

胃食管反流病药物治疗进展

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Advances in drug therapy for gastroesophageal reflux disease

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Abstract

The incidence of gastroesophageal reflux disease (GERD) is increasing drastically in China. GERD could probably cause reflux esophagitis, chronic cough, asthma, Barrett's esophagus and adenocarcinoma, and frequently affects health-related quality of life. The use of proton pump inhibitors (PPIs) provides effective symptomatic relief in most patients; however, some patients appear refractory to the treatment with PPIs. The long term use of PPIs might also cause adverse effects, such as interstitial nephritis, fracture and small intestinal bacterial overgrowth. Many new drugs for GERD have emerged recently. This article reviews the advances in drug therapy for GERD.

Key Words: Gastroesophageal reflux disease; Drug; Therapy

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摘要

我国胃食管反流病(GERD)发病率逐年升高。GERD可能引起反流性食管炎、慢性咳嗽、哮喘、Barrett's食管和食管腺癌等并发症,并且严重影响人们的生活质量。质子泵抑制剂(PPIs)的应用,使多数患者症状得到了缓解。但近年来发现PPIs对部分GERD患者无效,且长期使用会出现间质性肾炎、骨折和小肠细菌增生过多等并发症。近年来,一些新型药物逐渐应用于临床。本文就GERD药物治疗进展作一综述。

关键词: 胃食管反流病; 药物; 治疗

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0 引言

胃食管反流病(gastroesophageal reflux disease, GERD)是指胃内容物反流引起不适症状和(或)并发症的一种疾病^[1],除引起糜烂性食管炎、Barrett's食管和食管腺癌外,还可引起慢性咳嗽、慢性喉炎、支气管哮喘、牙侵蚀症等食管外表现,严重影响患者的日常工作及生活质量。随着生活方式、饮食结构的改变,我国GERD发病率呈逐年上升的趋势。因此,持续有效的控制GERD症状,减少并发症及提高患者生活质量非常必要。随着对GERD病理生理机制研究的深入,近几年出现了许多新型的治疗GERD药物。本文就GERD药物治疗进展作一综述。

1 抑酸剂

抑酸剂类药物通过抑制胃酸分泌,降低反流物酸度及胃蛋白酶活性,缓解症状,促进食管黏膜愈合。目前主要包括质子泵抑制剂(proton pump inhibitor, PPI)和H₂受体拮抗剂(H₂-receptor antagonist, H₂RA)两类。

1.1 PPI PPI具有不可逆性抑制H⁺-K⁺-ATP泵的作用,是目前治疗GERD的主要药物。传统的PPI包括奥美拉唑、泮托拉唑、兰索拉唑和雷贝拉唑。

■背景资料

随着生活方式的改变,我国GERD发病率逐年升高,已经严重影响了人们的生活质量。虽然PPI是GERD治疗的首选药物,但对部分患者无效,且长期使用会出现不良反应。临床研究也证实,促动力药及黏膜保护剂对GERD疗效有限。许多针对GERD其他病理生理机制的新型药物开始涌现。

■同行评议者

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抗反流药可减少TLESR,从而同时减少酸性和非酸反流。 γ -氨基丁酸 β (GABA β)受体激动剂和亲代谢谷氨酸盐受体5(mGluR5)拮抗剂成为抗反流药物的研究热点。

近几年出现的新型PPI制剂包括替那拉唑和艾普拉唑。替那拉唑是异咪唑吡啶衍生物的一种新型PPI制剂,可将血浆半衰期延长至9.3 h,是传统PPI的5-7倍^[2]。这使替那拉唑有长时间的抑酸能力,尤其是抑制夜间胃酸分泌效果较好,并基本不受进食及给药时间的影响^[3]。艾普拉唑为苯并咪唑类衍生物,具有不可逆抑制 H^+-K^+-ATP 酶,半衰期可达3.6 h,抑酸效果是奥美拉唑的2-3倍。研究表明,对GERD的疗效艾普拉唑10 mg/d优于奥美拉唑20 mg/d^[4]。

埃索美拉唑是奥美拉唑的S型异构体,具有比奥美拉唑更低的首过消除效应及更高的生物利用度。有系统综述表明,埃索美拉唑40 mg对食管炎的愈合率,优于兰索拉唑30 mg、奥美拉唑20 mg、泮托拉唑40 mg及雷贝拉唑20 mg^[5]。之后研发了泮托拉唑S型异构体。S-泮托拉唑(20 mg)在烧心、反酸、腹胀症状缓解上均优于外消旋泮托拉唑(40 mg),在食管炎和胃糜烂愈合率上两者疗效相当,并且两者的安全性及耐受性都很好^[6]。最近,右旋兰索拉唑(兰索拉唑的R型异构体)得到了美国食品药品监督管理局(FDA)的批准上市。右旋兰索拉唑缓释胶囊的药物成分可以分两次释放,从而达到延长抑制胃酸的时间,且服药时间不受进食影响^[7]。Sharma等^[8]比较了右旋兰索拉唑缓释胶囊与兰索拉唑对反流性食管炎(reflux esophagitis, RE)愈合的疗效。右旋兰索拉唑缓释胶囊治疗8 wk后可使92%-95%的RE愈合。与传统兰索拉唑相比,虽然两者无明显差异,但对于中重度RE,前者的疗效明显优于后者。与安慰剂相比,右旋兰索拉唑缓释胶囊30 mg/d或60 mg/d均能使非糜烂性反流病(nonerosive reflux disease, NERD)患者白天及夜间的烧心症状明显缓解,并且耐受性较好^[9]。S-替那拉唑钠是替那拉唑的左旋异构体,目前正在临床试验阶段。研究表明其抑酸作用能持续24 h或更长时间,夜间pH>4的时间是埃索美拉唑的1.5倍^[10]。

钾竞争性酸受体阻滞剂(potassium-competitive acid blockers, P-CABs)是一种有别于PPI的新型抑酸剂。该类物质通过和 K^+ 竞争性地与质子泵结合,从而抑制 H^+-K^+-ATP 酶活性,达到抑酸作用。该类物质起效迅速,抑酸持久,在酸性环境下稳定。与PPI只能抑制激活状态的质子泵相比,该药对静止状态质子泵亦有抑制作用。但有研究显示,不同剂量的AZD0865与埃索美拉唑相比,RE的治愈率与烧心症状缓解率无明显差异^[11]。另一项研究也发现,尽管AZD0865

维持pH>4的时间长于埃索美拉唑,但两者对NERD患者烧心症状的缓解无明显差异^[12]。因此,P-CABs的临床疗效有待进一步评估。

有调查显示,约30%-50%的GERD患者服用标准剂量的PPI仍有症状,被称为难治性GERD(或PPI抵抗性GERD),这可能与药物快速代谢、内脏感觉高敏、胃排空延迟、精神心理异常及非酸反流等因素有关^[13]。Bajbouj等^[14]发现,给予埃索美拉唑40 mg/d治疗无效的难治性GERD患者,80 mg/d能显著减少液体及混合反流。Becker等^[15]也发现,对服用标准剂量PPI无效的病理性GERD患者,增加PPI剂量可使90%以上的患者达到症状缓解。因此,对难治性GERD可尝试增加PPI剂量以达到患者症状缓解^[16]。而换用其他类型PPI则是难治性GERD的另一种治疗方法。一项对服用兰索拉唑30 mg/d无效的GERD患者采用埃索美拉唑40 mg/d治疗的研究显示,标准剂量埃索美拉唑能有效改善烧心症状,且疗效近似双倍剂量兰索拉唑^[17]。

目前对PPI治疗GERD食管外表现的疗效存在争议。不少学者经验性认为,合并有食管外症状的GERD患者需给予双倍剂量PPI持续2-3 mo,如果症状未完全缓解,则继续治疗至6 mo;如果PPI疗效仍然不佳,则需完善检查明确GERD诊断,或加用其他药物和行抗反流手术^[18]。一项大剂量埃索美拉唑与安慰剂8 wk随机对照试验表明,对合并慢性咳嗽而罕有烧心的GERD患者,强效抑酸治疗并不能提高其生活质量及缓解症状^[19]。另一项对哮喘控制不佳的无症状GERD患者,经大剂量抑酸治疗,也未见明显效果^[20]。因此,目前PPI对GERD食管外症状的最佳疗程及剂量仍不明确,PPI疗效的预测因素也需在未来研究中进一步探讨。

虽然PPI是GERD主要的治疗药物,但停药后常导致患者症状复发。长期维持治疗也给患者带来巨大的经济负担和一定的不良反应,其中最常见的是轻至中度的头痛、腹痛、呕吐、腹泻等。长期使用PPI的不良反应也引起了人们的重视。Chiu等^[21]的大样本病例对照研究结果显示髌骨骨折发生风险与PPI剂量呈正相关。Corley等^[22]认为抑酸剂导致髌骨骨折发生风险增加,但只发生在有额外危险因素情况下,如使用非甾体类消炎药。其可能机制是PPI抑制胃酸分泌,从而影响肠道钙吸收,长期使用可导致整个机体钙平衡,故易发生骨折^[23]。当胃内酸度下降后,致病菌会在上消化道繁殖,上段小肠细菌也

会过度繁殖,并可导致肠道菌群失调。Lombardo等^[24]对服用36 mo PPI的200例GERD患者、至少3年内未服用PPI的200例肠易激综合征患者及至少10年内未服用PPI的50名健康对照者进行的对比研究显示,50%服用PPI的患者小肠细菌过度生长,显著多于肠易激综合征患者(24.5%)和健康对照者(6%)。Compare等^[25]对42例服用6 mo PPI的NERD患者调查研究发现,长期服用PPI会引起腹胀、腹痛、腹泻等肠道症状,并导致小肠细菌过度生长。艰难芽孢梭菌感染,则是PPI致肠道菌群失调的突出表现。一项大型药物流行病学队列研究显示,院内艰难芽孢梭菌相关性腹泻的发病率和抑酸剂明显相关(未服用抑酸剂-0.3%,服用H₂RA-0.6%,每天服用1次PPI-0.9%,每天多次服用PPI-1.4%^[26])。对艰难芽孢梭菌感染患者,出院90 d内服用PPI,其复发风险会增加42%^[27]。不少心血管患者常使用PPI预防抗凝药可能导致的胃肠道出血。Pezalla等^[28]却发现,高度依赖PPI的患者其急性心肌梗死的发生风险是未使用PPI患者的300%。Juurlink等^[29]也发现,急性心肌梗死患者在服用氯吡格雷的同时,合并使用除泮托拉唑以外的PPI时,会降低氯吡格雷的疗效及增加再发心梗的风险。

1.2 H₂RA H₂RA通过抑制壁细胞H₂受体,达到减少胃酸分泌。该类药易受饮食影响,抑酸持续时间短,且患者容易快速耐受,因此常用于轻中度GERD患者。

虽然多数研究认为PPI对GERD疗效优于H₂RA,尤其是对于RE的黏膜愈合。但Fujiwara等^[30]发现,奥美拉唑对控制*H. pylori*阴性的NERD患者症状优于法莫替丁,而对*H. pylori*阳性的NERD患者则疗效相似。还有研究显示,罗沙替丁75 mg bid与奥美拉唑20 mg/d,经8 wk治疗后对NERD患者疗效相当,因而对于NERD患者,罗沙替丁也是一种不错的选择^[31]。

夜间酸突破(nocturnal acid breakthrough, NAB)是指夜间胃内pH<4的时间持续超过1 h,发生在午夜及凌晨6点之间。一项双倍剂量的PPI和睡前联合与不联合单剂量H₂RA对比研究显示,在服用双倍剂量的PPI情况下,64%的患者有NAB现象,在睡前联合H₂RA后,只有17%的患者存在NAB现象,H₂RA被认为是加强抑酸的辅助疗法,能有效控制NAB现象^[32]。但也有学者认为,长期使用H₂RA会使部分患者产生耐药,半衰期较长的新型PPI也许能有效控制NAB^[33]。

2 促动力药物

促动力药能增加食管下括约肌(lower esophageal sphincter, LES)压力、促进胃排空、刺激食管蠕动及增强食管收缩幅度。单独使用该类药物只对轻GERD有效。因该类物质有一定不良反应,限制了其临床上的应用。

莫沙必利为新型5-HT₄受体激动剂,直接作用于肠肌间神经丛,促进乙酰胆碱释放,增强胃及十二指肠运动,生物利用度高,不良反应少。Cho等^[34]对健康对照者服用莫沙必利,发现其有助于食管内容物通过,并能改善无效食管蠕动,因而推断其能促进食管酸廓清。Ruth等^[35]对GERD患者研究发现,莫沙必利对食管肌肉收缩总数及推进能力无明显作用,但能增加单次食管肌肉收缩的时程及波幅,食管pH<4的时间百分比也显著降低。Koshino等^[36]分别纳入9例及13例健康对照者进行交叉对照试验,发现莫沙必利15 mg/d并不能刺激唾液分泌及增强食管运动功能,也不能阻止餐后酸及非酸反流,有待更大样本及剂量的研究。

替加色罗是一种5-HT₄受体部分激动剂,主要应用于便秘型肠易激综合征及慢性便秘患者。研究发现其能促进胃排空,改善胃容受性,缓解饱胀不适症状,并能增加疼痛阈值及改变食管机械扩张敏感性^[37,38]。目前替加色罗对GERD研究报道较少,在部分研究中表现出一定的疗效。替加色罗1 mg/d及4 mg/d可降低餐后反流、pH<4的时间百分比和一过性下食管括约肌松弛(transient lower esophageal sphincter relaxation, TLESR),但对LES压力无影响^[39]。美国大样本调查研究发现替加色罗会增加心血管事件风险而被FDA限制使用。Al-Judaibi等^[40]对67例中51例服用替加色罗的肠易激综合征或慢性便秘的患者研究发现,37例患者无不良反应事件、14例患者至少有一个不良反应事件(6例患者有严重不良反应事件,包括4例晕厥,其中2例合并不典型胸痛,2例死亡,但并不是替加色罗直接导致)。因此认为替加色罗可用于无心血管事件风险的患者。

伊托必利是一种新型的促动力药,具有阻断多巴胺-D₂受体及抑制乙酰胆碱酯酶活性的双重作用。其能抑制TLESR,但对食管蠕动及LES压力无明显影响^[41]。Kim等^[42]对GERD患者随机给予伊托必利150 mg/d或300 mg/d,结果显示两组患者症状评分均显著下降,且大剂量组对降低食管pH<4时间百分比、pH<4总时间及

■相关报道

有相关研究报道,对难治性GERD患者行24 h食管阻抗-pH监测,发现7%-28%为酸反流,30%-40%为弱酸反流,而30%-60%的症状与反流无关。

■创新盘点

本文就新型PPI制剂、抗反流药、抗氧化剂、褪黑素等新近出现的GERD治疗药物作一综述,并对不同种类药物的优缺点作介绍。

DeMeester评分均优于小剂量组,所有患者均未出现严重不良反应。

新近研究发现,静脉注射阿奇霉素可通过激活胃动素受体,促进胃排空,减少胃食管反流次数及食管酸暴露时间^[43]。但长期使用会导致受体敏感性下降,疗效降低。恶心和胃肠痉挛的不良反应也常导致患者无法耐受。必须静脉使用也限制了其在临床上的广泛应用^[44]。因此,可口服的高选择性胃动素受体激动剂有待进一步研发。

目前对GERD抑酸治疗效果不佳时,加用动力药是否能提高疗效还存在不少争论。Madan等^[45]发现泮托拉唑单独使用和联合莫沙比利的疗效在NERD患者中无明显差异,但在RE患者中联合莫沙必利组的疗效较好。Hsu等^[46]发现除重度反流患者,与安慰剂相比,标准剂量的兰索拉唑联合莫沙必利,并不能提高RE患者的疗效。Futagami等^[47]对PPI抵抗并有胃排空延迟的NERD患者给予奥美拉唑联合莫沙必利治疗12 wk,研究显示两者联合使用可显著改善反流症状及促进胃排空。故目前有学者认为,PPI抵抗联合莫沙比利,只对重度反流患者有效。

3 抗反流药

虽然PPI能通过抑制胃酸分泌,减少胃食管酸反流,但却不能减少非酸反流。非酸反流在GERD发病机制中的作用已得到确认。GERD的终极治疗目标应能同时抑制胃食管酸反流和非酸反流。TLESR异常是GERD主要发病机制之一。研究显示,健康人中只有小部分的生理性胃食管反流在TLESR时发生,而GERD患者中高达90%的反流和TLESR有关^[48]。抗反流药可减少TLESR,从而同时减少酸性和非酸反流。 γ -氨基丁酸 β (GABA β)受体激动剂和亲代谢谷氨酸盐受体5(mGluR5)拮抗剂成为抗反流药物的研究热点。

3.1 GABA β 受体激动剂 巴氯芬是第一种认为有潜在治疗价值的GABA β 受体激动剂,可降低40%-60%的TLESR,增加LES基础压力,并减少反流次数。GERD患者服用4 wk巴氯芬后能显著缓解症状及减少食管酸暴露时间^[49]。与PPI相比,巴氯芬最大优势在于其不仅可减少酸反流,也可以减少非酸反流。Vela等^[50]发现巴氯芬40 mg能同时减少餐后酸及非酸反流次数,以及缓解反流相关症状。Koek等^[51]也发现,给予GERD患者巴氯芬5 mg tid,也能减少十二指肠胃食管反流,缓解难治性GERD的症状。

尽管诸多研究证实巴氯芬对GERD有一定

疗效,但患者症状缓解程度有限,只能和抑酸剂联合应用治疗难治性GERD。且该药半衰期较短(3-4 h),需多次服用,降低了患者的服药依从性。且血药浓度达峰时易导致头晕、嗜睡、乏力及肌肉震颤等中枢神经系统不良反应,因此未被广泛应用。Arbaclofen placarbil(AP, XP19986)是R-巴氯芬的前体,动物实验证实其比R-巴氯芬更容易吸收、分布、代谢、排泄。由于其释放缓慢,血药浓度没有明显的峰值,因此,中枢神经系统不良反应明显减少^[52]。一项50例GERD患者药物试验显示,AP耐受性较好,能减少反流事件及缓解反流相关症状,但临床疗效仍然有限^[53]。近年来,作用于周围神经系统的外周性GABA β 受体激动剂已在研发当中。该药由于中枢神经系统不良反应少而患者的耐受性较好。Lesogaberan(AZD3355)就是一种竞争性、选择性外周性GABA β 受体激动剂,与巴氯芬有相似的药物作用机制,但其作用于周围神经系统,中枢神经不良反应较少。研究显示,Lesogaberan使TLESR发生次数减少36%,酸反流次数也有所减少,并增加LES压力,不良反应更少,但症状缓解程度有限^[54]。能否加大剂量提高其疗效有待进一步研究。

3.2 mGluR5拮抗剂 谷氨酸能把肠道内的感觉信息传递到中枢神经系统,其中就包括触发TLESR的迷走神经信号。谷氨酸与代谢型谷氨酸受体(mGluRs)结合,而后者与GABA β 受体结构有关。动物研究证实,选择性mGluR5拮抗剂能有效抑制TLESR及反流事件^[55,56]。还有研究显示,mGluR5拮抗剂能降低结直肠痛觉敏感性^[57],而内脏痛觉过敏在功能性烧心及PPI抵抗性GERD中发挥了一定作用^[58],说明其对GERD,尤其是PPI抵抗性GERD有一定疗效。ADX10059是mGluR5的变构调节剂。有一项研究纳入了23例GERD患者,随机分成50 mg tid和250 mg tid。结果显示,服用1 d后,250 mg组能明显减少食管酸暴露时间、症状性反流的次数及持续时间,以及明显改善患者症状,但50 mg组的疗效和安慰剂相似^[59]。但该研究样本量小,服药时间短,而且是单盲设计。一项大样本随机对照试验($n = 103$)发现,和安慰剂相比,ADX10059 120 mg bid服用2 wk后能明显缓解患者烧心反流症状,减少总反流和酸反流次数。只有少部分患者出现头晕(16%)和眩晕(12%)的不良反应^[60]。另一项研究纳入8例男性健康对照者,发现ADX10059缓释剂能减少总反流次数及餐后弱

酸反流次数,且125 mg bid和250 mg bid的疗效相似^[61]。但该药由于其肝脏毒性限制了其长期应用。

3.3 其他抗反流药 动物研究显示,大麻素受体激动剂WIN55212-2可以减少80%的TLESR,从而减少胃食管反流^[62]。胆囊收缩素A(CCK-A)受体激活后会增加TLESR, CCK-A受体拮抗剂氯谷胺能减少GERD患者TLESR,减低进餐后LES压力下降的程度,从而减少反流,但临床疗效仍然有限^[63]。另一项研究发现静脉使用阿片受体激动剂吗啡能减少50%的TLESR,从而减少反流次数,但对健康对照者影响较小^[64]。但由于其成瘾性及便秘的不良反应,目前无法在临床上推广应用。还有动物实验证明, NO合成酶抑制剂可以减少75%TLESR,但只能减少25%进餐相关的TLESR。但由于尚无口服制剂,且对心脏、膀胱和呼吸道的动力有所影响而不能应用于临床。高选择性的NO合成酶抑制剂有待进一步研发^[65-67]。

虽然抗反流药可能是未来治疗PPI抵抗性GERD很有前景的药物,但目前其临床疗效有限,多将其和PPI联合应用,且有一定的不良反应。强效、安全、高选择性的抗反流药有待进一步研发。

4 内脏痛觉调节剂

到目前为止,内脏痛觉调节剂对难治性GERD的疗效评价研究仍较少。鉴于大部分PPI治疗无效的患者主要来自NERD患者,40%左右PPI治疗失败的患者既缺乏酸反流,又缺乏弱酸反流^[15,68]。研究表明三环抗抑郁药、曲唑酮、选择性5-羟色胺再摄取抑制药(SSRIs)等能缓解非心源性胸痛患者症状,并有可能改善PPI治疗无效患者的症状^[69-71]。有学者认为,该类物质作用于中枢神经系统或感觉传导通路,从而缓解痛觉。目前还没有食管特异性的痛觉调节剂,现有的药物由于选择性不高,有一定的不良反应,最好从小剂量开始使用。

5 抗酸剂

临床常用的抗酸剂主要包括氢氧化铝凝胶、铝碳酸镁、铝碳酸钙等。该类物质通过中和胃酸能迅速缓解症状,但持续时间短,不能充分治愈食管炎及预防GERD并发症。某些抗酸剂由于含铝盐或镁盐,会导致腹泻或便秘等不良反应。即将在国内上市的海藻酸盐制剂是一种抗酸剂和海藻酸的复合物,其在胃酸作用下产生一种黏性凝胶的抗反流屏障,且其中的抗酸剂又能短

暂中和胃酸。海藻酸盐不仅能清除反流的胃蛋白酶及胆汁酸,还能显著降低胃蛋白酶活性,这两种作用能明显减轻反流物对食管黏膜的损伤^[72]。通过阻抗-pH监测还发现,海藻酸盐能显著减少酸反流事件、pH<4时间百分比及近端反流事件,但对非酸反流无效^[73]。海藻酸盐与氢氧化镁铝疗效的对比研究显示,海藻酸盐起效更快,持续时间更长,症状缓解程度更明显,没有明显的不良反应^[74]。而且该药疗效和其剂型无关,片剂和水剂疗效相似^[75]。因而,海藻酸盐能有效缓解典型GERD症状。

6 其他

食管黏膜下腺体可分泌碳酸氢盐、粘蛋白、表皮生长因子、前列腺素E₂、转化生长因子 α 等物质保护食管黏膜^[76],因而加强黏膜防御因子的合成,并覆盖在病变表面形成保护膜,可有效抵抗胃内反流物对食管黏膜的损害。替加色罗能促进十二指肠碳酸氢盐的分泌,在受胃酸侵蚀的猪食管模型中也发现其可促进食管黏膜下腺体分泌碳酸氢盐,但在兔的食管模型中未发现^[77]。传统的黏膜保护剂如替普瑞酮、麦滋林-S、吉法酯等,因其疗效不佳已不常使用。食管上皮细胞在胆汁酸的刺激下,会增加细胞内活性氧簇,而导致食管黏膜的损害。动物实验显示,抗氧化剂如N-乙酰半胱氨酸和C族维生素能阻止胆汁酸对食管黏膜的损害,缩小扩大的食管黏膜细胞间隙,降低食管黏膜通透性^[78]。褪黑素最近也被发现对GERD患者有一定疗效。有研究显示,和健康对照者相比,GERD患者体内褪黑素明显下降。褪黑素治疗后GERD患者LES压力有所上升,LES松弛率和松弛时间百分比有所下降,胃酸分泌和食管酸暴露时间有所下降。与单用奥美拉唑相比,联合使用褪黑素虽能稍提高LES压力及减少松弛率,但食管酸暴露时间并没有减少。因此褪黑素对GERD疗效有待进一步评估^[79]。

7 结论

目前临床上治疗GERD的主要药物仍然是PPI。随着PPI异构体、缓释剂和新型抑酸剂的出现,其抑酸疗效将会更快、更强、持续时间更持久。但目前临床上仍有不少PPI抵抗性GERD患者,其症状不一定与酸相关。长期服用PPI也发现有一定不良反应。新型的抗反流药虽是最近研究的热点,但多数是短期、小样本的临床研究,且也有明显的不良反应。其他新型治疗GERD的药

■应用要点

抑酸剂与其他种类药物的联合应用,及合理选择药物,将促进GERD症状缓解,提高生活质量。

同行评价

本文内容详实, 有助于读者对胃食管反流病药物治疗有较全面的了解。

物, 如褪黑素、抗氧化剂等, 仍然处在动物实验阶段或者疗效不尽如人意。未来GERD的治疗方案将会按照患者不同的病理生理机制给予不同种类的药物, 而不是单一的抑酸治疗。相信随着对GERD发病机制的研究深入, 更安全有效的新型药物将不断出现, 为GERD治疗带来新的曙光。

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