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胃内占容干预儿童及青少年肥胖的研究进展

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【摘要】 全球儿童及青少年肥胖率呈现快速增长趋势，其远期合并症对人口素质及预期寿命构成严重威胁。针对儿童及青少年肥胖的干预措施主要包括生活方式干预和心理行为干预等。药物治疗以及代谢减重手术等的应用有严格的指征，因此在临床应用上存在一定局限性。近年来，胃内占容因其具有显著的减重效果、广泛的人群适用性、良好的安全性特征以及持久的远期疗效，为儿童及青少年肥胖的临床干预提供了新的思路。本综述系统回顾了儿童及青少年肥胖现有干预方法的优缺点，并探讨了胃内占容干预方式的作用机制、临床应用进展及其减重效果评估。仍需开展多中心、大样本研究，系统揭示胃内占容技术对儿童青少年肠道微生态的调控机制，并据此为其向肥胖干预临床实践转化建立循证基础。

【关键词】 儿童及青少年肥胖 肥胖干预 胃内占容 胃内球囊 综述

Research Advancements in Gastric Capacity Intervention for Childhood and Adolescent Obesity

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[Abstract] The global prevalence of obesity among children and adolescents is rising rapidly, and the long-term comorbidities of obesity pose serious threats to the population health and life expectancy. Interventions for childhood and adolescent obesity mainly include lifestyle and psycho-behavioral approaches. Pharmacological treatment and metabolic bariatric surgery are subject to strict clinical indications and, hence, have limited clinical application. In recent years, the concept of intragastric volume occupancy has emerged as a promising approach to the clinical management of childhood and adolescent obesity, for it has demonstrated notable weight-loss efficacy, broad applicability across different populations, a favorable safety profile, and sustained long-term effectiveness. Herein, we systematically evaluated the advantages and limitations of existing intervention strategies for childhood and adolescent obesity. We discussed the mechanisms of action, clinical application progress, and evaluation of weight loss effects of intragastric volume occupancy intervention methods. Further multicenter, large-sample studies are warranted to systematically elucidate the regulatory mechanisms of intragastric occupancy technology on the gut microbiota of children and adolescents, and to establish an evidence-based foundation for its translation into clinical practice for obesity intervention, accordingly.

[Key words] Childhood and adolescent obesity Obesity intervention Gastric capacity Gastric balloon Review

随着全球经济和生活水平的提升，生活方式的改变使肥胖成为突出的全球公共卫生问题，儿童及青少年肥胖患病率的上升尤为显著。肥胖已成为儿童及青少年最常见的慢性疾病之一。2020年数据显示，中国儿童的体质量指数（body mass index, BMI）增长水平位居全球前列[1]。若不干预，预计到2030年，儿童肥胖症患病率将达15.1%，即每7名儿童中有1名肥胖，这将对我国卫生系统造成巨大压力[2]。研究表明，儿童和青少年肥胖与高血压、2型糖尿病、非酒精性脂肪性肝病、哮喘及社会心理问题等多种疾病密切相关，且部分肥胖可持续至成年期，严重影响人口素质，甚至导致过早死亡[3-7]。因此，对儿童及青少年肥胖进行有效干预迫在眉睫。然而，目前干预手段有限，依从性较差，体重易反弹，难以实现显著且持久的减重效果[8-10]。鉴于此，本综述简述目前干预方式的优缺点，着重阐述目前新的胃内占容方法和作用机制，临床应用前景及禁忌证。

1 儿童及青少年肥胖干预方法的优缺点

为有效遏制儿童及青少年肥胖的流行趋势并促进其健康成长，制定科学合理的干预措施至关重要。当前儿童及青少年肥胖的干预管理策略主要包括生活方式干预及心理行为干预。生活方式干预作为基础性干预措施，

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包括膳食干预及运动干预[11]。美国洛杉矶儿童医院开展的一项为期12周的限时进食干预研究表明,约33.3%的肥胖青少年可实现具有临床意义的体重减轻(超过基线体重的5%)[12]。膳食干预不仅能帮助肥胖儿童及青少年建立健康的生活方式,还增加家庭成员的参与度[11]。然而,这一干预措施中饮食方案制定需要专业指导,且对儿童及青少年依从性要求较高,部分儿童及家庭难以长期坚持[13-14]。运动干预在改善肥胖相关并发症、提升身体素质及生活质量方面具有不错效果[15]。由于受限于儿童青少年的适应性及体能水平,运动干预的实施周期往往较长,临床依从性欠佳,这在一定程度上限制了其长期疗效和可持续性[16]。基于认知行为疗法(cognitive behavioral therapy, CBT)的干预措施已被证实可改善儿童青少年的饮食行为、社会心理健康、生活质量、自尊水平等心理社会指标,并在人体测量学指标方面取得显著改善。然而,这种干预方式并非完美无缺。它存在可及性有限的问题,且需要家庭-学校多方协同合作,这在实际操作中可能会面临诸多困难。因此,仍需进一步完善和推广,以充分发挥其潜力[17]。REHANA等[18]开展的系统评价聚焦于生活方式改变对儿童和青少年肥胖的影响,结果表明,综合干预措施,如饮食与运动相结合用于肥胖预防,以及饮食、运动与行为疗法三者联合用于肥胖管理,对于BMI、BMI z评分、体重、皮褶厚度以及代谢指标均具有显著益处。对于强化生活方式干预效果欠佳或存在运动禁忌的肥胖儿童及青少年,可考虑药物治疗。目前,美国食品药品监督管理局已批准奥利司他、利拉鲁肽、司美格鲁肽和芬特明-托吡酯用于12岁及以上青少年肥胖的治疗,但国内尚未获批相关适应证[19]。值得注意的是,药物治疗可以作为生活干预的辅助手段,且短期效果显著,但存在适用年龄范围的限制、潜在的不良反应风险以及停药后可能出现的体重反弹现象。对于生活方式及药物干预均未达到预期效果且符合手术适应证的儿童青少年重度肥胖患者,可考虑代谢减重手术。儿童青少年代谢手术可明显减轻体重,实现体重控制,但其实施要严格把握适应证,且相关手术经验及术后管理方案仍在探索中,需进行全面的术前评估、充分知情告知并谨慎决策[20-22]。

2 胃内占容方法

近年来,胃内占容作为一种新兴干预手段,在儿童及青少年肥胖领域展现出潜在应用价值。该技术可作为生活方式干预失败后的替代治疗方案,或作为重度肥胖儿童青少年代谢手术前的桥接治疗[23-24]。胃内占容技术包括胃内球囊及胃内胶囊。胃内球囊装置的植入需借助内镜完成,这一操作具有明确的侵入性特征,因此在儿童及青少年群体中的应用受到显著限制[25]。儿童及青少年的生理与心理特点决定了他们在接受此类操作时的配合度较低,同时,潜在风险较高以及目前缺乏针对该年龄段人群的明确临床指南和充分循证医学证据,使得可吞咽胃内胶囊在儿童及青少年中的应用同样受到诸多限制[26]。新型胃占容食品的出现为儿童青少年肥胖的无创治疗提供了新的研究方向[27]。与传统胃内球囊相比,胃占容食品具有良好的安全性,且操作简便,无需借助内镜等侵入性手段,从而显著降低了治疗相关风险,其在肥胖儿童及青少年中的应用前景值得进一步探索。

3 胃内占容作用机理

胃内占容通过物理占容与饱腹感调节、食欲相关激素调节以及肠道微生态调节等多重机制发挥减重作用,实现无创化体重管理,改善肥胖相关症状(图1)。

3.1 物理占容与饱腹感调节

胃内占容通过物理性减少胃内容积,限制过量食物摄入;同时,胃内占容食品可延缓胃排空时间,延长进食间隔,从而降低全天能量摄入[28]。其次,胃内占容通过机械性扩张胃壁,激活胃牵张感受器,经迷走神经传入通路将信号传递至孤束核和室旁核,进而抑制下丘脑外侧区摄食中枢活动,增强腹内侧核饱食中枢活性,最终产生饱腹感并降低饥饿感[29-31]。这一调节机制有助于改善进食行为,实现控制增重目标。

3.2 食欲相关激素调节

胃内占容的另一重要作用机制涉及食欲相关激素的调节[32]。胃生长激素释放肽(ghrelin)是目前已知的唯一促食欲肽类激素。研究表明,体质量减轻过程中胃底部生长激素释放肽细胞数量呈现代偿性增加,而胃内占容可抑制这一代偿机制,从而维持体质量减轻[32-33]。同时,胃内占容食品可显著提升胰高血糖素样肽-1(glucagon-like peptide-1, GLP-1)和肽YY(peptide YY, PYY)等抑食欲激素水平[34]。这种双重调节机制有效控制食欲,为体质量管理提供了生理基础。

3.3 肠道微生态调节

胃内占容食品对肠道微生态具有调节作用[35]。其作用机制包括:(1)降低促肥胖菌群丰度,增加抗肥胖菌群数量;(2)作为微生物代谢底物,产生有益代谢产物[36-37]。研究表明,厚壁菌门(Firmicutes)与拟杆菌门(Bacteroidetes)的相对丰度与儿童BMI z评分呈独立负相关,提示儿童BMI增加会导致肠道菌群失调[38]。值得注意的是,嗜黏蛋白阿克曼菌(*Akkermansia muciniphila*)丰度

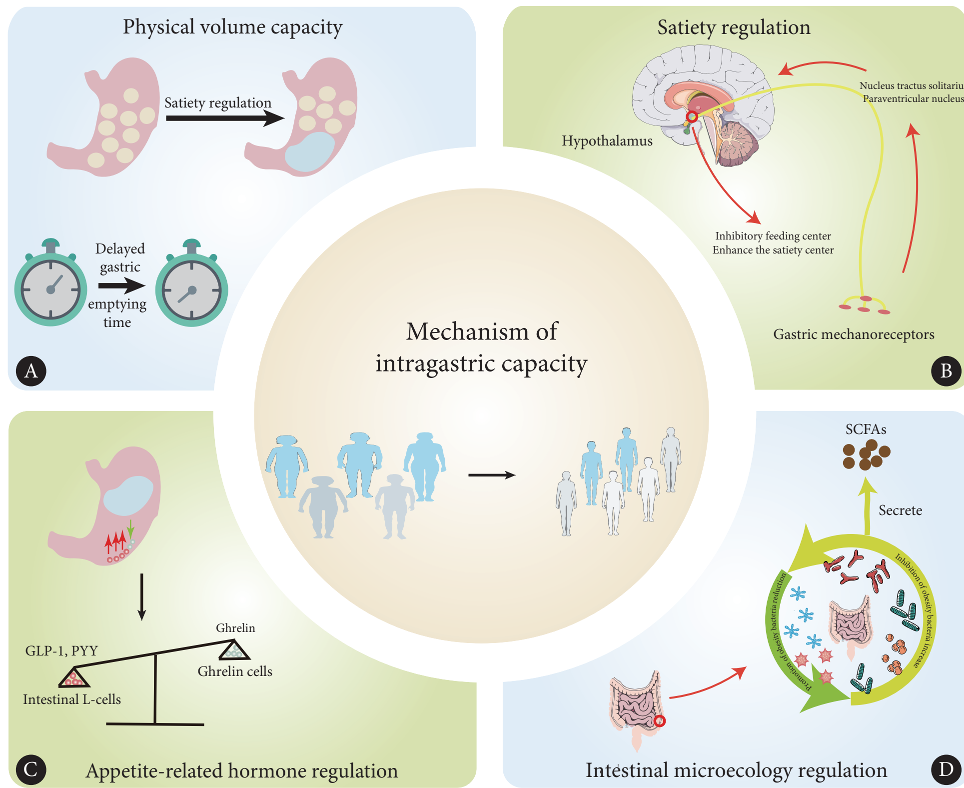

图 1　胃内占容机制示意图

Fig 1　Schematic diagram of the intragastric capacity mechanism

A, Through intragastric occupancy, the intragastric capcity is reduced, which limits excessive food intake; gastric occupancy extends gastric emptying time and prolongs the eating interval. B, Intragastric occupancy activates gastric baroreceptors and transmits signals to the solitary tract nucleus and paraventricular nucleus via the vagus nerve, which in turn affects the activity of hypothalamic ingestion and satiety centers. C, Intragastric occupancy regulates the secretion of Ghrelin, glucagon-like peptide-1 (GLP-1), and peptide YY (PYY). D, Intragastric occupancy affects the abundance of pro- and anti-obesity flora and is involved in the production of short-chain fatty acids (SCFAs) metabolites.

的增加与体脂分布改善、体重减轻及代谢异常风险降低密切相关[39]。胃内占容超吸水性水凝胶可通过其物理化学特性维持拟杆菌门丰度，促进嗜黏蛋白阿克曼菌增殖[40]。一项随机对照试验证实，胃占容食品中的菊粉补充剂可显著增加肥胖儿童肠道菌群多样性，促进双歧杆菌(*Bifidobacterium*)、巨球型菌属(*Megasphaera*)、优杆菌属(*Eubacterium*)和亚多里菌属(*Subdoligranulum*)等有益菌群增殖[41]。胃占容食品通过调节微生物代谢产生短链脂肪酸(short-chain fatty acids, SCFAs)，包括乙酸盐、丙酸盐和丁酸盐，对宿主代谢产生多重有益影响[41-42]。SCFAs可通过激活G蛋白偶联受体和腺苷-5'-单磷酸活化蛋白激酶信号通路，或通过表观遗传调控改善葡萄糖和脂质代谢，维持肠道稳态，缓解肥胖相关症状[43]。此外，SCFAs可刺激结肠肠内分泌细胞分泌PYY和GLP-1，通过体循环增加外周血中抑食欲激素水平，从而降低食欲，减少能量摄入[44]。总之，胃内占容可通过重塑肠道菌群结构，调节微生物代谢产物，实现食欲控制和代谢改善，最终达到由肥胖功能状态转变为正常功能状态的目的。

4　胃内占容技术的临床应用

随着医疗技术的进步，以胃内球囊(intragastric balloon, IGB)和胃占容食品为代表的胃内占容技术逐渐成为肥胖干预领域的研究热点(表1)。一项回顾性研究纳入91例15～17岁肥胖青少年(BMI≥27 kg/m^2)，在接受可吞咽胃内球囊(Allurion气球)，并联合个性化生活方式/营养改变计划，干预4个月后平均体重由基线(99.70±21.33) kg降至(86.37±18.83) kg，BMI由基线(35.60±5.59) kg/m^{2}降至(30.86±5.16) kg/m^2，总体重减轻百分比达(13.05±7.64)%(P< 0.000 1)[26]。CASTELLANI等[45]研究者开展了队列研究，纳入接受胃内球囊治疗、胃束带手术以及袖状胃切除术的肥胖青少年患者，并对其进行了长期随访。研究中接受胃内球囊治疗的肥胖青少年，其基线BMI为(43±6) kg/m^2。干预后，该组患者在6个月、3年和5年时的BMI分别为(41±5) kg/m^2、(34±5) kg/m^{2}和(33±6) kg/m^2。与接受胃束带手术和袖状胃切除术的患者相比，接受胃内球囊治疗的患者在3年内的超重减轻百

表 1 不同胃内占容方式减重效果比较表

Table 1 Comparison of weight loss effects of different intragastric occupancy methods

Gastric volume capacity method	Target population	Operation method	Initial weight/kg	Initial BMI/(kg/m^2)	Initial BMI z-score	Intervention Time	Post-intervention Weight/kg	Post-intervention BMI z-score	Adverse reactions
Intragastric balloon[25]	Obese teenagers	Endoscopy insertion	138.5 ± 23.9	46.4 ± 5.6	4 ± 0.3	6 months	Compared to the baseline, −7.1 (−27, 12.8)	Compared to the baseline, −0.2 (−0.37, −0.03)	Gastrointestinal reactions (nausea, vomiting, and abdominal discomfort); 1 case had subconjunctival hemorrhage (after vomiting)
Intragastric balloon[45]	Obese teenagers	Endoscopy insertion	59 ± 22	43 ± 6	—	6 months	41 ± 5	—	No gastroesophageal reflux disease, gastritis, hiatal hernia or dyspepsia
Intragastric balloon[26]	Overweight or obese teenagers	Self-swallowing oral administration	99.70 ± 21.33	35.60 ± 5.59	—	4 months	86.37 ± 18.83	—	Gastrointestinal reactions (nausea and vomiting)
Gastric capacity food[49]	Overweight or obese children and teenagers	Oral administration	56.6 (43.9-77.7)	—	2.5 (2.2-3.1)	3 months	—	Compared to the baseline, −0.2 (−0.3, −0.1)	Gastrointestinal reactions (abdominal pain, loose stools, fullness, and loss of appetite)
Gastric capacity food[50]	Overweight or obese children and teenagers	Oral administration	—	28.3 ± 4.5	3.3 ± 1.0	6 months	—	3.0 ± 0.9	No obvious gastrointestinal side effects
Gastric capacity food[54]	Overweight or obese children and teenagers	Oral administration	70.1 ± 21.3	28.1 ± 4.1	2.7 ± 0.7	3 months	—	2.49 ± 0.76	Gastrointestinal reactions (abdominal pain, abdominal distension, and diarrhea)

分比表现较为理想。多数研究已经证明胃内占容可为肥胖儿童及青少年实现控制增重目标，但胃内球囊的临床应用仍受限于疗效稳定性、安全性、耐受性及患者依从性等因素，其远期影响尚缺乏高质量循证医学证据，其在儿科领域的应用仍需谨慎[46-47]。

相比之下，胃占容食品通过在胃内吸水膨胀占据体积，达到占容的目的。其优点在于无需内镜参与，安全性高，操作简便，直接口服即可在胃内起效。胃占容食品作为一种无创减重方式，逐渐进入临床应用，为治疗超重和肥胖提供了新的选择。葡甘露聚糖和菊粉等胃占容成分因其独特的理化性质和生理功能，展现出显著的潜在应用价值。葡甘露聚糖作为一种高黏度的可溶性膳食纤维，能够在胃内形成凝胶状结构，延缓胃排空，从而增加饱腹感并调节食欲[48]。此外，其低剂量即可发挥显著的饱腹效果，且对胃肠功能具有调节作用[28]。菊粉作为一种益生元，不仅能够通过增加胃内容积来延缓胃排空，还能调节肠道菌群，改善肠道健康[41]。波兰一项纳入97例超重/肥胖儿童的随机对照试验表明，每日补充3 g葡甘露聚糖持续12周可大幅降低能量摄入，BMI较基线下降约0.9 kg/m^2，且与安慰剂组相比，12周时总胆固醇和低密度脂蛋白胆固醇浓度较低[49]。另有研究证实，每日晚餐前补充30 g菊粉可显著降低肥胖儿童的BMI z评分、脂肪质量指数和躯干脂肪质量指数，同时可能增加瘦体重并提高基础代谢率[50]。SILVESTRI等[40]研究发现，口服胃内占容超吸水性水凝胶可模拟富含纤维的蔬菜，产生饱腹感而不增加热量摄入，改善葡萄糖和脂质代谢，降低胆固醇水平，减轻肝脏脂肪变性，并改善胰岛素抵抗，最终改善代谢综合征，然而，目前该水凝胶尚未在肥胖儿童及青少年中应用。尽管胃内占容食品较胃内球囊可能具有更好的依从性，但目前研究仍存在以下局限性：（1）样本量较小；（2）缺乏不同种族肥胖儿童及青少年的验证数据；（3）长期有效性、安全性和减重持续性证据不足；（4）对肠道微生物群组成、多样性及代谢产物的影响机制仍需进一步探索。未来需要开展大规模、长期随访的临床研究以明确胃内占容食品在儿童及青少年肥胖治疗中的应用价值。

5 禁忌证与不良反应

在儿童及青少年肥胖治疗中，胃内占容干预作为一种新兴的减重手段，在部分研究中已显示出一定的有效性，但在临床应用中仍需谨慎评估其禁忌症和潜在不良反应。这些禁忌症主要基于对儿童青少年胃肠道及整体

健康状况的评估。具体禁忌证包括但不限于:消化道系统疾病、既往胃肠道手术史、精神疾病、激素或遗传性肥胖、慢性使用类固醇或非甾体抗炎药等[26, 51]。然而,在严格筛选适应证的情况下,胃内占容干预也可能引发一些不良反应。目前在相关研究中,不良反应的发生率相对较低,多数受试者未报告明显不良事件。胃内球囊治疗后,常见的不良反应包括恶心、呕吐、腹痛、腹胀、消化不良、便秘、胃酸反流和嗳气,极少出现严重的不良事件,如胃穿孔、球囊移位、胃溃疡、出血、胃肠梗阻、吸入性肺炎等[25-26]。胃占容食品的不良反应相对较少,可能出现腹胀、腹泻、便秘等轻微症状,通常可自行消退[49]。目前的研究尚未观察到该胃内占容干预对儿童及青少年的社会心理健康、生长发育等产生有害影响[52-53]。

6　总结与展望

本文综述了儿童及青少年肥胖干预领域的生活方式调整、心理行为干预、药物疗法及代谢减重手术等治疗方案的优缺点,重点探讨了胃内占容技术的机制及其在儿童及青少年中的应用进展。作为新兴干预手段,胃占容食品因其良好的安全性和便捷的操作性展现出显著的临床优势。未来研究应着力于:(1)开展多中心、大样本的长期随访研究;(2)建立多维度的观测指标体系;(3)完善临床疗效评价系统。此外,需深入探究胃占容食品在体重调控及代谢改善中的作用机制,特别应关注其对肠道菌群结构重塑及微生物代谢产物调节的潜在影响,以期实现从肥胖病理状态向正常代谢状态的转化,从而为儿童及青少年肥胖群体开发更具循证依据、安全有效的干预策略。

*　　*　　*

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