

新生儿感染性休克预后预测因素研究进展

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摘要

新生儿感染性休克是败血症的危重阶段, 病死率高, 早期识别预后不良风险对于指导治疗至关重要。本文旨在综述新生儿感染性休克的临床特征、当前治疗现状, 并重点探讨其预后预测指标的研究进展。通过梳理现有文献发现, 除低胎龄、低出生体重等传统高危因素外, 乳酸及其动态变化(如清除率)是重要的预后生化标志物。近年来, 血管活性 - 正性肌力评分(VIS)这一整合治疗强度的指标在儿童感染性休克中显示出优越的预测价值, 但在新生儿群体的证据仍有限。本综述总结现有证据, 提出未来应致力于构建整合临床特征、实验室指标及治疗相关指标(如VIS)的新生儿特异性预后预测模型, 以改善临床决策。

关键词

新生儿, 感染性休克, 预后, 预测因素, 血管活性 - 正性肌力评分

Advances in Prognostic Predictors of Neonatal Septic Shock

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Abstract

Neonatal septic shock is a critical stage of sepsis with a high mortality rate. Early identification of the risk of poor prognosis is crucial for guiding treatment. This article aims to review the clinical

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features and current treatment status of neonatal septic shock, with a focus on recent advances in prognostic predictors. A review of the existing literature reveals that, in addition to traditional high-risk factors such as low gestational age and low birth weight, lactate and its dynamic changes (e.g., clearance rate) serve as important biochemical prognostic markers. In recent years, the Vasoactive-Inotropic Score (VIS), an indicator integrating therapeutic intensity, has demonstrated superior predictive value in pediatric septic shock, though evidence in the neonatal population remains limited. This review summarizes the current evidence and suggests that future efforts should focus on developing neonatal-specific prognostic models that integrate clinical characteristics, laboratory indicators, and therapeutic indicators (such as VIS) to improve clinical decision-making.

Keywords

Neonatal, Septic Shock, Prognosis, Predictors, Vasoactive-Inotropic Score

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1. 引言

新生儿败血症是新生儿期发病和死亡的主要原因,而感染性休克作为其最严重的并发症,病死率极高。由于新生儿,尤其是早产儿,其心血管系统代偿能力有限且临床表现隐匿,感染性休克的早期诊断与预后评估面临巨大挑战。及时识别可能进展为不良预后的高危患儿,是调整强化治疗、改善结局的关键。因此,明确新生儿感染性休克的临床特征并探索有效的预后预测指标具有重要临床意义。本文将从该病的临床特征与病理生理基础、当前核心治疗与预后关联、以及预后预测指标三个方面进行综述,以期临床早期风险评估提供参考。

2. 新生儿感染性休克的临床特征与病理生理基础

2.1. 流行病学与高危因素

败血症在活产新生儿中的发生率约为 1%~8%,而在极低出生体重儿中可高达 21%。当进展为感染性休克时,病死率显著增加。研究表明,低胎龄、低出生体重是新生儿发生败血症及感染性休克的独立高危因素,其发病率和死亡率与之呈负相关[1]-[4]。许多死亡病例发生在休克治疗初期,特别是 48~72 小时内[5]。因此,早期识别新生儿感染性休克,并给予恰当的液体复苏和管理对于优化新生儿败血症患儿的预后至关重要。

2.2. 临床表现与多器官功能障碍的病理生理

新生儿感染性休克的早期表现常不典型,可仅表现为需液体复苏或血管活性药物支持的心血管功能障碍,或伴有肌张力下降、肤色改变等非特异性体征[6][7]。其本质是由宿主对感染反应失调引起的危及生命的器官功能障碍[8]。

心血管系统:是核心受累系统,机制包括血管内皮损伤致毛细血管渗漏和有效血容量不足;心肌抑制致心输出量下降;以及血管舒缩功能障碍,导致血流分布异常[9][10]。**呼吸系统:**可发展为急性呼吸窘迫综合征,涉及炎症性肺损伤和表面活性物质功能障碍[11]。**泌尿系统:**急性肾损伤常见,与肾脏灌注不足及炎症介质损伤相关[12]。**凝血系统:**新生儿,尤其是早产儿,凝血系统发育不完善,易出现凝血功

能异常,甚至弥散性血管内凝血,增加颅内等重要脏器出血风险[13][14]。中枢神经系统:可因灌注不足、炎症介质等影响,出现意识改变或惊厥[13]。

这些多器官功能障碍的病理生理过程是疾病严重程度的基石,也直接决定了患儿的预后。

3. 治疗现状与核心干预措施对预后的影响

3.1. 抗感染与支持治疗

感染性休克一经怀疑,立即使用广谱抗菌药物是治疗的基石[15]。此外,呼吸、凝血等器官功能支持也至关重要。2020 拯救脓毒症运动国际指南:儿童脓毒症休克和脓毒症相关器官功能障碍管理指南建议在不显著延迟抗菌药物给药前提下,在使用抗生素之前获取血培养对指导抗菌药物的使用及疗程至关重要,是识别多重耐药菌的重要途径,在休克早期建议经验性使用抗生素,选择一种或几种联合使用,以尽量覆盖所有可能的病原体[16]。作为直接针对病因的有力治疗,抗菌药物应在确诊 1 小时内使用,多项研究表明早期静脉使用抗菌药物能改善败血症预后[17],并且越早使用抗菌药物对预后越有利[18]。指南建议感染性休克引起急性呼吸窘迫综合征的患儿使用机械通气以较少呼吸做功;建议在无禁忌时早期肠内营养;建议在存在感染性休克引起器官功能障碍时进行血浆置换等支持治疗[16]。

3.2. 液体复苏与容量管理

早期液体复苏是纠正休克的关键,但对于新生儿,尤其是早产儿,液体过负荷与不良预后(如肺水肿、动脉导管开放、颅内出血风险增加)明确相关[19]。目前新生儿感染性休克的液体复苏策略尚无统一标准,液体的种类与剂量均是影响预后的重要变量[20]。因此,液体复苏本身既是一项治疗,其反应和需求也可视为预后的间接预测指标。

3.3. 血管活性药物应用

对于液体复苏无反应的休克,需尽早使用血管活性药物。由于新生儿生理特征,低血压标准并不明确,对于新生儿液体难治性休克暂无明确管理方案,针对血管活性药物的使用,最新国际儿童脓毒症生存指南建议使用肾上腺素及去甲肾上腺素,而非多巴胺(弱推荐)[16]。对于血管活性药物实际临床效果是否有差异这一问题,部分研究发现与多巴胺相比,选择肾上腺素或去甲肾上腺素作为一线药物可能与更低的死亡率相关[21][22]。最新一项以新生儿感染性休克患儿为研究对象的随机对照试验发现肾上腺素及多巴胺作为一线血管活性药物治疗新生儿感染性休克时疗效相当[23]。此外,血管活性药物的使用强度和持续时间,直观反映了休克的顽固性和心血管失代偿的严重程度,对于判断预后具有一定指示作用。

3.4. 其他治疗

广谱抗生素、液体复苏及血管活性药物的使用以外,一些研究证明糖皮质激素对于感染性休克可能存在一定疗效[24]。当所有治疗均无法有效改善时可使用 ECMO。

4. 预后预测指标的研究进展

4.1. 基于临床资料的预测指标

多项研究证实,低胎龄、低出生体重、感染时低体重、低 Apgar 评分、代谢性酸中毒(低 pH 值)以及革兰氏阴性菌感染与新生儿感染性休克预后不良独立相关[25]。这些因素是风险评估的基础。

4.2. 实验室指标——乳酸

乳酸水平是反映组织灌注与缺氧的核心生物标志物。初始乳酸值升高及乳酸清除率迟缓,已被广泛

证实是成人和儿童感染性休克患者死亡的强预测因子[26]-[30]。在儿童中,甚至有研究提出“乳酸面积积分”这一整合动态变化的指标,其预测价值优于单次测量[31]。因此,临床指南推荐动态监测乳酸[32]。一些研究证明血乳酸水平、乳酸清除率与新生儿休克预后相关[33] [34]。

4.3. 治疗相关预测指标——血管活性 - 正性肌力评分(VIS)

血管活性 - 正性肌力评分(VIS)最初用于量化心脏术后患儿血管活性药物支持强度,并预测死亡率[35]。后续研究发现其在儿童感染性休克预后预测中具有重要价值。例如, Dipu 等的研究显示 VIS 预测儿童感染性休克死亡的曲线下面积(AUC)达0.88 [36]。另一项前瞻性研究指出,96小时VIS累计值(AVIS96)与死亡率高度相关,其预测准确性(AUC 0.976)甚至优于乳酸水平[37]。

然而,将VIS应用于新生儿感染性休克预后预测的研究极为有限。目前仅有一项回顾性单中心研究表明VIS可用于预测新生儿感染性休克的死亡率[38]。这一领域存在明显的证据缺口。VIS的优势在于它整合了治疗反应和疾病严重程度,但其在新生儿中的最佳计算方式(是否需要根据新生儿生理调整药物权重)、预测的截断值以及与其他指标(如乳酸)的联合预测效能,均有待在前瞻性、大样本的新生儿队列中验证。

4.4. 生物标志物预测指标

在成人感染性休克预后预测指标的研究中,生物标志物是一个重要研究方向。

例如,急性期炎症蛋白正五聚蛋白3(pentraxin-3, PTX3)与感染性休克预后不良相关,在一项前瞻性观察分析中,PTX3、IL-6、PCT和乳酸的联合测量脓毒性休克患者28天全因死亡率的预测效果非常好,其预测性能甚至高于序贯性器官功能衰竭评分(sequential organ failure assessment, SOFA) [39]。S100钙结合蛋白100b(S100b)作为神经胶质细胞损伤和激活的标志,与感染性休克患者神经系统预后不良相关,在一项22例感染性休克患者的小样本量观察性研究中,其中10例患者出现谵妄,S100B水平超过0.15 ug/L与谵妄18.0的比值比相关[40]。此外,肾上腺髓质素(Adrenomedullin, ADM)、IL-6、PCT水平亦有研究发现与脓毒症及感染性休克预后相关[41][42]。但目前生物标志物尚未被纳入指南中,并且其中大多数非临床常规检测项目,此类标志物在新生儿感染性休克中的研究极少。

4.5. 各项预测指标的特点

Table 1. Comparison of the predictive performance of different indicators for the prognosis of septic shock
表 1. 不同预测指标预测感染性休克预后的性能对比

指标来源	预测指标	结局指标	AUC	灵敏度	特异度	截断值
袁文浩等[33]	复苏开始前血乳酸水平	因休克死亡	0.846	88.9%	74.1%	10.65 mmol/L
王义等[34]	入院1小时内血乳酸水平	60天内全因死亡率	0.875	89.65%	77.18%	4.03 mmol/L
王义等[34]	液体复苏后6小时乳酸清除率	60天内全因死亡率	0.699	83.32	72.52	9.83%
Demirhan S [38]	48小时内VISmax	因感染性休克死亡	0.819	81.4%	71.8%	20
Krishnamurthy [36]	平均VIS	在PICU内死亡	0.88	83.7%	80.6%	42.5
Song [39]	确诊感染性休克6小时内PTX3水平	28天全因死亡率	0.734	88.9%	49.5%	26.9 ng/ml

综上所述, 新生儿感染性休克的预后预测正从依赖单一指标, 向整合实验室指标、治疗相关指标及生物标志物的方向发展。传统因素奠定了风险基线, 乳酸实时反映灌注, 而 VIS 则量化了心血管失代偿的严重程度与顽固性。目前, 建立以 VIS 为核心、结合传统风险与乳酸清除率的多维度新生儿特异性预测模型, 是证据缺口所在, 也是最具潜力的研究方向。现有相关研究中不同预测指标的效能见表 1。

5. 总结与展望

5.1. 总结

新生儿感染性休克病情凶险, 预后差。其预后受胎龄、出生体重等固有因素影响, 也与反映疾病动态过程的指标密切相关。目前, 乳酸作为组织灌注的敏感标志物, 其预测价值明确。VIS 作为一项量化心血管支持强度的客观工具, 在儿童群体中展现出卓越的预测潜力, 为新生儿领域的预后评估提供了新思路, 但亟待新生儿特异性研究证实。

5.2. 临床启示

在临床实践中, 评估新生儿感染性休克预后时, 应综合传统高危因素、动态乳酸变化及血管活性药物使用强度。建议在监护中常规计算并记录 VIS 评分, 将其作为评估病情严重程度和治疗反应的重要补充。

5.3. 研究展望

基于现有证据的不足, 未来研究应聚焦于以下几点: 1. 验证与优化 VIS 在新生儿中的应用: 开展多中心前瞻性研究, 明确 VIS 在新生儿感染性休克中的预测效能, 并探讨是否需要建立新生儿特异的 VIS 计算标准。2. 探索多维预测模型: 研究应超越单一指标, 致力于构建整合胎龄、发病日龄、初始乳酸、乳酸清除率、VIS 峰值及持续时间等多维度指标的临床预测模型或风险评分。3. 评估预测模型对治疗的影响: 最终目标是验证此类预测模型能否有效识别高危患儿, 并引导早期目标导向性治疗, 从而真正改善临床结局。4. 通过深化对预后预测因素的理解和工具开发, 有望实现新生儿感染性休克的精准风险分层, 为临床决策提供有力支持, 最终降低这一危重疾病的死亡率。

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