



在线全文

去甲万古霉素治疗急性血源性骨髓炎患儿的疗效及对炎症指标的影响^{*}

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【摘要】 目的 观察感染相关急性血源性骨髓炎(acute hematogenous osteomyelitis, AHO)患儿采用去甲万古霉素治疗的临床效果及其对炎症指标的影响。**方法** 本研究对2016年1月–2024年12月河北省儿童医院收治的感染相关AHO患儿进行回顾性分析,根据用药方案分为万古霉素组(A组, $n=103$)和去甲万古霉素组(B组, $n=107$)。两组在年龄、性别、体重及病变部位等基线资料方面经倾向评分匹配及多因素回归分析以控制混杂因素。比较两组患儿的临床疗效及炎症指标变化,包括白细胞(white blood cell, WBC)、中性粒细胞(neutrophils, NE)、C反应蛋白(C-reactive protein, CRP)和淀粉样蛋白A(serum amyloid A, SAA)水平。**结果** 两组临床治愈率差异无统计学意义($P>0.05$)。治疗1周和3周后,CRP和SAA水平在时间效应上差异有统计学意义($F_{\text{时间}}=503.00, 703.400, P<0.05$);WBC和NE水平在时间效应与组间效应上均差异有统计学意义($F_{\text{时间}}=259.100, 203.500, F_{\text{组间}}=8.403, 6.884, P<0.05$)。WBC、NE、CRP和SAA水平在治疗后1周和3周均呈逐步下降趋势($P<0.05$)。A组在治疗1周时WBC水平高于B组($P<0.05$),治疗3周时NE水平高于B组($P<0.05$)。A组WBC和NE恢复至正常水平的时间均长于B组($t=2.051, 2.001, P<0.05$),而两组CRP和SAA的恢复时间差异无统计学意义($P>0.05$)。A组发热消退时间长于B组($t=2.010, P<0.05$),两组在疼痛、肿胀等临床症状消失时间方面差异无统计学意义($P>0.05$)。A组与B组不良反应总发生率分别为14.56%和7.48%,组间差异无统计学意义($P>0.05$)。A组的人均治疗费用及成本效果比均高于B组($t=14.385, P<0.05$)。**结论** 去甲万古霉素治疗感染相关AHO与万古霉素在临床治愈率方面相当,但去甲万古霉素在促进WBC、NE水平恢复及发热消退方面有一定的优势,同时人均费用及成本效果比值方面低于万古霉素。

【关键词】 血源性骨髓炎 去甲万古霉素 白细胞 中性粒细胞 C反应蛋白

Efficacy of Norvancomycin in the Treatment of Acute Hematogenous Osteomyelitis in Children and Its Effect on Inflammatory Indicators

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【Abstract】 Objective To evaluate the clinical efficacy of norvancomycin in pediatric patients with infection-related acute hematogenous osteomyelitis (AHO) and its impact on inflammatory markers. **Methods** This study retrospectively analyzed children with infection-related AHO admitted to Hebei Children's Hospital from January 2016 to December 2024. Patients were divided into the vancomycin group (Group A, $n=103$) and the norvancomycin group (Group B, $n=107$) based on medication regimens. Baseline characteristics, including age, gender, weight, and lesion location, were adjusted for confounding factors using propensity score matching and multivariate regression analysis. Clinical efficacy and changes in inflammatory markers were compared between groups, including white blood cell (WBC) count, neutrophil (NE) count, C-reactive protein (CRP), and serum amyloid A (SAA) levels. **Results** There was no statistically significant difference in clinical cure rates between the two groups ($P>0.05$). At 1 and 3 weeks post-treatment, CRP and SAA levels showed statistically significant time effects ($F_{\text{time-point}}=503.00$ and 703.400 , respectively, $P<0.05$). Both WBC and NE levels showed statistically significant time effects and between-group effects ($F_{\text{time-point}}=259.100$ and 203.500 , respectively; $F_{\text{between-group}}=8.403$ and 6.884 , respectively; $P<0.05$). WBC, NE, CRP, and SAA levels gradually declined at both 1 week and 3 weeks post-treatment ($P<0.05$). Group A had higher WBC levels than Group B at 1 week post-treatment ($P<0.05$) and higher NE levels at 3 weeks post-treatment ($P<0.05$). The time required for WBC and NE to return to normal levels was longer in Group A than in Group B ($t=2.051, 2.001, P<0.05$), while the difference in recovery time for CRP and SAA between the two groups was not statistically significant ($P>0.05$). Group A had a longer duration of fever resolution than Group B ($t=2.010, P<0.05$). No statistically significant intergroup difference was observed in the time to resolution of clinical symptoms such as pain and swelling ($P>0.05$). The overall incidence of adverse reactions was 14.56% in Group A and 7.48% in Group B, with no statistically significant intergroup difference.

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($P > 0.05$). The per-patient treatment cost and cost-effectiveness ratio were higher in Group A than in Group B ($t = 14.385$, $P < 0.05$). **Conclusion** Norexvancomycin achieved clinical cure rates comparable to those of vancomycin in treating infection-associated AHO. Furthermore, it demonstrated advantages in accelerating the recovery of WBC and NE counts and the resolution of fever. These clinical benefits were coupled with lower per-patient costs and more favorable cost-effectiveness ratios compared to vancomycin.

[Key words] Hematogenic osteomyelitis Norvancomycin White blood cell Neutrophils C-reactive protein

近年来临床急性血源性骨髓炎(acute hematogenic osteomyelitis, AHO)的发生率日益增长,儿童是AHO的高危人群,发病后易引起骨质破坏导致骨质缺损、肢体畸形,具有较高的致残率^[1-3]。金黄葡萄球菌是诱发AHO的主要病原体,随着近年来细菌耐药问题的日益严峻,AHO的治疗也面临极大的挑战,尤其是耐甲氧西林金黄葡萄球菌(methicillin resistant staphylococcus aureus, MRSA)菌株对常规抗菌药敏感性不理想,导致临床治疗手段日益受限。万古霉素对MRSA具有较好的抗菌活性,然而万古霉素药物成本较高,儿童AHO又是一种需长时间用药的疾病,这会大大增加医疗负担,与药物资源配置的合理性相悖^[4-6]。去甲万古霉素为国产糖肽类抗生素,抗菌谱与万古霉素相似,但药物成本相对较低,故而去甲万古霉素用于AHO可能有助于降低医疗负担^[7-9]。然而现临床仍较为缺乏去甲万古霉素治疗儿童AHO有效性和安全性的循证依据。为此本研究拟通过观察去甲万古霉素在儿童AHO治疗中的应用效果,在确保治疗效果和安全性的前提下以期为临床探寻更具经济价值的治疗方案,促进临床药物的合理应用。

1 资料与方法

1.1 研究对象

本研究为回顾性研究,纳入2016年1月-2024年12月河北省儿童医院收治因MRSA感染诱发的214例AHO患儿。纳入标准:①来院就诊的AHO患儿,依据患儿的临床表现、实验室、影像学 and 病原微生物等检查确诊;②MRSA感染或社区MRSA分离率 $>10\%$;③年龄 <18 岁;④静脉使用去甲万古霉素和万古霉素的疗程均需 ≥ 1 周;⑤患儿家属知情同意。排除标准:①入组前使用去甲万古霉素/万古霉素等抗菌药物;②合并其他类型的慢性感染或炎症,如结核杆菌、乙肝病毒、人类免疫缺陷病毒感染;③近2周内有关抗炎药物、免疫抑制剂或其他可能与研究药物存在相互作用的药物使用史;④合并血液病、肝肾等脏器功能障碍等。入组患儿按治疗方案分为A、B两组(按年龄、性别、体重、病变部位等分层进行倾向性评分匹配,并采用多因素回

归分析调整混杂因素),分别给予万古霉素($n=107$)和去甲万古霉素($n=107$)治疗。A组中有3例后续治疗过程中新发现混合感染病原菌(链球菌,可能是初始未检测出或新发感染),1例病例中症状消失时间记录异常;最终A组剔除了4例。本研究经河北省儿童医院医学研究伦理委员会审批(批准号:医研伦审第20222289号)。

1.2 方法

1.2.1 A组治疗方法

入组时,患儿经验性用药给予头孢曲松+万古霉素静脉滴注。明确感染后,停用头孢曲松,仅给予万古霉素静脉滴注。头孢曲松(国药准字H53020673)用量 $20 \sim 80$ mg/kg,每日1次。万古霉素(国药准字HJ20140174)用量 40 mg/kg,溶于 $100 \sim 250$ mL 0.9% 氯化钠液,缓慢静脉滴注(不少于1 h),每日分2~4次静脉滴注。

1.2.2 B组治疗方法

入组时,患儿经验性用药给予头孢曲松+去甲万古霉素(国药准字H20023137)静脉滴注。明确感染后,停用头孢曲松,仅给予去甲万古霉素静脉滴注。头孢曲松用法同A组。去甲万古霉素(国药准字H20023137) 30 mg/kg,溶于 $100 \sim 250$ mL 0.9% 氯化钠液,缓慢静脉滴注(不少于1 h),每日分2~3次静脉滴注。

1.3 观察指标

1.3.1 主要指标

用药6周后评估患儿的治疗临床治愈率,定义为:临床症状体征消失和WBC、NE、CRP、SAA水平降至本院正常参考范围以内。临床治愈率 = (达到临床治愈标准的患儿例数 / 该组总患儿例数) $\times 100\%$ 。

1.3.2 次要指标

1.3.2.1 炎症指标

治疗前及治疗1、3周分三次采集所有患儿空腹肘静脉血液样本,进行指标评估。取部分全血行血常规及肝肾功能检测,记录白细胞(white blood cell, WBC)、中性粒细胞(neutrophils, NE)水平;另取血液样本使用离心机以 3000 r/min的转速分离血清与血浆备用;取血清样,采用酶联免疫吸附法测定C反应蛋白(C-reactive protein,

CRP)及淀粉样蛋白A(serum amyloid A, SAA)水平。记录WBC、NE、CRP、SAA首次恢复正常时间,其中“恢复正常”的判定以末次评估时间为截止点。

1.3.2.2 症状改善

每日观察两组患儿发热、肿胀、疼痛症状,并记录持续时间。

1.3.2.3 治疗安全性

根据临床指南^[10]及药品说明书监测不良事件类型,并记录两组患儿治疗期间不良事件的发生情况,包括皮疹、静脉炎、耳毒性以及血常规异常等),最后一次评估时统计整体发生情况。

1.3.2.4 成本效果

在临床经济学中诊疗成本包括诊疗的直接成本、间接成本和隐性成本,本研究只考虑直接成本,包括药品

费、检查与耗材费、住院费等,以最后一次评估为准。成本效果比值=人均费用/临床治愈率。

1.4 统计学方法

以SPSS 22.0统计学软件处理数据,分类变量如性别等以百分比描述,组间以 χ^2 检验进行比较;连续正态分布变量如年龄、SAA恢复时间等服从正态分布以 $\bar{x} \pm s$ 描述,采用 t 检验进行比较;多时间点测量数据如WBC、NE、CRP、SAA水平采用重复测量方差分析进行比较, $P < 0.05$ 表示差异有统计学意义。

2 结果

2.1 两组一般资料比较

两组患儿入组时一般资料基线可比,组间差异无统计学($P > 0.05$),见表1。

表 1 两组患儿一般资料比较

Table 1 Comparison of general data between the two groups

Item		Group A (n = 103)	Group B (n = 107)	χ^2/t	P
Sex/case (%)	Male	62 (60.19)	59 (55.14)	0.549	0.459
	Female	41 (39.81)	48 (44.86)		
Lesion site/case (%)	Tibial and femoral segments	68 (66.02)	69 (64.49)	0.603	0.740
	Humeral and radial segments	24 (23.30)	29 (27.10)		
	Other	11 (10.68)	9 (8.41)		
Empirical treatment/case (%)	Yes	51 (49.51)	49 (45.79)	0.291	0.589
Age/yr., $\bar{x} \pm s$		7.43 $\pm$ 2.57	7.29 $\pm$ 2.66	0.387	0.699
Height/cm, $\bar{x} \pm s$		121.46 $\pm$ 21.25	122.08 $\pm$ 20.50	0.215	0.830
Body mass/kg, $\bar{x} \pm s$		25.86 $\pm$ 7.18	26.08 $\pm$ 7.35	0.219	0.827
Medication administration duration/d, $\bar{x} \pm s$		26.65 $\pm$ 3.42	26.28 $\pm$ 3.51	0.773	0.440
Length-of-stay/d, $\bar{x} \pm s$		34.75 $\pm$ 4.72	35.54 $\pm$ 4.65	1.222	0.223

2.2 两组WBC、NE、CRP、SAA水平比较

两组治疗前WBC、NE、CRP、SAA水平差异无统计学意义($P > 0.05$),治疗1周、3周两组CRP、SAA水平在时间效应上差异有统计学意义($P < 0.01$),两组WBC、NE水平在时间、组间效应上差异有统计学意义($P < 0.05$),WBC、NE、CRP、SAA水平在治疗1、3周依次下降($P < 0.05$),A组治疗1周的WBC高于B组,治疗3周NE高于B组($P < 0.05$),见表2。

2.3 两组WBC、NE、CRP、SAA恢复正常时间

A组WBC、NE恢复正常时间长于B组($P < 0.05$),两组CRP、SAA恢复正常时间差异无统计学意义($P > 0.05$),见表3。

2.4 两组临床症状持续时间

A组发热时间长于B组($P < 0.05$),两组疼痛、肿胀等临床症状持续时间差异无统计学意义($P > 0.05$),见表4。

表 2 两组WBC、NE、CRP、SAA水平比较

Table 2 Comparison of WBC, NE, CRP, and SAA levels between the two groups

Item	Time point	Group A (n = 103)	Group B (n = 107)
WBC/($\times 10^9/L$)	Before treatment	17.92 $\pm$ 4.35	17.87 $\pm$ 4.28
	1 week of treatment	14.53 $\pm$ 3.41 ^{ac}	13.06 $\pm$ 3.34 ^a
	3 weeks of treatment	10.48 $\pm$ 2.73 ^{ab}	9.54 $\pm$ 2.85 ^{ab}
	Before treatment	65.97 $\pm$ 19.35	66.28 $\pm$ 18.54
NE/%	1 week of treatment	46.44 $\pm$ 14.16 ^a	43.03 $\pm$ 13.62 ^a
	3 weeks of treatment	41.53 $\pm$ 10.28 ^{abc}	35.39 $\pm$ 9.65 ^{ab}
	Before treatment	85.27 $\pm$ 22.35	83.52 $\pm$ 20.38
	1 week of treatment	49.37 $\pm$ 14.61 ^a	51.48 $\pm$ 15.28 ^a
CRP/(mg/L)	3 weeks of treatment	32.46 $\pm$ 15.33 ^{ab}	30.54 $\pm$ 14.28 ^{ab}
	Before treatment	78.17 $\pm$ 17.25	78.55 $\pm$ 16.58
	1 week of treatment	44.82 $\pm$ 10.54 ^a	46.52 $\pm$ 11.35 ^a
	3 weeks of treatment	31.26 $\pm$ 12.34 ^{ab}	29.87 $\pm$ 10.25 ^{ab}

WBC: white blood cell; NE: neutrophils; CRP: C-reactive protein; SAA: serum amyloid A. ^a $P < 0.05$, compared with before treatment; ^b $P < 0.05$, compared with 1 week of treatment; ^c $P < 0.05$, compared with group B.

表 3 两组WBC、NE、CRP、SAA恢复正常时间
Table 3 Time to normalization of WBC, NE, CRP, and SAA levels in the two groups

Group	WBC recovery time/d	NE recovery time/d	CRP recovery time/d	SAA recovery time/d
A (n = 103)	30.96 ± 4.84	31.65 ± 5.04	32.68 ± 4.56	32.85 ± 4.73
B (n = 107)	29.54 ± 5.18	30.28 ± 4.88	31.72 ± 4.75	32.22 ± 4.27
t	2.051	2.001	1.493	1.104
P	0.042	0.047	0.137	0.312

The abbreviations are explained in the note to Table 2.

2.5 两组治疗安全性

A组不良反应总发生率为14.56%, B不良反应总发生

表 4 两组临床症状持续时间
Table 4 The duration of clinical symptoms in the two groups

Group	Fever	Pain	Swelling
A (n = 103)	26.18 ± 4.87	28.84 ± 5.65	29.27 ± 5.24
B (n = 107)	24.82 ± 4.93	27.62 ± 5.08	29.08 ± 4.81
t	2.010	1.647	0.274
P	0.046	0.101	0.784

率为7.48%, 两组治疗安全性差异无统计学意义 (P>0.05), 见表5。

表 5 两组治疗安全性比较〔例(%)〕

Group	Skin rash	Phlebitis	Tinnitus	Granulocytopenia	Kidney injury	Gastrointestinal reaction	Total incidence rate
A (n = 103)	1 (0.97)	2 (1.96)	4 (3.88)	2 (1.96)	2 (1.96)	4 (3.88)	15 (14.56)
B (n = 107)	2 (1.87)	3 (2.80)	0 (0.00)	1 (0.93)	0 (0.00)	2 (1.87)	8 (7.48)
χ^2							2.702
P							0.100

2.6 两组治疗经济性

两组临床治愈率差异无统计学意义 (P>0.05), A组

人均费用及成本效果比值均明显高于B组 (P<0.05), 见表6。

表 6 两组治疗经济性比较

Group	Per capita cost/yuan	Clinical cure/case(%)	Cost-effectiveness ratio
A (n = 103)	56 762.26 ± 13 362.30	101 (98.06)	578.85
B (n = 107)	35 458.65 ± 7 352.48	106 (99.07)	357.92
t/ χ^2	14.385	0.001	N/A
P	<0.001	0.973	N/A

N/A: not applicable.

3 讨论

目前临床AHO的诊疗仍面临着许多困难, AHO需要长期给予抗菌药物治疗, 但用药方案的选择、剂量、途径和持续时间仍存在较大的差异, 且近年来抗菌药物的不合理应用导致耐药菌株的不断演化, 进一步增加了临床治疗的复杂程度, 甚至有部分患者会因治疗失败而需要面临手术干预^[11-14]。在国内金黄葡萄球菌是AHO的主要致病菌, 其中MRSA的分离率高达29.3%~30.9%, 不仅促使临床治疗方法进一步受限, 也增加了临床的用药周期, 此外由于许多MRSA感染患儿需要应用万古霉素治疗, 这也使得患者家庭需要承担较重医疗负担, 而去甲万古霉素在治疗MRSA的AHO方面目前仍缺乏大样本临床数据支持^[15-18]。

本研究对比了万古霉素与去甲万古霉素治疗AHO的临床效果, 结果显示去甲万古霉素与万古霉素治疗的临

床治愈率相当, 揭示这两种药物在抗MRSA方面均有良好的效果, 临床可根据实际情况灵活选择用药。在临床应用和现有的研究成果方面万古霉素已有大量的临床报道, 而去甲万古霉素则较为缺乏, 也缺少两种药物的对比报道, 在分子在结构上去甲万古霉素仅比万古霉素缺少一个甲基, 一般认为抗菌谱、抗菌活性二者是大致相当的^[19-22]。从这方面来看二者在治疗AHO上差异不大。然而治疗患儿的治疗1周的WBC、治疗3周的NE水平相对较低, WBC、NE恢复正常及发热消退时间也早于万古霉素方案, 这揭示在MRSA感染的AHO患儿中去甲万古霉素方案可能存在一定的优势。这可能由于去甲万古霉素的烷基较万古霉素短, 其与细菌细胞壁的亲和力略强于万古霉素, 0.5 mg/L的去甲万古霉素可抑制74.5%的MRSA生长, 而同浓度的万古霉素仅能抑制38.6%MRSA生长, 故而在抗菌活性方面也略强一些^[23-24]。在既往研究^[25]的观察中去甲万古霉素在治疗AHO患儿中用药1周、2周时

WBC、CRP水平及红细胞沉降率大致相当,但也观察到NE水平存在差异,揭示去甲万古霉素与细菌细胞壁的亲合力相对较强,能更好抑制细菌活性,从而抑制细菌的增殖和生长,促进临床症状的消退。而本次研究也观察到在降低WBC、NE及发热消退方面优于万古霉素,显然去甲万古霉素在治疗AHO疗效上略有优势。同时WBC、NE等血细胞变化不仅能反映用药后感染的控制情况,同时也是临床监测药物血液毒性的重要指标,是AHO临床治疗有效性和安全性的重要监测项目。在治疗安全性方面,主要观察到耳鸣、肾损伤和粒细胞减少等类型,两组不良反应发生率整体上无明显差异。万古霉素与去甲万古霉素在毒理性质方面相似,长时间用药时均具有一定的耳毒性和肾毒性,尤其是药物排泄主要经肾脏排泄,会导致肾组织线粒体嵴减少、断裂和肾小管上皮细胞形态异常、增殖抑制等病理,故而应用时需要谨慎监测,一般临床正常剂量内安全性较好,但需要注意长时间用药导致的蓄积效应^[26]。合并有肾功能异常的患者在血药浓度方面万古霉素/去甲万古霉素存在差异,故而在临床实际应用中对于存在肾功能异常的患者需要根据患者情况调整剂量,并严格监测血药浓度^[27-28]。此外在医疗成本方面万古霉素属于进口药品,价格较高,长时间用药会极大加重患者的经济负担,临床成本效果比值相对较高,国产药则价格相对低廉,疗效相当的前提下则具有更高的经济学优势,目前一些国产药物或替代药物是现临床应考虑的优化方案,包括去甲万古霉素^[29-30]。本研究还通过成本-效果法证明在近年来的价格体系下相对于万古霉素,去甲万古霉素在治疗人均费用和成本效果比值上更低,揭示去甲万古霉素更具有经济学上的优势,能减轻患儿家庭的医疗经济负担,这也有利于临床医疗资源合理配置,从而降低资源浪费。

综上所述,相对于万古霉素,针对MRSA感染诱发的AHO采用去甲万古霉素进行抗菌治疗安全性大致相当,在降低WBC、NE水平和促进发热消退方面有一定的优势,且去甲万古霉素还具有更高的治疗经济学优势,能减轻临床医疗负担,促进医疗资源的合理配置。然而本研究仅为单中心回顾性研究,结果可能存在一定的偏倚,后期需要开展多中心、前瞻性研究,进一步对比二者在临床的应用效果,以指导临床合理用药。

* * *

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参 考 文 献

- [1] PALMER B, WANG ME. Clinical guideline highlights for the hospitalist: Diagnosis and management of acute hematogenous osteomyelitis in children. *J Hosp Med*, 2022, 17(2): 114-116. doi: 10.1002/jhm.2742.
- [2] COCHARD B, HABRE C, PRALONG-GUANZIROLI N, *et al*. Transphyseal Hematogenous Osteomyelitis: An Epidemiological, Bacteriological, and Radiological Retrospective Cohort Analysis. *Microorganisms*, 2023, 11(4): 894. doi: 10.3390/microorganisms11040894.
- [3] ALEXANDER KM, LAOR T, BEDOYA MA. Magnetic resonance imaging protocols for pediatric acute hematogenous osteomyelitis. *Pediatr Radiol*, 2023, 53(7): 1405-1419. doi: 10.1007/s00247-022-05435-2.
- [4] HACHEM AA, FILKINS LM, KIDANE YH, *et al*. Staphylococcus aureus isolates from children with clinically differentiated osteomyelitis exhibit distinct transcriptomic signatures. *PLoS One*, 2023, 18(8): e0288758. doi: 10.1371/journal.pone.0288758.
- [5] HOYER EA, JOSEPH M, KAPLAN SL, *et al*. Predictive Factors to Guide Empiric Antimicrobial Therapy of Acute Hematogenous Osteomyelitis in Children. *Pediatr Infect Dis J*, 2023, 42(6): 449-455. doi: 10.1097/INF.0000000000003875.
- [6] 李兵兵, 汪浩, 杨鹏飞, 等. 淮南市临床分离金黄色葡萄球菌耐药性及全基因组测序分析. *现代预防医学*, 2024, 51(9): 1689-1694, 1701. doi: 10.20043/j.cnki.MPM.202312350.
- [7] LI B B, WANG H, YANG P F, *et al*. Analysis of drug resistance and whole genome sequencing of clinically isolated Staphylococcus aureus in Huai'an City. *Mod Prev Med*, 2024, 51(9): 1689-1694, 1701. doi: 10.20043/j.cnki.MPM.202312350.
- [8] YANG Q, LI X, JIA P, *et al*. Determination of norvancomycin epidemiological cut-off values (ECOFFs) for Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus and Staphylococcus hominis. *J Antimicrob Chemother*, 2021, 76(1): 152-159. doi: 10.1093/jac/dkaa414.
- [9] GUAN D, CHEN F, SHI W, *et al*. Single Modification at the N-Terminus of Norvancomycin to Combat Drug-Resistant Gram-Positive Bacteria. *ChemMedChem*, 2023, 18(9): e202200708. doi: 10.1002/cmdc.202200708.
- [10] 姜锡娟, 雷蓉, 秦亚彬, 等. 用HPLC-MS/MS法测定重症感染患儿微量血浆/血清中利奈唑胺和万古霉素浓度. *中国临床药理学杂志*, 2024, 40(7): 1044-1048. doi: 10.13699/j.cnki.1001-6821.2024.07.023.
- [11] JIANG X J, LEI R, QIN Y B, *et al*. The concentrations of linezolid and vancomycin in plasma/serum of children with severe infection determined by HPLC-MS/MS method. *Chin J Clin Pharmacol*, 2024, 40(7): 1044-1048. doi: 10.13699/j.cnki.1001-6821.2024.07.023.
- [12] 范亚新, 郭蓓宁. 万古霉素治疗严重耐甲氧西林金黄色葡萄球菌感染的治疗药物监测: 2020年美国卫生系统药师协会、美国感染病学会、儿童感染性疾病学会和感染病药师学会更新修订的共识指南. *中国感染与化疗杂志*, 2021, 21(3): 374-376. doi: 10.16718/j.1009-7708.2021.03.024.

- FAN Y X, GUO B N. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Chin J Infect Chemother*, 2021, 21(3): 374-376. doi: 10.16718/j.1009-7708.2021.03.024.
- [11] BRADLEY JS. What Is the Appropriate Dose, Route, and Duration of Antibiotic Therapy for Pediatric Acute Hematogenous Osteomyelitis (AHO)? I Wish I Knew. *J Pediatric Infect Dis Soc*, 2023, 12(2): 61-63. doi: 10.1093/jpids/piac108.
- [12] UPASANI VV, BURNS JD, BASTROM TP, et al. Practice Variation in the Surgical Management of Children With Acute Hematogenous Osteomyelitis. *J Pediatr Orthop*, 2022, 42(5): e520-e525. doi: 10.1097/BPO.0000000000002123.
- [13] ZAIRI M, MOHSENI AA, MSAKNI A, et al. Acute hematogenous osteomyelitis in children: Management of pandiaphysitis with extensive bone destruction: A case series of thirteen child. *Ann Med Surg (Lond)*, 2022, 82: 104578. doi: 10.1016/j.amsu.2022.104578.
- [14] SARMIENTO CLEMENTE A, MCNEIL JC, HULTÉN KG, et al. Assessing risk for complications in acute hematogenous osteomyelitis in children: validation of 2 predictive scores. *J Pediatric Infect Dis Soc*, 2023, 12(12): 610-617. doi: 10.1093/jpids/piad095.
- [15] MCDONALD ACE, JULIAN J, VOSS LM, et al. An update on pediatric acute hematogenous osteomyelitis in new zealand - a decade on. *J Pediatr Orthop*, 2023, 43(8): e614-e618. doi: 10.1097/BPO.0000000000002443.
- [16] 富洋, 王宏胜, 陆凤娟. 儿童急性血源性骨髓炎诊断及药物治疗研究进展. *世界临床药物*, 2023, 44(1): 90-93. doi: 10.13683/j.wph.2023.01.015.
- FU Y, WANG H S, LU F J. Research progress in diagnosis and drug treatment of acute hematogenous osteomyelitis in children. *World Clin Drug*, 2023, 44(1): 90-93. doi: 10.13683/j.wph.2023.01.015.
- [17] ZHANG X, PEI Y, ZHAO Y. Acute Hematogenous Osteomyelitis in Pediatric Patients. *Pediatr Ann*, 2024, 53(10): e392-e395. doi: 10.3928/19382359-20240811-08.
- [18] 中华医学会儿科学分会感染学组, 中华儿科杂志编辑委员会. 儿童急性血源性骨髓炎治疗专家共识. *中华儿科杂志*, 2022, 60(8): 745-750. doi:10.3760/cma.j.cn112140-20220214-00118.
- Infection Group of Society of Pediatrics of Chinese Medical Association, Editorial Board of Chinese Journal of Pediatrics. Expert consensus on the treatment of acute hematogenous osteomyelitis in children. *Chin J Pediatr*, 2022, 60(8): 745-750. doi:10.3760/cma.j.cn112140-20220214-00118.
- [19] FLINT AJ, DAVIS AP. Vancomycin mimicry: towards new supramolecular antibiotics. *Org Biomol Chem*, 2022, 20(39): 7694-7712. doi: 10.1039/d2ob01381a.
- [20] CAFARO A, STELLA M, MESINI A, et al. Dose optimization and target attainment of vancomycin in children. *Clin Biochem*, 2024, 125: 110728. doi: 10.1016/j.clinbiochem.
- [21] LI Y, LU W, ZHENG X, et al. Norvancomycin for the treatment of central nervous system MRSA infections: A randomized controlled trial. *Eur J Pharm Sci*, 2022 Oct 1;177: 106266. doi:10.1016/j.ejps.2022.106266.
- [22] BIAN X, CHEN Z, LI F, et al. Single amine or guanidine modification on norvancomycin and vancomycin to overcome multidrug-resistance through augmented lipid ii binding and increased membrane activity. *J Med Chem*, 2024, 67(22): 20639-20663. doi: 10.1021/acs.jmedchem.4c02196.
- [23] 胡佳丽, 范亚新, 郭蓓宁, 等. 去甲万古霉素临床药理学研究综述. *中国感染与化疗杂志*, 2021, 21(6): 745-751. doi: 10.16718/j.1009-7708.2021.06.024.
- HU J L, FAN Y X, GUO B N, et al. Review of clinical pharmacology of norvancomycin. *Chin J Infect Chemother*, 2021, 21(6): 745-751. doi: 10.16718/j.1009-7708.2021.06.024.
- [24] 谢志杰, 宋国斌, 仇新军, 等. 去甲万古霉素治疗老年耐甲氧西林金黄色葡萄球菌下呼吸道感染效果观察. *河北医药*, 2022, 44(22): 3430-3433. doi: 10.3969/j.issn.1002-7386.2022.22.017.
- XIE Z J, SONG G B, QIU X J, et al. Efficacy observation: norvancomycin for lower respiratory tract infection caused by Methicillin-resistant *Staphylococcus aureus* in the elderly. *Hebei Med J*, 2022, 44(22): 3430-3433. doi: 10.3969/j.issn.1002-7386.2022.22.017.
- [25] ZHANG X, ZHANG N, PEI Y, et al. Effectiveness, safety, and cost-effectiveness of norvancomycin in the management of acute hematogenous osteomyelitis in pediatric patients: A retrospective case study. *Medicine (Baltimore)*, 2024, 103(45): e40335. doi: 10.1097/MD.00000000000040335.
- [26] 王金龙, 薛明, 王皓飞, 等. 万古霉素曲线下面积的列线图预测重症患者万古霉素相关肾损伤的临床应用价值. *中华内科杂志*, 2022, 61(3): 291-297. doi: 10.3760/cma.j.cn112138-20211011-00688.
- WANG J L, XUE M, WANG H F, et al. An area under curve-based nomogram to predicts vancomycin-associated nephrotoxicity in critically ill patients: a retrospective cohort study. *Chin J Intern Med*, 2022, 61(3): 291-297. doi: 10.3760/cma.j.cn112138-20211011-00688.
- [27] 杨翠, 何娜, 闫盈盈, 等. 肾功能亢进对(去甲)万古霉素治疗结局的影响. *中国临床药理学杂志*, 2023, 39(7): 924-927. doi: 10.13699/j.cnki.1001-6821.2023.07.003.
- YANG C, HE N, YAN Y Y, et al. Effects of augmented renal clearance on the outcome of vancomycin/norvancomycin. *Chin J Clin Pharmacol*, 2023, 39(7): 924-927. doi: 10.13699/j.cnki.1001-6821.2023.07.003.
- [28] 韦秀平, 王娟, 龙剑海. 老年肺部感染患者不同剂量去甲万古霉素谷浓度分析. *中国临床药理学杂志*, 2021, 37(11): 1311-1314. doi: 10.13699/j.cnki.1001-6821.2021.11.002.
- WEI X P, WANG J, LONG J H. Analysis of trough concentrations of different norvancomycin dosages in elderly patients with pulmonary infection. *Chin J Clin Pharmacol*, 2021, 37(11): 1311-1314. doi: 10.13699/j.cnki.1001-6821.2021.11.002.
- [29] 胥甜甜, 吕燕妮, 张秀莹, 等. 利奈唑胺和万古霉素治疗化脓性脊柱炎的疗效, 安全与经济性比较. *中国感染控制杂志*, 2023, 22(10): 1232-1238. doi: 10.12138/j.issn.1671-9638.20234423.
- XU T T, LV Y N, ZHANG X Y, et al. Comparison between linezolid and vancomycin treatment of purulent spondylitis in effectiveness, safety and economy. *Chin J Infect Contrl*, 2023, 22(10): 1232-1238. doi: 10.12138/j.issn.1671-9638.20234423.
- [30] 张海霞, 陈杏凯, 梁培, 等. 两个厂家注射用盐酸万古霉素有效性和安全性及经济性的真实世界研究. *医药导报*, 2023, 42(12): 1850-1855. doi: 10.3870/j.issn.1004-0781.2023.12.018.
- ZHANG H X, CHEN X K, LIANG P, et al. Real-world study on the efficacy, safety and economics of vancomycin hydrochloride for injection from two manufacturers. *Herald Med*, 2023, 42(12): 1850-1855. doi: 10.3870/j.issn.1004-0781.2023.12.018.

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