

## 炎症性肠病患者营养支持的研究进展

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### Nutritional support in inflammatory bowel disease

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#### 背景资料

营养支持治疗作为炎症性肠病(inflammatory bowel disease, IBD)治疗中重要的组成部分, 因其专业性强的特点而与药物治疗和手术治疗具有同等重要的价值和地位, 营养支持治疗技术的不断提升对改善IBD的治疗效果具有重要的临床意义, 因此, 本文是为了更好的了解营养支持治疗在IBD中的研究进展.

### Abstract

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a group of autoimmune diseases mainly characterized by chronic inflammation in the small and large intestine. The incidence and prevalence of IBD are high and stable. Since IBD is characterized by the wide range of lesions, recurrence, long duration, severe gastrointestinal symptoms and metabolic change, IBD patients often have nutritional disorders. The drug use and surgical operation in the process of IBD treatment will further aggravate nutritional disorders. Therefore, proper nutrition support in IBD is of great value and significance for the recovery and prognosis of the disease.

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Key Words: Inflammatory bowel disease; Nutritional support; Progress

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## ■ 相关报道

van Nood等研究将健康捐献者未分离的粪便微生物输入IBD患者中, 具有很好的创新, 如果能将粪便微生物分离出来, 会有更大的临床价值。

## 摘要

炎症性肠病(inflammatory bowel disease, IBD)是一组以机体肠道炎症反应为特征的自身免疫性疾病, 包括溃疡性结肠炎(ulcerative colitis, UC)和克罗恩病(Crohn's disease, CD), 发病率和患病率一直居高而稳定, 因其病变范围广泛, 且具有反复发作、病程长、消化系症状重、代谢改变等特点, 易发生营养不良, 而IBD在治疗过程中药物的使用和手术治疗又进一步加重了营养障碍。因此, 恰当的营养支持对于IBD患者病情的恢复及预后具有重要的价值和意义。

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关键词: 炎症性肠病; 营养支持; 进展

**核心提示:** 炎症性肠病(inflammatory bowel disease, IBD)包括溃疡性结肠炎(ulcerative colitis)和克罗恩病(Crohn's disease), 营养与IBD的发病机制和治疗有极其重要的意义。关于营养是否和发病有关、如何营养支持等问题一直受到关注。随着我国IBD发病率的不断提高, 此方面的研究将越来越受到重视。

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## 0 引言

炎症性肠病(inflammatory bowel disease, IBD)是一种病因不明、以机体肠道慢性非特异性炎症反应为特征的自身免疫性疾病。包括溃疡性结肠炎(ulcerative colitis, UC)和克罗恩病(Crohn's disease, CD)<sup>[1]</sup>。在北美及欧洲等发达国家IBD的发病率和患病率一直居高而稳定<sup>[2,3]</sup>, 小儿或青春期的IBD发病率高达25%<sup>[4]</sup>, 近期一项流行病学研究<sup>[5]</sup>表明: 世界IBD高发地区小儿发病率呈持续增高状态。由于IBD病变范围广泛, 且具有反复发作、病程长、消化系症状重、代谢改变等特点, 因此易发生营养不良, 而药物的使用和手术治疗又进一步加重营养障碍。营养支持治疗作为IBD治疗中重要的组成部分, 因其专业性强的特点而与药物治疗和手术治疗具有同等重要的价值和地位, 因此营养支持治疗技术的不断提升对改善IBD的治疗效果具有重要的临床意义。

## 1 IBD患者营养状况

国内外学者对IBD患者营养状况做了大量调查研究<sup>[6-8]</sup>, 相关数据显示20%-85%的IBD患者、特别是CD患者存在营养不良<sup>[9]</sup>, 但也有研究<sup>[10]</sup>显示在活动期IBD患者中, CD和UC营养不良状况没有明显差别。其中约25%-80%的IBD患者存在不同程度的蛋白质热能营养不良<sup>[11]</sup>, 丹麦一项基于人群的前瞻性研究<sup>[12]</sup>发现, 患有CD的儿童较正常人群更易处于营养不良的状态。

IBD患者由于代谢改变等因素易出现低体质量指数或肥胖症状, 澳大利亚学者Aurangzeb等<sup>[13]</sup>在一项病例对照研究中发现, 被诊断为IBD的儿童患者较对照组均存在体质量指数和年龄别体质量偏低的情况, 其中22%-24%的CD儿童患者和7%-9%的UC儿童患者存在低体质量指数情况<sup>[14]</sup>, 20%-40%的CD患者存在体质量减轻<sup>[15]</sup>, 而Griffiths等<sup>[16]</sup>对386例被诊断为CD的儿童患者随访10年发现80%的患者都有体质量减轻的表现, 但也有学者研究结果相反, Sousa Guerreiro等<sup>[17]</sup>与Long等<sup>[18]</sup>调查结果显示40.0%门诊CD缓解期患者及23.6%的IBD儿童青少年患者有体质量超重或肥胖的症状, 而体脂的增加是导致肥胖的主要原因<sup>[19]</sup>, 巴西学者研究<sup>[10]</sup>发现以BMI作为评价指标, 14%的CD患者与5.7%的UC患者存在营养不良, 但一半以上的患者存在肌肉损耗, 德国的研究<sup>[20]</sup>也显示, 74%的IBD缓解期患者与健康人群相比手握力和体细胞质量下降。

贫血在IBD患者中也普遍存在, 其不仅严重影响患者的生活质量, 还能导致并发症或死亡<sup>[21,22]</sup>, 有数据显示27%的CD患者和21%的UC患者存在贫血现象, 而其中57%为缺铁性贫血<sup>[23]</sup>, 感染、维生素B<sub>12</sub>缺乏、过敏反应和骨髓增生异常综合征等是导致缺铁性贫血的主要原因<sup>[24]</sup>。

矿物质和维生素缺乏也是炎性肠病患者营养不良的表现。研究<sup>[25]</sup>发现维生素C缺乏与UC的发生呈正相关, 而维生素D缺乏在IBD儿童及青少年患者中较正常人群也更常见<sup>[26,27]</sup>, 且低骨转换普遍存在于CD和UC儿童患者中<sup>[28]</sup>, 20-50岁的IBD患者中, 24.4%骨量减少, 5.8%患有骨质疏松<sup>[29]</sup>。除此之外, IBD的青少年患者还会出现青春期延迟<sup>[30]</sup>, 18%-88%儿童会出现生长发育迟缓, 这结果在一系列研究中都得到了证实<sup>[31-34]</sup>。

## 2 IBD患者营养支持国内外研究现况

2.1 IBD患者营养膳食干预 饮食习惯的差异是导致IBD患病原因之一<sup>[35]</sup>, 长期以来国内外学者对饮食与IBD患病关系做了大量研究, 结果显示大量摄入肉类、牛奶、甜食、油炸食品以及高脂食物特别是大量动物脂肪、n-6多不饱和脂肪酸等可增加患IBD的风险, 且罹患IBD的风险随着蔗糖、牛奶、脂肪等摄入量的增加逐渐增加<sup>[36-39]</sup>, Cohen等<sup>[40]</sup>研究发现辛辣的食物、水果、坚果、绿叶蔬菜、红肉、汽水、爆米花、乳制品、酒精、高纤维食物、玉米、高脂肪食品、咖啡等食物的摄入能导致IBD症状加重。某些食物中含的食品添加剂、防腐剂、污染物等也可增加IBD患病率<sup>[36]</sup>。而摄入大量的肉类和酒精饮料等可导致UC复发<sup>[41]</sup>, 朱元民等<sup>[42]</sup>调查发现短时间或无母乳喂养者也易发生UC。牛乳喂养的儿童IBD患病率有升高倾向, 而延长母乳喂养时间, 可降低IBD的患病率<sup>[43]</sup>。但n-3多不饱和脂肪酸的摄入与IBD患病率呈负相关, 起保护作用<sup>[44]</sup>。摄入酸奶、大米、香蕉也能使IBD症状得到改善<sup>[41]</sup>。

在饮食因素与IBD关系的研究中, 免疫球蛋白G介导的食物不耐受(food intolerance, FI)已成为目前国内外研究的热点课题<sup>[45-47]</sup>。近期研究<sup>[48]</sup>显示, 难治性UC患者食物不耐受发生率达到78.57%。北美儿童胃肠病、肝病和营养组织达成一致共识, CD儿童患者一定要基于食物金字塔指南及遵循膳食参考摄入量平衡膳食<sup>[49]</sup>。特殊的饮食营养是导致IBD风险因子之一<sup>[50]</sup>, 因此合理的营养膳食干预能有效缓解IBD症状, 在IBD治疗恢复中起到重要作用。

2.2 IBD患者肠内营养 肠内营养是指通过经口服或导管输送方式提供机体所需营养素的营养支持方法<sup>[51]</sup>。其目的是维持正常胃肠道运动功能、各种肠道菌群的合理分布及稳定, 提高免疫功能, 最终达到改善肠道功能、病变及机体营养状态的作用。国内外学者一致认为肠内营养应作为肠道功能存在且没有明显禁忌证时营养支持的首选途径<sup>[52,53]</sup>, 一项来自美国、加拿大、西欧及以色列的167名内科医师研究显示: 分别有4%、62%的北美儿童胃肠科的医师及欧洲医师规律使用肠内营养, 65%的科室将肠内营养的使用作为新诊断为CD患者的首要治疗方式<sup>[54]</sup>。

IBD患者营养状况明显受损, 尤其是CD患

者。而针对UC患者的营养治疗在国外文献中鲜见报道, 当前研究主要集中在探讨肠内营养与IBD、特别是CD的关系上, 但近几年来国内开始关注UC肠内营养的治疗, 辛丽敏等<sup>[55]</sup>将肠内营养作为对活动期UC患者的辅助治疗方式疗效显著, 特别是个性化营养支持对缓解病情较重UC患者能达到更好的治疗效果<sup>[56]</sup>, 国外学者研究<sup>[6]</sup>发现肠内营养和半肠内营养对儿童和成人患者能有效维持和诱导CD缓解, 20.0%-84.2%的CD急性期患者能通过肠内营养得到缓解, 特别针对激素治疗的成人CD患者肠内营养更具有特别重要的作用<sup>[57]</sup>。采用肠内营养治疗CD患者在不同时间结果也不相同, 日本学者一项前瞻性研究<sup>[58]</sup>发现, 选用夜间肠内营养治疗CD患者更有利于临床症状缓解及体质增加。同时大量研究<sup>[59,60]</sup>认为, 肠内营养不仅能有效地改善CD活动期的病情, 并且在治疗CD儿童患者生长发育过缓上要优于激素治疗, 可以作为激素的替代治疗选择。肠内营养治疗IBD具有效果明显, 并发症少等优点<sup>[61]</sup>, 因此, 可根据病情需要延长使用, 肠内营养以其不可替代的优势在IBD患者的治疗中起着重要的作用。

2.3 IBD患者肠外营养 肠外营养(parenteral nutrition, PN)治疗是指通过静脉给患者提供足够的热量、电解质、氨基酸及微量元素等营养, 使患者在进食受限的情况下仍能满足营养需要<sup>[51]</sup>。PN主要用于不同原因导致的肠瘘或严重肠梗阻、手术吻合口瘘、UC合并便血或严重腹泻、短肠综合征初期、不能耐受肠内营养或严重水电解质紊乱等情况<sup>[62]</sup>。相关数据统计, 1988-2006年, PN在CD和UC住院患者中使用率分别为4.29/100000和3.80/100000<sup>[63]</sup>。IBD患者PN的使用受多方面因素影响, 美国研究结果显示, 不同地区PN使用率不同, 无医疗保险者PN使用率仅占有医疗保险者的一半, 拉美裔患者较白人患者花更长的时间来接受PN治疗, 且具有更高的导管感染率<sup>[64]</sup>。

PN在疾病的进展期和加重期可明显缓解腹泻、腹痛及呕吐等症状。Dudrick等<sup>[65]</sup>首先提出了PN临床治疗安全有效。针对活动期CD患者, PN的使用与管理是基于能使肠道得到休息的理论优势之上的, 这可以减少病变肠蠕动及抗原刺激, 促进蛋白质合成, 加快细胞更新和肠黏膜愈合<sup>[66]</sup>。同时针对严重UC围手术期患者, 术前选用PN使用5 d以上可减少术后并发

**■创新盘点**  
本文在阅读了大量的外文文献基础上, 将近几年来IBD营养治疗的发展进行了充分的总结, 能使研究者更充分的了解近期的研究现状。

### 应用要点

本文能使研究者更好的了解营养支持治疗在IBD中的研究进展, 了解最前沿的发展, 可以使自己的研究方向更清楚。

症, 且可降低病死率<sup>[67]</sup>.

但是尽管PN能使肠道得到休息, 仍没有被证明其方法优于肠内营养。国内外学者对此也做了大量研究, Guagnozzi等<sup>[57]</sup>认为除了提供正常的食物, 肠内营养在IBD患者营养不良的管理上可能比PN更有用。采用PN治疗IBD患者, 可增加静脉血栓的风险, 同时更易出现导管相关感染、胃肠功能减退、代谢紊乱等并发症, 因此, 根据病情在接受PN治疗后, 临床症状有所缓解且能耐受肠内营养的条件下, 应过渡为肠内营养治疗。

**2.4 IBD患者生态营养** 生态营养是由学者Parker 1974年提出的“微生态制剂”发展而来, 直至20世纪90年代才逐渐被人们所认识并运用, 并越来越受到人们的关注。IBD的发病机制人们至今还不完全清楚, 除了基因、免疫、环境因素及肠道微生物群的相互作用, 肠道菌群结构及肠道功能的改变对IBD的发病和进展也有着重要影响。研究<sup>[68]</sup>发现与未患IBD的对照组人群相比较, IBD患者肠道处于变形菌属细菌增加, 厚壁菌属细菌减少的状态。最新一项大样本数据显示, 447例3-17岁新诊断为CD的患者与221例无炎症的对照组进行回肠及直肠活组织检查, 结果发现, 患有CD的患者肠杆菌科、巴斯德氏菌科、韦荣氏菌科、奈瑟氏菌科、梭杆菌科均增加, 而双歧杆菌、丹毒丝菌、拟杆菌、梭菌目却减少<sup>[69]</sup>。可见肠道菌群失调普遍存在于IBD患者中, 肠道菌群的调整在IBD患者中起着非常重要的作用, 基于此, 国内外学者对IBD患者提出了生态营养治疗方式。

1989年, 堪萨斯城的外科医生将不含药物成分的粪便微生物移植给IBD患者, 1 wk后症状得到缓解<sup>[70]</sup>。益生菌的益处在于<sup>[71]</sup>: (1)生产SCFAs和乳酸, 抑制潜在的致病微生物的生长并对肠道有抗炎作用; (2)增加了水净流量从血液到肠道通过时间, 影响细菌黏附在肠壁; (3)减少可能导致IBD的有毒物质产生。国外学者van Nood等<sup>[72]</sup>研究将健康捐献者未分离的粪便微生物输入IBD患者中, 反复证实粪便微生物移植对IBD的治疗具有显著作用。

随着生态营养在IBD治疗中的发展, 益生菌也引起了学者们的关注。研究<sup>[73,74]</sup>发现益生菌能抑制炎症并激活先天免疫来恢复宿主肠道微生物群, 大量报道<sup>[75-77]</sup>显示益生菌在提高IBD患者生活质量上有明显功效, 且对胃肠道

的功能恢复和IBD的诱导缓解及维护有显著效果<sup>[78]</sup>。王坚强等<sup>[79]</sup>将植物乳杆菌用于小鼠肠道, 连续灌注植物乳杆菌4 wk后, 较对照组在肠道菌群失衡及细菌移位的情况得到了明显改善。**2.5 IBD患者激素营养** 大量临床研究<sup>[80]</sup>表明激素在诱导活动性CD缓解方面治疗效果显著。国内外学者大量实验显示转化生长因子、生长激素、胃泌素、肠高血糖素等能促进肠道黏膜的修复及重建, 从而使全身营养状态得到改善。IBD治疗的主要目标是控制肠道炎症反应, 而生长激素有助于提升促炎症细胞因子并激活巨噬细胞, 从而可作为IBD潜在的治疗目标。Coëffier等<sup>[81]</sup>研究发现转化生长因子(transforming growth factor-β, TGF-β)可通过减少炎症标志物水平有效诱导CD患者疾病的缓解, 以促进黏膜愈合来达到治疗的目的。实验证明胰高血糖素样肽-2(glucagon-like peptide-2, GLP-2)是一种强大特定的胃肠道生长因子, 通过增加GLP-2生物活性循环水平, 促进肠道黏膜上皮细胞修复, 在预防和治疗IBD有显著效果<sup>[82]</sup>, 激素营养在预防治疗IBD的作用已得到大量的实验支持, 并将会在IBD治疗中得到越来越广泛的运用。

## 3 结论

营养支持治疗是IBD管理的重要组成部分, 是IBD治疗成功的基础。成功的营养支持治疗需要专业的、强大的学科团队, 包含了医师、护士、营养师等相互协作。IBD治疗决策过程中必须设定目标, 包括减轻缓解疾病症状、促进肠黏膜愈合, 改正错误营养方式。在未来的营养支持治疗研究中, 将会具有更大的挑战, 比如解决患者不喜欢就餐时重复的饮食等问题, 因此探索具有药物性能的食品, 寻找更有效且适合的营养治疗方法, 将手术、药物、营养治疗相结合, 以达到缓解IBD症状, 最终达到改善患者生活质量的目的。

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**名词解释**

发病率：指一定时期内，一定人群中，某病新病例出现的频率。其分子是一定期间内的新发病人数，分母是可能发生该病的人群；患病率：指某特定时间内总人口中，曾患有某病（新旧病例之和）所占的比例。

**■同行评价**

本文针对国内外研究现状进行归纳、总结, 反映出了IBD最新营养支持的研究进展, 条理清楚, 论证充分, 总体效果好。

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• 消息 •

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**本刊讯** 为了促进消化护理学领域的事业发展,《世界华人消化杂志》已成立消化护理学编辑委员会. 将主要报道消化护理学的基础研究,临床研究,临床护理实践和护理管理等原始和综述性文章.

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