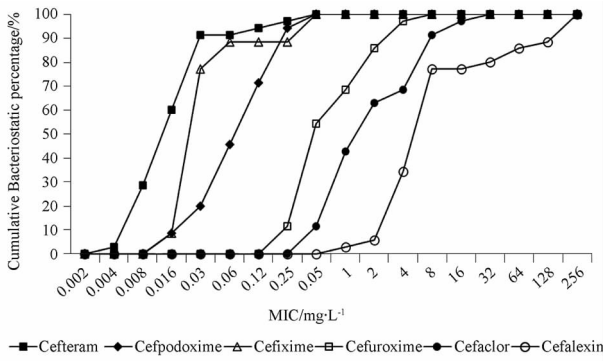

图 10 头孢特仑及对照药对 35 株氨苄西林敏感流感嗜血杆菌的累积抑菌百分比

Figure 10 Cummulative bacteriostatic percentage of cefteram and compared agents against 35 ampicillin susceptible *Haemophilus influenzae*

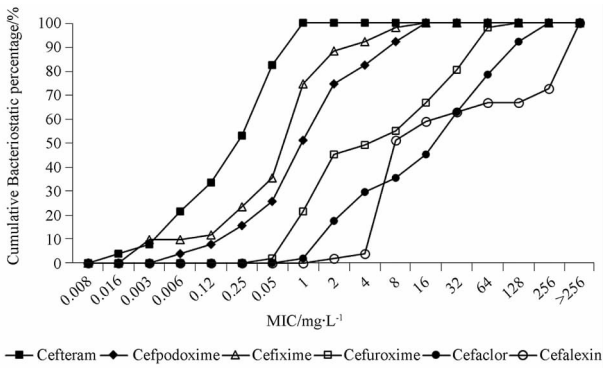

图 11 头孢特仑及对照药对 51 株氨苄西林耐药产 β－内酰胺酶流感嗜血杆菌的累积抑菌百分比

Figure 11 Cummulative bacteriostatic percentage of cefteram and compared agents against 51 β－lactamase positive ampicillin resistant *Haemophilus influenzae*

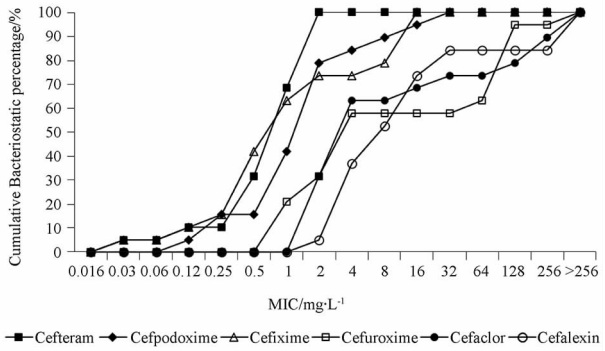

图 12 头孢特仑及对照药对 19 株氨苄西林不敏感非产 β－内酰胺酶流感嗜血杆菌的累积抑菌百分比

Figure 12 Cummulative bacteriostatic percentage of cefteram and compared agents against 19 β－lactamase negative ampicillin non－sensitive *Haemophilus influenzae*

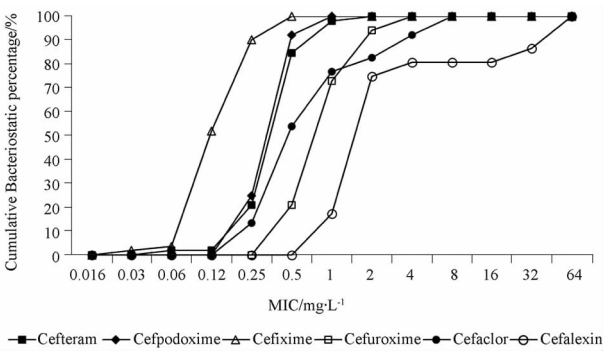

图 13 头孢特仑及对照药对 52 株卡他莫拉菌的累积抑菌百分比

Figure 13 Cummulative bacteriostatic percentage of cefteram and compared agents against 52 *Moraxella catarrhalis*

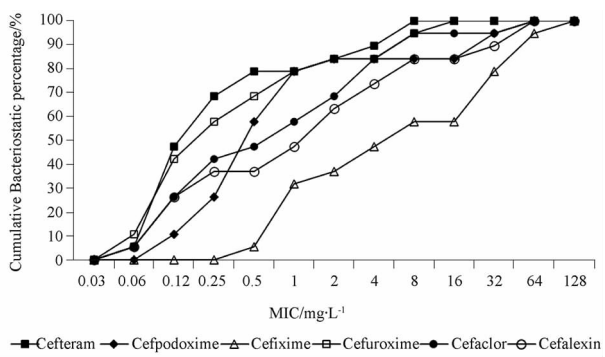

图 14 头孢特仑及对照药对 19 株消化链球菌属细菌的累积抑菌百分比

Figure 14 Cummulative bacteriostatic percentage of cefteram and compared agents against 19 *Peptostreptococcus spp.*

讨　论

本研究结果显示,头孢特仑具有广谱抗菌作用,特别对革兰氏阳性菌中链球属细菌、革兰氏阴性菌中大肠埃希菌、流感嗜血杆菌以及厌氧菌中消化链球菌属细菌具有较好抗菌活性,优于本研究中其他对照药。头孢特仑对青霉素敏感、中介肺炎链球菌以及对氨苄西林敏感流感嗜血杆菌、非产 β 内酰胺酶氨苄西林耐药流感嗜血杆菌结果与既往研究结果[10]相似,对青霉素耐药肺炎链球菌和产 β 内酰胺酶氨苄西林耐药流感嗜血杆菌 MIC 值较既往研究结果略高。既往研究[11-12]中,头孢特仑对青霉素敏感肺炎链球菌(未涉及不敏感肺炎链球菌)、化脓链球菌、无乳链球菌、大肠埃希菌、肺炎克雷伯菌、奇异变形杆菌及氨苄西林敏感的流感嗜血杆菌的 MIC 结果均与本研究结果基本一致,对产 β 内酰胺酶氨苄西林耐药流感嗜血杆菌活性优于本研究。而在 WISE 等[3]的研究显示,头孢特仑对产酶耐药流感嗜血杆菌 MIC 值与本研究相似。

经研究表明,头孢特仑口服后血药浓度可在 2~3 h达到峰值,半衰期 1 h,具有较好的组织分布,如扁桃体、耳分泌物、上颌窦黏膜、鼻息肉、筛骨窦黏膜、尿道等[13-17]。头孢特仑主要经过肾排出,少部分经胆汁排泄,饭后服用效果更佳。此外,该药的药物不良反应发生率低。

头孢特仑对近年中国临床分离链球菌属细菌、ESBLs 阴性常见肠杆菌目细菌,包括大肠埃希菌、肺炎克雷伯菌和奇异变形杆菌以及流感嗜血杆菌、卡他莫拉菌、消化链球菌仍保持较好抗菌作用,对敏感菌株 MIC 值较研发时没有明显升高,抗革兰氏阳性菌、阴性菌作用均衡,为口服头孢菌素中较好品种。

参考文献:

[1] 李光辉. 第三代口服头孢菌素头孢特仑酯[J]. 国外医药抗生素分册,1996,17(2):101—104.

[2] 曾晓辉,徐新军,石磊,等. 头孢特仑新戊酯的药动学和临床评价进展[J]. 实用药物与临床,2011,14(5):431—434.

[3] WISE R, ANDREWS J M, PIDDOCK L J V. *In vitro* activity of Ro 15-8074 and Ro 19-5247, two orally administered cephalosporin metabolites [J]. *Antimicrob Agent Chemother*, 1986, 29(6):1067—1072.

[4] FASS R J, HELSEL V L. *In vitro* activites of Ro 19-5247 and Ro 15-8074, new oral cephalosporins [J]. *Antimicrob Agents Chemother*, 1986, 30(3):429—434.

[5] 彭英,张洪. 头孢地尼和头孢特仑酯治疗细菌感染疗效及其抗菌活性分析[J]. 中国医药导报,2011,8(30):82—84.

[6] 赵晓莹,付鑫,刘露. 药物变态反应与药物交叉变态反应[J]. 医药导报,2009,28(10):1369—1370.

[7] CLSI. *Performance Standards for Antimicrobial Susceptibility Testing* [M]. 34th ed. Wayne, PA: Clinical and Laboratory Standards Institute, 2024: CLSI supplement M100.

[8] THE EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING. Breakpoint tables for interpretation of MICs and zone diameters. Version 14.0 [EB/OL]. 2024-01-01 [2024-05-30]. http://www.eucast.org.

[9] BESKID G, FALLAT V, SIEBELIST J, *et al*. *In vitro* activites of Ro 19-5247 (T-2525) and interpretive criteria for disk diffusion susceptibility testing [J]. *J Clin Microbiol*, 1987, 25(7): 1186—1190.

[10] 松崎薫,渡部惠美字,古木梓,等. *Streptococcus pneumoniae* およびHaemophilus influenzae の新鮮臨床分離株に対するcefteramの抗菌力に関する検討[J]. *Jpn J Antibiot*, 2004, 57(6):475—480.

[11] CHAU P Y, LEUNG Y K, NG W W S, *et al*. Comparative *in vitro* antibacterial activities of two new oral cephalosporins, ceftetrame (Ro 19-5247) and cefetamet (Ro 15-8074) [J]. *Antimicrob Agent Chemother*, 1987, 31(3):473—476.

[12] NEU H, CHIN N X, LABTHAVIKUL P. *In vitro* activity and β-lactamase stability of tow oral cephalosporins, ceftetrame (Ro 19-5247) and cefetamet (Ro 15-8074) [J]. *Antimicrob Agent Chemother*, 1986, 30(3):423—428.

[13] 张惠民,汪东,王嵩,等. 儿科医生如何正确使用头孢菌素类第三、四代新药[J]. 中国临床医生,2002,30(11):49—50.

[14] WEI F, ZHU R, ZHAO W, *et al*. Pharmacokinetics and bioequivalence studies of cefteram pivoxil in healthy Chinese volunteers [J]. *Eur J Drug Metab Pharmacokinet*, 2009, 34(3—4):157—162.

[15] YAMAGISHI Y, IZUMI K, TANAKA K, *et al*. Evaluation of antimicrobial prophylaxis after normal delivery [J]. *Jpn J Antibiot*, 2009, 62(2):103—115.

[16] 朱新昌,张霞,吴小丽. 抗感染药物的处方用药交代与指导[J]. 实用药物与临床,2009,2(1):39—41.

[17] MATSUMOTO F, SAKURAI I, MORITA M, *et al*. Effects of the quantity of water and milk ingested concomitantly with AS-924, a novelester-type cephem antibiotic, on its pharmacokinetics [J]. *Int J Antimicrob Agents*, 2001, 18(5):471—476.

(收稿日期 2024-09-27)