

肛裂治疗方式的选择

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Choice of treatments for anal fissure

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Abstract

Chronic anal fissure (CAF) is one of the most common and painful proctologic diseases. Its treatment has long been discussed and several different therapeutic options have been proposed. The understanding of its pathophysiology has led to a progressive reduction of invasive and potentially invalidating treatments in favor of conservative treatment. Lateral internal sphincterotomy (LIS) is a surgical treatment that is considered the 'gold standard' therapy for CAF. It relieves CAF symptoms with a high rate of healing. The risk of incontinence after this procedure seems to be severe. Chemical sphincterotomy (CS) is safe, with the rapid relief of pain, no risk of surgery or anesthesia, but is a statistically less effective therapy for CAF than LIS. In recent years, fissurectomy coupled with CS has been demonstrated to be a satisfactory

treatment for chronic anal fissure and an alternative to lateral sphincterotomy when conservative measures fail.

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Key Words: Anal fissure; Treatment; Anal fissurectomy

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摘要

慢性肛裂是一种常见的肛门直肠疾病, 可以引起令人不快的疼痛。对于肛裂的治疗, 人们经过长期的研究, 建立了许多治疗肛裂的方法。随着对肛裂病理生理的研究不断深入, 手术治疗在逐渐减少, 而更倾向于应用药物保守治疗。内括约肌侧切术(lateral internal sphincterotomy, LIS)被认为是治疗肛裂的“金标准”, 但是术后可能导致肛门失禁; 化学性内括约肌切开(chemical sphincterotomy, CS)可以较快的缓解疼痛, 没有手术和麻醉的危险, 但是有效率不及LIS。近年来肛裂切除术联合术后CS作为一种新的治疗方式正在逐渐被人们所接受, 若药物治疗失败后, 其可以作为LIS的一种代替治疗方法。

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关键词: 肛裂; 治疗方式; 肛裂切除术

核心提示: 肛裂切除术联合术后化学性内括约肌切开, 可以作为药物治疗肛裂失败后的首选治疗方式, 能够提高治愈率, 并且能够避免肛门失禁的危险。其可以作为肛门内括约肌侧切术的一种代替治疗方法。

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■背景资料

随着人们对生活质量要求的提高, 对肛裂的治疗也从单一的治愈变成治愈的同时能够最大程度的减少痛苦、缩短病程并减少术后并发症, 这就要求肛肠外科医生需要在众多的治疗肛裂的方法中选择最佳的方式。

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■ 研发前沿

为了更好的预防和治疗肛裂, 人们在不断探寻肛裂的病因及病理生理, 而在治疗肛裂时越来越重视肛管内括约肌的保护, 故在提高治愈率的同时避免肛管内括约肌的损伤成为今后研究的重点和热点。

0 引言

肛裂的发病机制未明, 现在较为公认的肛裂的本质是缺血性溃疡, 可以概括为缺血-痉挛-缺血, 这一恶性循环。而对于肛裂的治疗一般采取的方式是括约肌切开, 包括化学性内括约肌切开(chemical sphincterotomy, CS)和手术括约肌切开。但是从远期疗效来看, CS治愈率低, 复发率高, 而行手术括约肌切开术则可能导致严重的并发症, 如肛门失禁等。所以如何在手术治疗慢性肛裂的同时最大程度地保留肛管内括约肌的功能就成为重要的课题。本文对肛裂产生的原因、病理生理及治疗方式的选择进行阐述。

1 肛裂

肛裂, 指肛管皮肤全层纵行裂开而形成的溃疡, 可见于各个年龄阶段, 其发生率无性别差异^[1], 如果肛裂6 wk未愈, 就被认为是慢性肛裂, 但是根据时间来判断肛裂的分期是不确切的^[2], 根据形态学来判断可能会更加合理, 如: 创缘增厚、溃疡较深、创缘底部内括约肌的暴露、肛乳头肥大、赘皮外痔, 这些都是由于慢性的感染及纤维结缔组织的增生引起的^[1-3]。

1.1 肛裂的病因 肛裂的病因目前仍不清楚, 比较多的从解剖学上进行了不懈的探索, 并提出了许多学说: Ball肛瓣学说、Miles栉膜带学说、Rankin肛窦学说、Blaisdell栅门学说、Arnous上皮学说、Shafik残留上皮学说、Eisenhammer内括约肌学说等。损伤学说认为: 干燥的粪便引起的创伤和内括约肌的痉挛是导致肛裂的最初原因。但在肛裂患者中, 仅有25%的患者存在便秘的情况^[4], 而6%的患者存在腹泻的情况^[3,4]。

山地车运动员由于长时间在车座上的颠簸, 导致肛管的裂口, 可引起慢性感染并形成肛裂^[5]; 有证据表明应用坐便器的喷水装置可引起前部肛裂^[6]; 3%-11%的肛裂的产生与分娩有关, 而且这种肛裂更易发生在肛门的前部^[7]。性虐待也和肛裂有一定的关系^[8]。应用尼可地尔(ATP敏感的钾离子通道开放剂)可能会增加患肛裂的风险^[9,10]。饮食情况会引起症状的改变, 如进食辛辣食物, 会加重肛裂患者的症状^[11]。调查显示饮食习惯、排便习惯及工作性质都会对肛裂的产生有一定的影响。

由于肛裂发生的部位特殊, 人们在肛裂产生时并没有在第一时间就诊。一项研究表明, 约40%的肛裂患者可以坚持数月甚至数年, 所以大部分患者来就诊时就已经发展到慢性肛裂。

1.2 肛裂产生的部位 肛裂最常见的部位是肛管后正中线, 仅有10%的女性及1%的男性发生前位肛裂^[3,4,12]。肛裂的位置有时发生在肛门侧方, 产生的原因可能是: 炎性肠病、肛门部手术、性病、皮肤病、感染或者肿瘤。

1.3 肛裂的病理生理 肛裂与肛管内括约肌的痉挛有关, 但是痉挛产生的机制未明。Schouten等^[13,14]研究发现肛管后正中线皮肤的血供与肛管静息压成负相关, 肛裂处皮肤的血流灌注要少于正常肛管后中线处的皮肤血供。Klosterhalfen等^[15]发现, 正常人两侧肛门动脉的分支在肛后连合处约85%的人无吻合, 形成乏血管区。

近代, 随着国内外对肛裂研究的深入, 越来越多的学者认可肛裂的本质是缺血性溃疡, 可以概括为缺血-痉挛-缺血, 这一恶性循环。所以内括约肌切断术可以降低肛管的压力, 增加肛管皮肤的血供, 从而促进肛裂的愈合。

肛裂的病理生理实质是高血压低血流。降低肛管静息压反射性地使内括约肌张力降低, 有利于恢复皮肤血供, 但有研究显示, 应用CS治疗肛裂时, 肛管静息压的下降未与肛裂的治愈率成正比^[16,17]。

如果肛管静息压下降而肛裂并未痊愈, 就需要另一种解释: 肛管静息压下降, 并不一定导致内括约肌在排便时完全扩张, 也未必改善局部血供, 因为肛裂局部的生化因素可能会影响到内括约肌的舒缩^[18]。

近年发现内皮细胞可以产生释放内皮源性血管舒张因子(endothelium-derived relaxing factor, EDRF), 有研究指出EDRF为一氧化氮(NO)^[19]。若内皮完整, 二磷酸腺苷(adenosine diphosphate, ADP)、三磷酸腺苷(adenosine triphosphate, ATP)、5-羟色胺(5-hydroxytryptamine, 5-HT)、血小板活化因子、凝血酶、组胺、P物质等这些物质会导致NO和前列环素的释放, 会放松小动脉的肌膜, NO还可以增加血管流量而防止血小板聚集; 若内皮损伤, 有证据表明, 这些物质会收缩平滑肌细胞。对于肛裂区再生的细胞, 只能释放较少的NO, 并且对5-HT和 α_2 -肾上腺素受体激动剂特别敏感, 故肛裂区域生化环境的改变, 也会引起平滑肌的舒缩。

肛周皮肤的血流灌注与肛管静息压呈负相关, 但血流灌注并不仅仅与内括约肌的机械收缩有关, 而且与肛裂区域的生化环境有关^[20]。当肛管不能产生足够的扩张时, 组织就会被撕裂损伤, 从而改变肛裂区域局部的生化环境, 继而

导致血管平滑肌和内括约肌的收缩, 这是导致肛裂不能顺利愈合的原因. 所以治疗肛裂应该: 降低排便时内括约肌的张力, 改善肛裂区域的生化环境, 从而缓解血管平滑肌和内括约肌的痉挛性收缩.

2 肛裂的药物治疗

肛裂产生的病因有多种, 但最终导致肛门静息压的增高, 而肛门静息压有70%-80%是由肛管内括约肌维持的, 所以治疗肛裂首先要降低内括约肌的张力. LIS仍然被认为是治疗肛裂的金标准, 治愈率高且复发率<10%^[21], 但LIS可导致: 肛周感染、出血、尿潴留等并发症^[22-24], 当然这些并发症发生的概率较小, 但是排气和排便失禁仍值得注意^[25]. Hancke等^[26]研究显示: 内括约肌侧切术后3 mo轻微的肛门失禁(如: 排气、污物)为20%, 术后79 mo达47.6%, 甚至更高.

并发症的发生还有麻醉的风险, 导致了医生们要寻找另一种方式去模拟手术治疗肛裂, 故化学性内括约肌切开被广大医生认为是治疗肛裂的一线治疗方法^[2,27], 而且也降低了治疗的费用^[28]. 最常用的药物有: 肉毒毒素、一氧化氮供体和钙离子通道阻滞剂等.

2.1 肉毒毒素 肉毒毒素于1993年被用于慢性肛裂的治疗, 其主要作用是降低肛管压力, 但在疗效方面, 结果却不尽相同: 一些实验证明他的有效性, 一些实验则认为等同于安慰剂^[29], 大剂量的肉毒毒素可能比小剂量的效果好^[30,31]. 肉毒毒素可引起暂时性的排气失禁(18%), 排便失禁(5%), 肛周的血栓、血肿及全身症状(3%), 但对于并发症的报道, 结果也是不尽相同^[32,33]. Valizadeh等^[34]研究发现, 注射肉毒毒素术后1年的治愈率为48%; 术后3-4年复发率为40%-55%^[35]. 这种治疗方式在治愈率和并发症等方面存在争议, 剂量应用方面没有统一的标准^[36-38]以及注射的部位、注射的深度、注射针与内括约肌的角度都会影响疗效及预后^[39].

2.2 一氧化氮供体 自从发现NO可以缓解肛管内括约肌的痉挛以来^[40], 硝酸盐就被用于降低肛管压力, 并且在许多临床试验中, 作为治疗肛裂的一线药物使用^[41]. 在欧洲许多国家, 硝酸盐的局部使用, 明显减少了需要手术治疗肛裂的人数^[42]. Velson等^[43]研究指出: 局部应用硝酸盐治疗肛裂要显著优于安慰剂, 能够明显减轻疼痛^[44-46], 但是硝酸盐最主要的不良反应是头痛(20%-30%^[12], 甚至更高^[47]), 还会出现头晕、肛

门区灼热等, 随着药物浓度的增大(0.2%-0.4%)治疗效果未见明显提高, 但不良反应明显增加. 为了减少硝酸甘油的不良反应. Pérez-Legaz等^[48]研究发现: 0.4%硝酸甘油软膏肛内给药与肛周给药相比, 前者降低了头痛的发生率, 并提高了治愈率. 但这种治疗方式远期复发率较高, Carapeti等^[47]经过9 mo的观察, 复发率为33%. Lund等^[49]经过28 mo的观察, 复发率为27%. Kirkil等^[50]经过5年的观察, 复发率为52.3%.

2.3 钙离子通道阻滞剂 钙离子通道阻滞剂, 一般用于治疗心血管疾病. 口服或肛周局部应用钙离子通道阻滞剂(硝苯地平、地尔硫卓)可以缓解内括约肌痉挛, 降低肛管静息压. Cook等^[51]研究发现, 健康志愿者和慢性肛裂患者口服硝苯地平, 他们的肛管静息压都降低了1/3. Carapeti等^[52]研究发现: 口服地尔硫卓60 mg, 2次/d, 肛管静息压降低17%, 并且还对不同浓度的地尔硫卓软膏进行试验, 发现2%的软膏能发挥最大作用, 肛管静息压约降低28%, 一次应用效果可维持3-5 h. 钙离子通道阻滞剂与NO供体相比, 在治疗效果方面与硝酸甘油相当, 但可以降低不良反应的发生(头痛、肛门瘙痒等). 其不良反应较小的原因, 可能是因为局部应用, 全身系统吸收较少. Jawaid等^[53]研究发现: 运用2%盐酸地尔硫卓和0.2%硝酸甘油治疗慢性肛裂, 随访8 wk, 疗效没有显著差异, 且不良反应前者小于后者. 比较局部应用地尔硫卓和0.2%硝酸甘油的研究显示经过后者治疗无效的患者采用地尔硫卓外用, 其治愈率接近70%^[54,55], 体外实验表明, 两者的联用效果更好^[56]. 高复发率是应用本类药物产生的主要问题, 在一项两年的随访试验中^[57], 复发率高达60%.

CS对肛裂的治愈率存在较大波动, 原因之一为: 应用药物的剂量和治疗时间的长短不同^[58-62]. Lysy等^[62]应用7.5 mg硝酸异山梨酯, 1 mo治愈率为83%; 另一项报道: 0.2%硝酸异山梨酯5 wk的治愈率为67%, 10 wk的治愈率为89%; Kirkil等^[50]运用5%和10%硝酸异山梨酯治疗40 d的治愈率分别为: 56.7%和63.3%. 另一个原因可能是未统一治愈标准, 如: 溃疡愈合为治愈还是症状消失为治愈? 有的医师建议后者为治愈, 因为对前者的评价增加了医师的主观因素. 非手术治疗的结果不同, 一定程度上也反应了药物的不稳定性.

CS可以较快的缓解症状, 并且没有手术和麻醉的危险, 但是从统计学上分析, 有效率不及

■ 相关报道

应用肛裂切除联合术后化学性内括约肌切开的方式来治疗肛裂, 国外对此研究较多, 能够减少对内括约肌的损伤, 提高治愈率, 并取得满意疗效.

■应用要点

明确肛裂各种治疗方式的适应症、治愈率、复发率及并发症,从而根据病情需要选择出最优治疗方式。

LIS^[63],并且有着较高的复发率。Abd Elhady等^[64],通过5年的随访:肛门内括约肌侧切术、局部应用地尔硫卓、硝酸甘油、肉毒毒素的复发率分别为:10.0%、65.0%、57.5%、52.5%。

2010年美国结肠与直肠外科医师协会(American Society of Colon and Rectal Surgeons, ASCRS)提出:肉毒毒素可以治愈60%-80%的肛裂患者,但是复发率高达42%。根据ASCRS,局部应用硝酸盐类药物的治愈率要高于安慰剂。虽然钙离子通道阻滞剂的不良反应少于硝酸盐类,但是没有充足的证据表明他优于安慰剂。Arroyo等^[65]指出行内括约肌切开术,手术要比CS疗效好。Nelson等^[24]的Meta分析指出:化学性括约肌切开的有效性可能稍高于安慰剂,但是远远要低于手术治疗。

综上所述,鉴于手术内括约肌切开术后的并发症与化学性内括约肌切开术后较高的复发率和不良反应,外科医师仍在寻找更好的治疗肛裂的方法。

3 肛裂的手术治疗

2004年, Lindsey等^[66]发明了一种新的术式,肛裂切除联合肉毒毒素(25 IU)内括约肌内注射,用来治疗应用药物治疗失败后的慢性肛裂,治愈率高达93%; Sileri等^[67]研究表明:肛裂切除联合肉毒毒素注射与内括约肌侧切术的治愈率分别为:83.3%和98.7%。

肛裂切除术,曾被报道用于儿童肛裂,但是很少有关于肛裂切除术单独用于治疗成人肛裂的研究报道。少量研究报道肛裂切除加内括约肌后位切开术获得较好效果^[68-71]。Meier等^[72]发现:肛裂切除术作为一个独立的术式,可取得令人满意的效果。对于肛裂切除的远期疗效, Schornagel等^[73]研究发现:肛裂切除术后5年治愈率为88.4%,且对肛门自制功能的影响较小。为评价肛裂切除术的疗效, Mousavi等^[74]通过对比肛裂切除术与内括约肌侧切术发现:术后1 wk两种术式疼痛、出血的症状消失;术后20 mo, 两组患者对手术的满意度分别为:87.5%和96.6%。现在内括约肌侧切术仍然是治疗肛裂的金标准,可获得非常好的效果:治愈率高达95%且术后疼痛较小。但是少数患者会出现排便失禁,虽然几率较小,一旦发生,治疗困难。

近几年肛裂切除术作为一种保护内括约肌的手术方式,取得了较好的治疗效果。现在肛裂切除术一般和其他治疗方式联用,如:药物或者手术。Patti等^[75]采用肛裂切除+肛门皮瓣推移成

形+内括约肌内30 IU肉毒毒素注射治疗肛门前方伴随肛管压力增高的慢性肛裂,术后30 d全部治愈,且术后肛管静息压显著下降。在之前的一些研究中,肛裂切除与术后NO供体联用,取得令人满意的效果,而且术后标本中仅有少量的内括约肌,肛门内超声也显示内括约肌并未受到损伤,这表明肛裂切除术对肛裂的治疗作用并不是直接作用于肛门内括约肌。Abramowitz等^[76]一项回顾性研究发现:肛裂切除联合肛门成形术后一年患者治愈率达100%。Patti等^[77]一项前瞻性研究发现:肛裂切除联合肛门皮瓣推移成形术后30 d全部治愈。Patel等^[78]在一项回顾性研究中发现:肛裂切除联合肛门皮瓣推移成形术与肛门内括约肌侧切术相比较,术后20 mo,前者治愈率为96%,后者为88%;症状的缓解分别为90%、72%。

4 肛裂治疗方式的选择

在治疗慢性肛裂方面,运用硝酸甘油、钙离子通道阻滞剂、肉毒毒素、内括约肌侧切术的顺序,于1999年在第七届欧洲联合胃肠病周上被提出^[79],在2001^[30]和2002^[33]年推广发行,随后考虑到药物的有效性和经济因素又在新英格兰杂志中发表^[79,80]。2005年Essani等^[28]从疗效和经济方面进行分析:采用这种顺序约有88%的患者不需要手术治疗就可痊愈,而且能够降低治疗费用。Gil等^[81]研究发现,慢性肛裂愈合的概率与收缩压和静息压百分比变化相关,若收缩压/静息压<150%则用药物治疗的可能性较小,需手术治疗。

从1999年, Madalinski等^[37,38,82]多次提出把大剂量应用肉毒毒素作为手术治疗肛裂前,化学性括约肌切开术的最后一道防线。2001年,在文献中第一次提到了联合硝酸甘油大剂量应用肉毒毒素(50-100 IU)可以提高慢性肛裂的治愈率^[67]。若应用大剂量肉毒毒素2-3 wk后,症状和注射之前没有明显的改善,就应该考虑内括约肌侧切术,但是在行内括约肌侧切术之前,肛裂切除术联合术后化学性内括约肌切开应被考虑。有研究表明在应用硝酸异山梨酯治疗肛裂失败以后,采取肛裂切除加局部应用硝酸异山梨酯,全部治愈,而且术后随访29 mo无一复发;肛裂切除联合肉毒毒素注射,随访16 wk,治愈率高达93%^[27]。

由于肉毒毒素价格昂贵且容易引起肛门失禁及肛周脓肿,越来越多的人希望用其他的替代方法去治疗肛裂。为了寻找更好的方法, Ar-

thur等^[83]研究发现肛裂切除配合40 IU肉毒毒素注射与肛裂切除配合术后8 wk的2%地尔硫卓外用, 治愈率分别为89.3%和82.6%, 无显著差异。肉毒毒素能够持久缓解肛门痉挛, 这是他的优势, 但同时也是他的劣势: 术后导致不同程度的肛门排气排便失禁, 故在选择这种术式的时候还是很谨慎的。虽然地尔硫卓的局部应用会导致肛门瘙痒, 但这是应用药物后导致肛门潮湿引起的, 而且是短暂的。

5 结论

在选择合适的方法治疗慢性肛裂的时候, 我们应该明白哪个阶段的肛裂适合化学性括约肌切开, 更应该明白内括约肌切开所带来的病理生理意义。随着社会发展, 对内括约切开后长时间随访研究的进行, 现在治疗肛裂越来越重视内括约肌的保护, 避免使其损伤。故在药物治疗肛裂失败后, 采用肛裂切除术联合术后化学性括约肌切开是一个较为理想的治疗方法。

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同行评价

本文介绍了肛裂治疗的最新进展, 对侧方内括约肌切开术、肛裂切除加皮瓣推移成形术、化学性内括约肌切开的优缺点进行了分析, 对临床实践具有一定的参考价值。

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