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重症急性胰腺炎诊疗现状及主要问题

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Diagnosis and treatment of severe acute pancreatitis: Current status and main problems

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Abstract

Acute pancreatitis (AP) is a disease of various

causes, characterized by pancreatic enzyme activation and local pancreatic inflammatory response. Serious cases may develop systemic inflammatory response syndrome and even organ dysfunction. Severe AP (SAP) as a category of AP associated with persistent organ failure (>48 h) has an acute onset and high fatality rate. SAP accounts for about 5%-10% of all AP cases, with 30%-50% mortality rate. In this paper, we discuss the current status and main problems on the diagnosis and treatment of SAP based on the literature and our experience.

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Key Words: Acute pancreatitis; Severe acute pancreatitis; Treatment; Review

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摘要

急性胰腺炎(acute pancreatitis, AP)是指多种病因引起的胰酶激活, 继以胰腺局部炎症反应为主要特征的疾病, 病情较重者可发生全身炎症反应综合征甚至器官功能障碍。重症急性胰腺炎(severe acute pancreatitis, SAP)是伴有持续的器官功能衰竭(48 h以上)的一类。SAP起病凶险、病死率高, SAP约占AP的5%-10%, 病死率却高达30%-50%。现结合国内外文献, 相关指南以及我们的经验与体会对SAP的诊治情况及存在的主要问题进行了综述。

背景资料

重症急性胰腺炎(severe acute pancreatitis, SAP)是一种发病多、进展快、并发症多、病死率高、治疗棘手的急腹症。近年来对于SAP的诊治已经达成一定的共识, 形成了以“个体化治疗方案”为基础的“综合治疗方案”, 但随着对其发病机制、病程进展及治疗方案研究的深入, 其诊疗在共识的基础上亦有相关问题存在争议。

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■ 研究前沿

本文主要介绍SAP的诊疗现状及其在治疗方面存在争议的主要问题, 为临床诊疗提供一定指导依据。

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关键词: 胰腺炎; 重症急性胰腺炎; 治疗; 综述

核心提要: 重症急性胰腺炎(severe acute pancreatitis, SAP)是一种发病多、进展快、并发症多、病死率高、治疗棘手的急腹症。虽然, 近年来对于SAP的诊治已经达成一定的共识, 但随着对SAP发病机制、病程进展及治疗方案研究的深入, 其诊疗在共识的基础上亦有相关问题存在争议。本文就SAP的诊疗基本情况及存在的主要问题进行了描述。

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0 引言

重症急性胰腺炎(severe acute pancreatitis, SAP)是一种发病多、进展快、并发症多、病死率高、治疗棘手的急腹症^[1]。近年来对于SAP的诊治已经达成一定的共识, 形成了以“个体化治疗方案”为基础, 按不同病因及不同病期进行处理的“综合治疗方案”^[2]。但随着对SAP发病机制、病程进展及治疗方案研究的深入, 其诊疗在共识的基础上亦有相关问题存在争议。本文就SAP的诊疗基本情况及存在的主要问题进行了描述。

1 SAP的病因及发病机制

SAP按病因分类主要包括胆道结石性、酒精性、高脂血症性、高钙血症性、药物刺激性、经内镜逆行性胰胆管造影术后胰腺炎以及部分病因不明的特发性急性胰腺炎(acute pancreatitis, AP)^[3,4]。随着对病因的研究深入, 部分特发性的病因可能为胆道微结石、Oddi括约肌功能障碍、胰腺分裂、十二指肠乳头旁憩室、胆总管囊肿、胰腺或壶腹肿瘤、自身免疫性、感染性、遗传性等因素^[5]。

近年来, 发病机制研究进一步深入, 主要学说包括胰酶的自身消化、腺泡细胞凋亡、炎症反应、微循环改变、钙超载、高甘油三酯血症、肠道细菌易位等^[6]。但SAP的发病机制复杂, 不能用单一因素解释, 往往是多种因素相互促进而形成的一条恶性循环链。

2 SAP的诊断标准

目前临床上符合以下3项特征中的2项即可诊断为AP: (1)与AP相符合的腹痛; (2)血清淀粉酶(或)脂肪酶活性至少高于正常上限值3倍; (3)腹部影像学检查符合AP影像学改变^[7]。其中尤其要注意血脂脂肪酶的意义, 当血清淀粉酶在3倍界值之内时, 检测脂肪酶的价值更大。平扫计算机断层扫描(computed tomography, CT)现在已成为胰腺炎的首选影像学诊断方法, 而增强CT有助于对胰腺炎发病1 wk后坏死情况的诊断。

依据改良Marshall评分系统(表1), 任何器官评分 ≥ 2 分可定义存在器官功能衰竭, 当AP存在持续性(超过48 h)的器官功能衰竭可诊断为SAP^[7]。

3 SAP的主要治疗措施

3.1 非手术治疗 SAP发病早期主要为炎症反应并组织出血坏死, 肠黏膜屏障功能的严重破坏, 手术不能终止胰腺炎的病情进程, 反而加重了全身循环、代谢紊乱, 增加了感染的发生率及死亡率, 因此对SAP早期多以积极、有效、综合的非手术治疗为主^[8]。主要包括禁食、胃肠减压、抗胰酶药物、补充容量、维持电解质平衡、营养支持、抗生素的应用、区域动脉灌注治疗、血液净化、免疫疗法、诱导细胞凋亡、早期腹腔灌洗、改善胰腺微循环、中药治疗、内镜治疗等。其中SAP患者早期的液体复苏治疗需要高度重视, 甚至可以决定治疗的成败^[9-11]。

另外胰腺区域动脉灌注治疗(LAI)因能大幅提高胰腺组织药物浓度而被作为SAP增效的非手术方法, 治疗SAP较常规用药途径好, 适用于早期非手术治疗者^[12,13]。LAI常用药物包括胰酶抑制剂、抗生素、改善微循环药物及激素类等^[14]。近十年来我们已对腹痛症状明显的早期AP患者采用该方法治疗90余例, 可及时有效缓解症状, 阻止病情的继续恶化患者, 较快得以康复, 是一种安全有效价廉的治疗方法, 值得普及推广^[15]。

3.2 手术治疗 手术治疗是治疗SAP的重要方法之一, 但手术适应证及手术时机的选择仍存在争议^[16]。手术适应证包括胰腺坏死感染^[17,18]、胰腺脓肿或假性囊肿^[19]、胆源性胰腺炎、腹腔筋膜室综合征^[20,21]、合并出血、穿孔、内科

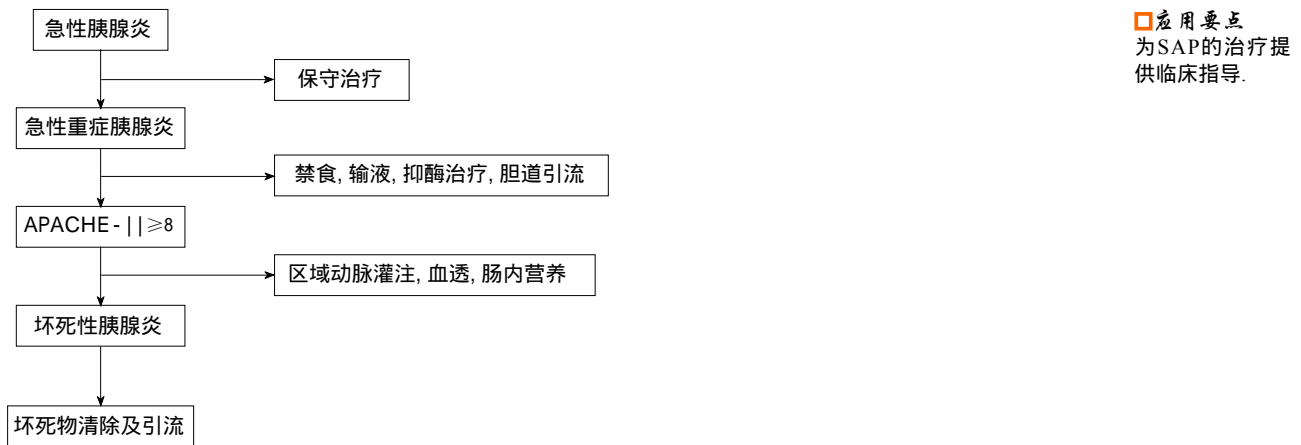


图1 重症急性胰腺炎治疗策略.

表1 改良Marshall评分系统

器官系统	评分				
	0	1	2	3	4
呼吸($\text{PaO}_2/\text{FiO}_2$)	>400	301-400	201-300	101-200	≤ 101
肾脏 ¹					
(血肌酐, $\mu\text{mol/L}$)	≤ 134	134-169	170-310	311-439	>439
(血肌酐, mg/dL)	≤ 1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
心血管(收缩压, mmHg) ²	>90	<90 , 输液 有应答	<90 , 输液 无应答	<90 , $\text{pH} < 7.3$	<90 , $\text{pH} < 7.2$
非机械通气的患者, FiO_2 可按以下估算:					
吸氧(L/min)	$\text{FiO}_2(\%)$				
室内空气	21				
2	25				
4	30				
6-8	40				
9-10	50				

¹既往有慢性肾衰竭患者的评分依据基线肾功能进一步恶化的程度而定, 对于基线血肌酐 $134 \mu\text{mol/L}$ 或 1.4 mg/L 者尚无正式的修订方案; ²未使用正性肌力药物.

保守治疗无法控制的腹膜炎等情况, 应根据患者的具体情况采取个体化治疗方案. SAP手术时机的观点经历了早期干预、胰腺坏死感染后干预、延期干预等多种变迁. 目前, 对于胰腺坏死感染后的外科干预治疗逐渐趋于认同, 其目的乃清除胰周局部坏死物, 减少毒素的吸收, 防止邻近血管的被腐蚀而导致的大出血^[22]. 手术方式多种多样, 原则应以最小的创伤达到治疗目的^[19,23,24], 适时适当的外科干预不可或缺, 应引起足够的重视^[25,26](图1).

4 SAP诊治存在的主要问题

4.1 SAP的诊断 根据《急性胰腺炎分类与定义国际专家共识——2012亚特兰大修订版》^[7],

中度SAP与SAP鉴别需到发病48 h以后, 对于SAP的早期分级诊疗有一定的限制.

4.2 诊断方法的选择 SAP的诊断除了根据特征性的症状及淀粉酶、脂肪酶等生化检查外, 还需必要的影像学检查. 美国指南推荐B超作为SAP的首选影像学检查方法, 理由是胆道结石是其主要病因, 但B超检查易受到周围组织干扰并且难以准确判断病变胰腺及周围情况. 我国和日本的指南均推荐CT作为SAP的首选影像学检查方法, 但目前对入院后先行平扫或增强CT检查仍存在争议, 推荐CT平扫的理由是胰腺灌注损伤和胰周坏死的演变需要数天, 早期增强CT有可能低估胰腺及胰周坏死的程度, 起病3 d到1 wk之后的增强CT更有价值^[27-30].

□ 同行评价
本文整体行文流畅, 具有一定的科学意义, 对临床工作具有一定指导意义。

4.3 缺乏病情严重程度判断的有效指标 AP严重度的评估标准除了AP的分级诊断标准, 还有Ranson评分、APACHE II评分、BISAP评分、Marshall评分、Balthazar CT评分等众多临床评分标准, 单一的评分系统往往无法有效帮助临床医师对病情作出准确而全面的判断并进行针对性处理, 临床医师更多的是结合自身经验对SAP的病情做出综合评价。目前临床推荐的病情评估指标还包括血糖水平、电解质水平(包括血钙)、炎症指标(C反应蛋白、降钙素原)、血气分析、全身性炎症反应综合征(systemic inflammatory response syndrome, SIRS)动态变化等^[31,32]。

4.4 肠内营养的时机和方式 国内相关指南及研究推荐早期实施肠内营养(enteral nutrition, EN), 理由是早期EN对于维护重症患者的肠道功能、预防感染等并发症有重要作用^[33-35], 但目前国际指南认为早期EN(48 h内)和后期EN的效果近似^[36,37]。关于EN途径, 国内指南推荐内镜引导或X线引导下放置鼻空肠管, 但近期也有经鼻胃内营养和经鼻空EN的疗效和安全性类似的报道^[38], 但是因部分患者存在胃流出道梗阻的情况, 因此鼻空肠管仍为首选途径^[39,40]。同样, 停用鼻空肠管的指征也存在争议。

4.5 外科手术的时机 目前国内外指南均推荐手术治疗SAP推迟到感染控制以后, 因为胰腺坏死感染后, 患者全身情况迅速恶化, 手术并发症和病死率增加^[41]。但也有人认为非手术疗法治疗伴有多器官功能衰竭的患者一旦发生感染性坏死病死率极高, 因此手术时间要适当提前^[42]。此外, 合并有急性胆管炎或疑为胆总管下端有梗阻时, 应立即行十二指肠乳头括约肌切开(内镜下乳头括约肌切开术)^[43,44]; 胆源性SAP患者, 为预防感染, 应推迟胆囊切除术至炎症缓解、液体积聚消退或稳定后尽早实施^[45]。我们的体会是对于因胆道疾病引起的AP宜早期行胆道手术以及胰床的引流^[46], 对于因胰腺炎后坏死物导致SIRS者也应积极清除坏死物, 同时腹腔引流, 以阻止病情的恶化尤其是腹腔血管遭腐蚀引起的大出血。有报道^[47,48]SAP发病后2 wk坏死组织与正常组织之间界限不清, 手术中易致出血。起病后四周行胰腺坏死物清除术可降低术中出血的机会, 同时提高手术的安全性。

4.6 抗生素的使用问题 SAP因为肠内细菌移位, 40%-60%的坏死性胰腺炎患者于发病1-3 wk内发生感染, 因此发病早期预防性应用抗生素十分必要, 应成为SAP标准治疗的一部分。抗生素预防或治疗性使用的种类方面, 有研究发现, 很多抗生素不能进入胰腺组织内, 治疗效果不佳, 如氨基糖苷类抗生素。目前认为, SAP患者具有多重感染, 混合感染比例高的特点, 首选碳青霉烯类或碳青霉烯类+糖肽类联合应用, 但另有研究^[49,50]表明抗生素的应用不能有效地控制和预防胰腺坏死感染。

4.7 抑制胰酶活性药物的选择 尽管国内的AP指南均建议使用胰酶抑制剂如乌司他丁、加贝酯等抑制胰酶活性, 但该类药物的疗效一直存在争议。国外临床研究^[51]表明, 二者对SAP的疗效有限, 并未显著降低病死率和感染率, 在美国的AP治疗指南里也没有相应的环节。

5 结论

SAP系常见病, 难治病。近些年来对SAP的认识在不断深化, 治疗理念在不断更新, 治疗手段在不断丰富, 但仍然有许多问题有待进一步探索 and 解决, 在尽快达成共识的基础上, 对临床实践予以规范, 有望较大幅度改善SAP的疗效。随着医学的进步, 我们有理由相信SAP的诊治水平在不久的将来达到一个新的水平。

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