

腹膜透析相关性腹膜炎危险因素的研究进展

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摘要

腹膜透析(peritoneal dialysis, PD)是终末期肾病(end-stage renal disease, ESRD)患者的主要治疗方法之一, 而腹膜透析相关性腹膜炎(peritoneal dialysis-associated peritonitis, PDAP)是腹膜透析常见且严重的并发症。尽管透析技术、连接系统和患者教育不断进步, PDAP的发生率仍居高不下, 深刻影响着患者的预后和生活质量。因此, 深入探究PDAP发生的危险因素, 对于实施精准化治疗、制定个体化干预策略具有至关重要的临床意义。本文旨在系统综述近年来国内外关于PDAP危险因素的研究进展, 以期为临床识别高危人群、优化管理方案提供理论依据。

关键词

终末期肾脏病, 腹膜透析, 腹膜炎, 腹膜透析相关性腹膜炎, 危险因素

Research Progress of Peritoneal Dialysis-Associated Peritonitis Risk Factors

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Abstract

Peritoneal dialysis (PD) is one of the main therapeutic modalities for patients with end-stage renal disease (ESRD), whereas peritoneal dialysis-associated peritonitis (PDAP) remains a common and serious complication of PD. Despite continuous advances in dialysis techniques, connection systems, and patient education, the incidence of PDAP remains unacceptably high, substantially affecting patient prognosis and quality of life. Therefore, a comprehensive understanding of the risk factors for

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PDAP is of critical clinical importance for the implementation of precision-based treatment and the development of individualized preventive and management strategies. This review aims to systematically summarize recent domestic and international research advances regarding the risk factors for PDAP, in order to provide a theoretical basis for identifying high-risk patients and optimizing clinical management.

Keywords

End-Stage Renal Disease, Peritoneal Dialysis, Peritonitis, Peritoneal Dialysis-Associated Peritonitis, Risk Factors

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1. 引言

腹膜透析(peritoneal dialysis, PD)是目前终末期肾病(end-stage renal disease, ESRD)患者的主要治疗方法之一,与血液透析相比,其具有便携性、饮食限制少、更好保留残余肾功能等优势[1]。腹膜透析相关性腹膜炎(peritoneal dialysis-associated peritonitis, PDAP)是腹膜透析常见且严重的并发症,是导致腹膜透析患者技术失败、导管拔除、转至血液透析和死亡的重要原因[2]。其发生是病原体、宿主防御能力及治疗环境等多因素复杂交织的结果。全面、深入地识别相关危险因素,是实现精准预防和改善患者预后的基石。本文系统综述近年研究揭示的PDAP危险因素,为临床实践提供参考。

2. 宿主内在因素

宿主的内在特性是构成感染易感性的基础,包括不可改变的人口学特征、基础疾病状态以及近年来备受关注的固有生物学特质。

2.1. 人口学与基础疾病状态

多项研究显示,高龄PD患者的腹膜炎发生率明显高于年轻人群,同时其腹膜炎相关死亡风险也更高[3][4]。一项大规模回顾性研究进一步指出,年龄偏大是首次腹膜炎发生的独立预测因素[5]。这可能与老年患者整体生理功能衰退、合并疾病增多、腹膜防御能力减弱,以及听力、视力下降和肢体协调性变差等因素有关,上述问题可能导致PD操作过程出现不规范甚至错误,从而增加感染风险。尽管多数研究将高龄视为PDAP的独立危险因素,但部分研究提示[6]-[8],在纳入营养状态与功能、自我护理相关指标后,年龄的独立效应可能减弱,提示其更可能反映衰弱与功能储备下降。因此,未来风险评估应结合衰弱指数和功能状态,而非单纯以年龄分层。

糖尿病患者,尤其是血糖控制不理想者,其腹膜炎发生概率显著升高[9]。Zhao [10]、Dai [11]等学者建立的风险预测模型同样提示,糖尿病是PDAP发生的重要预测因子。糖尿病被普遍认为是感染的高危因素,合并糖尿病的PD患者常存在更明显的微炎症状态;此外,糖尿病可造成血管壁损害,并诱发腹膜纤维化等病理改变,使有效腹膜表面积减少。已有证据表明,加强血糖管理可有效降低PDAP的发生风险[12]。因此,在强化血糖控制的基础上,合理规范使用胰岛素,对预防PDAP的发生具有关键意义。

BMI被认为是PDAP的独立危险因素,也是反映机体状态及营养不良的重要预测指标[13]。在临床观察中,肥胖患者更容易出现早期腹膜炎[14]。美国某大型透析机构对15,573名PD患者的研究发现[15],

BMI ≥ 30 kg/m² 的患者残余肾功能下降更为迅速, 且转为血液透析的可能性明显增加。其潜在机制可能包括伤口愈合延迟、出口处日常护理难度加大, 以及皮肤与软组织感染易感性增强等因素。然而关于 BMI 与 PDAP 风险的研究结果并不完全一致。透析人群中存在“肥胖悖论”现象, 轻中度超重患者并未显示显著更高感染风险[16]。BMI 未能区分脂肪分布与肌肉量, 内脏脂肪或肌少性肥胖可能才是关键因素[17]。未来研究应结合体成分分析, 以提高风险评估精度。

吸烟作为多种疾病的独立危险因素, 可显著提高 PDAP 的发生风险, 而戒烟则有助于降低腹膜炎的发生率[18]。宁丽娜等[19]的研究结果同样支持这一观点。其可能原因在于烟雾中的多种有害成分(如尼古丁)可抑制 T 淋巴细胞增殖, 削弱巨噬细胞吞噬能力及抗体应答, 从而干扰机体免疫功能。

血清白蛋白是评价营养状况及免疫能力的重要指标, 白蛋白水平偏低往往提示蛋白质能量消耗增加及炎症反应活跃。腹膜炎发生与低血清白蛋白水平之间存在较强相关性, 低白蛋白血症被视为 PDAP 的危险因素这一观点已被广泛认可[20]-[23]。白蛋白降低通常反映营养不良状态, PD 患者长期营养不足可导致免疫应答减弱及组织修复能力下降, 使其对病原体的易感性增加, 从而使腹膜炎发生率上升[24]。

2.2. 免疫功能障碍与慢性炎症状态

C 反应蛋白(CRP)是反应炎症状态最常见的指标, 是人类肝细胞在感染、炎症或组织损伤下产生的一种非糖化蛋白。PD 患者长期处于一种微炎症状态, 而长期的微炎症是 PDAP 发生的影响因素[25]。有研究表明血清 CRP > 10 mg/L 是 PDAP 的独立危险因素[26]。Tang 等[27]的研究也指出 CRP 是频发 PDAP 的危险因素。

白细胞介素-6(IL-6)作为关键的多效性细胞因子, 不仅是全身及局部炎症状态的敏感标志物, 更是直接参与病理过程的效应分子。PD 患者的微炎症状态使得其腹膜具有产生 IL-6 的能力, IL-6 可较好地反映腹膜内炎症状态[28]。前瞻性队列研究已证实, 腹透液 IL-6 水平是 PDAP 发生的潜在预测因子[29]。近年机制研究[30]-[32]进一步揭示, IL-6 通过其经典信号通路和反式信号通路, 不仅能驱动急性炎症反应, 还可能通过促进腹膜间皮细胞的上皮-间充质转化、血管生成和纤维化, 参与感染后腹膜长期的结构与功能损害。因此, 动态监测血清及透出液 IL-6 水平, 不仅有助于识别 PDAP 高危患者, 也可能为评估腹膜健康状态和预后提供重要信息, 并提示针对 IL-6 通路的干预或许是未来预防严重或复发性腹膜炎的潜在策略之一。

2.3. 肠道菌群失调与屏障功能障碍

多项队列研究[33][34]显示, 血钾持续偏低与 PDAP 发生风险升高相关, 且在对人口学、合并症、透析充分性及营养相关指标等进行多因素校正后, 该关联仍可观察到, 提示低钾可能是 PDAP 的独立风险标志物。机制上, 低钾可与肠麻痹或肠蠕动减弱相关[35]; 而肠内容物淤滞可导致肠管扩张、腔内压升高及肠壁微循环障碍[36]并削弱黏膜屏障, 从而增加细菌移位的可能性[37]。相关实验研究亦提示低钾状态可增加肠通透性并促进细菌移位[33][38]。因此, 监测并纠正低钾血症应被视为 PDAP 综合预防策略的重要环节。

近年来, 肠道菌群在 PDAP 发病机制中的作用成为研究热点。相关研究指出, PD 患者存在肠道菌群失调, 且这种失调可能与腹膜炎发生相关。例如, 一项实验[39]指出肠道微生物紊乱与肠道屏障功能受损、菌群与宿主免疫调节之间相互作用, 在腹膜炎发生机制中可能发挥作用。肠道菌群失调可能通过多种途径增加 PDAP 发生风险: (1) 肠道屏障完整性受损导致细菌及其代谢产物(如内毒素)易位至全身循环, 引发持续性低度炎症, 促进感染易感性[39]; (2) 有益菌及其抗炎代谢物(如短链脂肪酸)减少, 削弱机体局部及系统免疫调节功能[40]; (3) 部分致病菌或其成分可能通过淋巴途径或跨壁迁移进入腹腔, 直接参与

腹膜炎的发生[41]。基于这些机制,肠道菌群构成及其代谢特征已被视为 PDAP 新的、可干预的风险标志物。但当前关于肠道菌群与 PDAP 的研究多为观察性分析,因果关系尚未完全确立。尽管机制研究支持其生物学合理性,但仍需多中心前瞻性研究验证微生态干预的临床获益。

多项研究发现,质子泵抑制剂(proton pump inhibitors, PPI)的使用可能与 PDAP 发生风险增加相关。多项观察性研究及系统评价提示,接受 PPI 治疗的 PD 患者发生 PDAP 的风险较未使用者升高,且以肠源性或革兰阴性菌腹膜炎更为常见[42] [43]。其潜在机制可能与胃酸屏障功能受损及肠道菌群改变有关。PPI 通过显著抑制胃酸分泌,升高胃内 pH 值,削弱其对摄入病原体的杀灭作用,同时可致上消化道及肠道菌群结构发生改变,表现为条件致病菌相对丰度升高[44]。需要指出的是,目前相关证据主要来源于观察性研究,仍可能受到处方指征偏倚及残余混杂因素的影响。然而,在腹膜透析患者的临床管理中,仍应审慎评估 PPI 的长期用药指征,避免不必要的持续使用,以降低潜在感染风险。

3. 治疗相关因素

腹膜透析治疗本身的技术细节、材料生物相容性及管理方式,直接构成了感染发生的外部条件与内在环境。

3.1. 腹膜透析液生物相容性

传统葡萄糖腹膜透析液因其低 pH、高葡萄糖降解产物(glucose degradation products, GDPs)及高渗特性,被认为具有较差的生物相容性,可对腹膜防御系统产生直接损害作用。研究表明,此类透析液可诱导腹膜间皮细胞发生上皮-间充质转化(epithelial-mesenchymal transition, EMT),促进细胞衰老并破坏间皮屏障完整性,同时抑制腹腔巨噬细胞的吞噬和杀菌功能,从而削弱局部免疫防御能力[45]-[47]。大量临床研究和随机对照试验提示,采用低 GDPs、中性 pH、碳酸氢盐/乳酸盐缓冲的生物相容性腹膜透析液,可改善腹膜生物学环境,并在一定程度上降低 PDAP 的发生风险,其保护效应可能部分归因于对腹膜毒性的减轻[48] [49]。此外,腹膜溶质转运特性本身亦被认为是 PDAP 的重要风险指标。多项队列研究发现,高腹膜转运状态常伴随更显著的腹膜血管增生和慢性炎症基础,与 PDAP 发生风险增加独立相关[50]-[52]。

3.2. 导管相关因素

导管作为连接体外环境与腹腔的人工通道,构成腹膜透析相关感染的关键入口,导管相关感染可导致导管丢失并显著增加腹膜炎发生风险[53]。大量研究表明[54],导管相关感染,尤其是出口感染和隧道炎,是 PDAP 的明确前兆因素,其存在可显著增加后续腹膜炎发生风险。病原学研究显示[53],金黄色葡萄球菌和铜绿假单胞菌是导管出口及隧道感染中最具临床挑战性的致病菌,与腹膜炎发生、复发及不良导管结局密切相关。此外,导管表面生物膜的形成被认为是复发性及难治性腹膜炎的核心机制之一。生物膜内细菌可通过降低代谢活性、形成保护性基质等方式,对抗生素产生显著耐受,从而导致治疗失败和反复感染,尤其在铜绿假单胞菌相关感染中更为突出[55]。因此,在反复或难治性 PDAP 的管理中,应充分考虑导管相关因素及生物膜的潜在作用。

4. 病原体相关因素

病原体的种类、毒力及耐药特性决定了感染的严重程度和治疗难度。

病原体谱与耐药性

革兰阳性球菌,特别是凝固酶阴性葡萄球菌和金黄色葡萄球菌,仍是 PDAP 最常见的病原体[54]。然

而,近年来部分透析中心报道革兰阴性杆菌感染的比例呈上升趋势,且此类感染往往导致更严重的临床表现和更高的治疗失败率[56][57]。更为严峻的挑战是抗生素耐药性的增加,如耐甲氧西林金黄色葡萄球菌以及产超广谱 β -内酰胺酶的肠杆菌科细菌感染,其治疗选择有限,拔管率和转血液透析率显著升高[58][59]。真菌性腹膜炎虽然发生率相对较低,但其死亡率和技术失败率显著高于细菌性腹膜炎,且多与长期或反复使用抗生素、免疫抑制状态等因素密切相关[60]。

5. 小结

腹膜透析相关性腹膜炎的危险因素是一个多层次、相互关联的复杂网络。它既包含糖尿病、营养不良等经典宿主因素,也涵盖肠道菌群失调、表观遗传易感性等新兴生物学标志;既涉及透析液生物相容性、导管技术等治疗核心环节,也受操作规范及医疗体系质量等外部条件的深刻影响。未来研究应致力于整合多维度风险信息,构建精准预测模型,并探索针对特定易感通路(如调节肠道菌群、干预腹膜衰老)的靶向预防策略,从而最终实现PDAP发生率的有效降低和患者预后的全面提升。

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