·综述·

糖尿病性骨质疏松症患者疼痛管理的研究进展

祁佩瑶[1,2],沙薇薇[1,2],刘庭[3],李楠[1,2*]

(中国人民解放军总医院:[1]第二医学中心内分泌科,[2]国家老年疾病临床医学研究中心,[3]第二医学中心消化内科,北京 100853)

【摘 要】 糖尿病性骨质疏松症(DOP)是以骨量下降、骨微结构破坏及骨脆性增加为特征的糖尿病严重慢性并发症,显著增加骨折风险并损害骨折愈合能力,是导致患者残疾与生活质量下降的重要原因。DOP所致疼痛及其伴随的焦虑、抑郁等心理问题,易形成"疼痛-心理障碍-骨代谢恶化"的恶性循环,严重影响患者身心功能与社会适应。因此,有效缓解疼痛并促进心理社会适应是改善DOP患者整体预后的核心环节。本文系统综述DOP的流行病学特征、疼痛机制及多维度干预策略的研究进展,分析当前临床实践面临的挑战,以期为临床综合管理提供参考。

【关键词】 糖尿病;骨质疏松;疼痛管理

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Research progress in pain management for patients with diabetic osteoporosis

Qi Peiyao[1,2], Sha Weiwei[1,2], Liu Ting[3], Li Nan[1,2*]

([1]Department of Endocrinology, The Second Medical Center, [2]National Clinical Research Center for Geriatric Diseases, [2]Department of Gastroenterology, The Second Medical Center, Chinese PLA General Hospital, Beijing 100853, China)

【**Abstract**】 Diabetic osteoporosis (DOP) is a serious chronic diabetic complication characterized by reduced bone mass, impaired bone microstructure, and increased bone fragility. It significantly elevates fracture risk and compromises bone healing, constituting a major cause of disability and reduced quality of life. DOP-related pain, along with associated psychological issues such as anxiety and depression, tend to forms a vicious cycle of "pain-psychological impairment-worsened bone metabolism," severely affecting physical and mental functions as well as social adaptation. Thus, effective pain relieve and psychosocial support are essential for improving the overall prognosis in DOP patients. This review summarizes epidemiological features, pain mechanisms, and multidimensional interventions for DOP, discusses current clinical challenges, and provides a reference for comprehensive clinical management.

【**Key words**】 diabetes mellitus; osteoporosis; pain management

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Corresponding author: Li Nan, E-mail: wsln_may07@163.com

糖尿病性骨质疏松症(diabetic osteoporosis, DOP)是糖尿病(diabetes mellitus, DM)常见并发症,以骨代谢紊乱、骨微结构破坏及骨脆性增加为特征,显著升高骨折风险并影响骨折后愈合能力,是导致DM患者致死、致残的重要原因之一[1,2]。与健康人群相比,2型糖尿病(type 2 diabetes mellitus, T2DM)患者骨质疏松性骨折的发生率增加(30.6%和25.7%)[3]。DOP的发生发展与高糖环境、胰岛素抵抗、维生素D代谢异常等多种因素相关,其疼痛机制涉及神经病变与慢性炎症等[4]。持续的骨骼疼痛及功能障碍易引发心理社会适应问题,形成"疼痛-心理障碍-骨代谢恶化"的恶性循环[5,6]。本文旨在综述DOP的流行病学特征、疼痛机制及多维度管理策略的研究进展,以期为临床综合管理提供参考。

1 DOP的流行病学、病理生理机制

1.1 DOP流行病学

DOP作为DM的重要并发症,全球患病形势日益严峻。国际糖尿病联盟数据显示,2021年全球DM患者约5.37亿,预计2045年将突破7.83亿[7]。DOP发病率与DM病程显著相关,约50%~66%的

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通信作者:李楠,E-mail:wsln_may07@163.com

DM患者存在骨密度(body mass density, BMD)下降,其中约33%被诊断为DOP[8]。T2DM患者中超过35%出现骨质流失,约20%符合骨质疏松症(osteoporosis, OP)诊断标准[9]。随病程延长,T2DM患者骨折风险较非DM人群增加2.11倍,且骨折愈合受损更为显著[10,11]。DOP患者较原发性OP患者更易出现长期骨痛、运动功能障碍及更高骨折风险[12,13]。临床数据显示,89%的OP患者存在背部疼痛,其中45%为中重度疼痛,43%疼痛持续超过5年[6]。除糖尿病相关因素外,年龄、性别(女性风险高)及种族差异等也共同影响DOP发病风险[13]。

1.2 DOP及疼痛的病理生理机制

优化血糖控制和合理选择降糖方案是预防和管理DOP相关疼痛的基石,临床应将患者的血糖管理状况作为核心评估要素。

1.2.1 骨代谢异常 高血糖环境下,晚期糖基化终产物(advanced glycation end products, AGEs)积累与骨基质蛋白交联,增加骨脆性并抑制成骨细胞功能及骨矿化[12]。同时,高血糖会抑制胰岛素样生长因子与骨钙素合成,进一步降低骨矿物质含量[14]。部分降糖药物(如磺脲类、胰岛素)可能增加跌倒及骨折风险,而胰高糖素样肽-1类似物等则具骨骼保护潜力。上述因素共同导致骨强度下降、微骨折风险增高,并引发慢性疼痛及骨折愈合延迟[15]。

1.2.2 炎症、氧化应激与神经病变 DM患者常伴有慢性炎症状态,肿瘤坏死因子-α、白细胞介素-6等炎症因子被大量激活,可促进破骨细胞分化与骨吸收,并抑制成骨细胞功能,破坏骨重建平衡,成为DOP疼痛的重要机制[12,16]。高血糖诱发氧化应激、促进AGEs形成,在局部炎症共同作用下,进一步改变骨胶原结构,引起骨骼蛋白交联、力学性能下降,加剧骨质疏松与疼痛[12]。

糖尿病性神经病变(diabetic peripheral neuropathy, DPN)是导致DOP患者疼痛的重要因素。长期高血糖可损伤神经细胞,导致疼痛阈值下降及神经传导障碍;自主神经病变影响骨血供,而外周感觉神经中瞬时受体电位香草酸亚型1通道的激活可增强伤害感受器灵敏性。这些改变共同促成持续性、弥漫性骨痛,增加诊疗难度[17,18]。

1.2.3 疼痛与抑郁的相互作用 疼痛与抑郁在DOP中常形成"疼痛-功能丧失-心理障碍-疼痛加重"的恶性循环。长期疼痛及活动受限易引发社会隔离与抑郁;抑郁状态亦为骨质疏松的危险因素,并可通过降低痛阈加重疼痛感受[6]。髋部或椎体骨折等事件不仅导致急慢性疼痛,亦严重影响心理与社会功能,而部分降糖药物所致低血糖与跌倒风险进一步强化了上述循环[12]。

2 DOP疼痛管理的药物方法

2.1 骨代谢调节药物

此类药物主要通过抑制骨吸收或促进骨形成来缓解疼痛。双膦酸盐类药物(如阿仑膦酸钠、伊班膦酸钠)能有效抑制破骨细胞活性,并通过抗炎等机制发挥镇痛作用,可显著降低骨痛并改善功能[18,19]。地舒单抗作为RANKL抑制剂,在提升骨密度、降低骨折风险的同时,也能缓解相关疼痛,但其在DOP中的长期疗效与安全性尚需更多证据[20]。降钙素则通过抑制骨吸收及中枢镇痛作用短期缓解疼痛,可作为双膦酸盐的替代选择,但长期疗效有限[18]。对于严重患者,促骨形成剂如特立帕肽能有效增加骨密度并减轻背痛,但其成本与潜在不良反应限制了广泛应用。研究证实长期使用特立帕肽不仅能增加BMD,还能减轻与椎体骨折相关的背痛,其改善效果需持续12个月,且新发背部疼痛率低于传统药物[21]。

2.2 传统与新型镇痛药

传统镇痛药是DOP疼痛管理的重要辅助。对乙酰氨基酚与非甾体抗炎药常用于控制急性疼痛,但对慢性神经病理性疼痛效果不佳,且需关注其副作用。阿片类药物虽能控制中重度急慢性骨痛,但应遵循"最低有效剂量、最短疗程"原则以平衡风险[18]。研究也聚焦于新型靶点,如调节Akt-GSK3β-NFATc1信号通路或使用罗莫珠单抗等药物,旨在同时改善骨质量与缓解疼痛,代表了多靶点治疗的新方向[22]。

3 非药物管理策略

3.1 运动与物理康复

运动干预是改善骨密度、整体功能及疼痛的核心策略,其标准方案涵盖姿势纠正、肌力与平衡训练等要素,旨在预防跌倒、缓解疼痛并增强心理健康[17]。多系统整合性训练(如结合平衡与力量练习)在镇痛方面优于传统单一运动,机制涉及改善神经肌肉控制与促进内源性镇痛[23]。瑜伽、太极等身心运动也被证实有助于缓解疼痛、改善骨密度,但需个体化渐进实施[24]。

物理治疗是缓解DOP疼痛的常用手段。按摩与冷(热)疗可用于缓解肌肉骨骼疼痛;低频脉冲电磁场具有明确的镇痛效果;振动训练则通过增强肌力与平衡来降低跌倒风险;高强度激光与体外冲击

波等新型疗法在快速镇痛与促进组织修复方面展现出优势[25,26]。

3.2 营养、心理与综合支持

充足的钙与维生素 D 是骨骼健康的基石,维生素 D 的抗炎作用对缓解骨痛尤为重要[27]。推荐富含抗氧化剂与 ω-3 脂肪酸的地中海饮食模式,以拮抗氧化应激与慢性炎症对骨骼的不利影响[12]。心理干预针对疼痛伴发的情绪问题。认知行为疗法能够帮助患者重构疼痛认知、学习应对技巧,以打破“疼痛-情绪-行为”的恶性循环;基于正念的干预疗法则能够引导患者解构持续性疼痛体验,帮助其建立积极的应对策略[17,28]。构建完善的社会支持体系同样关键,包括家庭的理解与陪伴、社区的患者组织与资源链接,以及远程监测技术的应用,共同为患者提供心理支持与疾病管理便利。

3.3 中医与器械/手术干预

中医治疗 DOP 具有多途径、多靶点的特点,且不良反应小、患者依从性高。治疗以“健脾益肾、活血化瘀”为原则,通过健脾益气活血汤等方剂及针灸、推拿等外治法,在缓解疼痛、改善骨代谢及血糖控制方面体现了多靶点治疗特色[29]。

对于器质性病变,微创手术如经皮椎体成形术能通过稳定椎体快速缓解顽固性椎体骨折疼痛;而矫形器、支撑鞋等器械则为局部微骨折或骨痛提供了非侵入性的机械减负与保护[30,31]。这些方法共同构成了多学科管理的重要组成部分。

综上,当前 DOP 的疼痛管理在临床评估、个体化治疗及多学科协作方面仍面临严峻挑战。鉴于其复杂的病理机制,未来的管理策略需深度融合药物治疗、物理康复、心理支持与先进技术,构建整合性的干预框架。研究应优先探索精准的生物标志物,验证新型治疗靶点,并推动数字健康技术在长期随访和个性化管理中的应用。通过建立以患者为中心的全周期管理模式,有望显著缓解疼痛,改善功能状态,最终提升 DOP 患者的整体生活质量。

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