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残胃患者胃粘膜和血清中LPO与SOD-1含量研究*

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提 要 本文随访25例传统胃大部切除术(毕罗Ⅰ式11例, 毕罗Ⅱ式14例)手术患者和11例保留胃窦幽门浆肌瓣式胃大部切除术(PAFPG)患者, 并与11例健康者对照, 测定其胃粘膜和血清标本(共141份)的过氧化脂质(LPO)和铜锌超氧化物歧化酶(SOD-1)含量。发现: (1) PAFPG组、毕罗Ⅰ式组和毕罗Ⅱ式组的胃粘膜LPO含量依次明显升高, SOD-1含量依次明显下降; (2)36例残胃标本中, 残胃吻合口粘膜的LPO水平显著高于胃体, 而SOD-1却无明显差别; (3) 胃内LPO值与胃内pH正相关, SOD-1与pH负相关。提示胃切除方式和胃内pH影响着残胃的氧自由基反应, 氧自由基反应特别是脂质过氧化作用在残胃吻合口病变过程中起着某种作用。

关键词 过氧化脂质类; 超氧化物歧化酶类; 胃切除术; 氢离子浓度; 胃

炎症、溃疡和癌变等病理过程与超氧阴离子(O_2^-)或羟自由基(OH·)等氧自由基有关[1]。OH·与细胞膜发生脂质过氧化作用, 导致组织损伤。超氧化物歧化酶(SOD)是体内能清除O_2^-的唯一酶类, 包括铜锌SOD(SOD-1)、锰SOD和铁SOD[2]。大量动物实验证实, 缺血再灌注、酒精和阿斯匹林等刺激所致的急性胃粘膜溃疡病变过程中肯定存在着氧自由基反应[3]。但有关人类慢性胃疾患尤其是术后残胃粘膜病变中氧自由基的作用问题, 所见研究报道无几。本文通过检测溃疡病各种胃切除术后患者胃粘膜和血清的过氧化脂质(LPO)和SOD-1含量, 着重探讨氧自由基在残胃病变过程中的作用。

1 材料与方法

1.1 病例选择与分组

从随访患者中选择36例残胃患者, 按不同术式分为3组: PAFPG(Pylorus and Antroseromuscular Flap Preserving Gastrectomy)组11例, 毕罗Ⅰ式(B-Ⅰ)组11例, 毕罗Ⅱ式(B-Ⅱ)组14例, 并从胃镜和病理证实为健康胃的29例志愿者中随机选择11例作对照组, 4组年龄在20~60岁, 平均43岁左右; 所有病例均除外心肝肺肾等脏器严重器质性病变; 残胃3组术后随访时间为1~8年, 平均1.83~2.16年; 所有病例胃镜检查前禁药1周、禁烟3 d。

按Hoffmeister氏法行B-Ⅱ手术, B-Ⅰ采用封闭残胃小弯侧、残胃十二指肠端端吻合法, PAFPG按晏氏法进行, 详见有关报道[4]。

1.2 方法与指标

取外周血样常规分离血清标本待用。胃粘膜标本分别取自残胃大弯侧、残胃吻合口附近以及健康胃的胃窦和胃大弯, 每部位取3小块: 1块送常规病检, 以Watt等[5]制定的标准作为病理诊断依据; 其余2块于冰盐水中清洗、立即置入0.5mmol EDTANa_2的Tris-HCl缓冲液(pH7.8)中低温匀浆。按Ohkawa法[6]或Yagi法[7]分别测定匀浆液或血清的LPO含量, 用每mg蛋白或每ml的丙二醛(MDA)之nmol数表示胃粘膜或血清的LPO水平, 采用日产RF-540型荧光分光光度仪。

胃粘膜匀浆液低温离心, 其上清液同血清标本一起置-20℃保存, 参照二医大生理教研室的药盒说明书用放免法[8]测定SOD-1含量, 以μg/mg蛋白或μg/ml表示。

胃粘膜蛋白含量经Lowry氏法[9]检测, 胃液pH用美制pH计测定。数据处理包括t检验、双因素方差分析或线性回归分析等。

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2 结 果

PAFPG组与B-Ⅰ组或B-Ⅱ组相比，LPO水平明显降低而SOD-1含量明显升高（$P<0.05\sim0.001$，见表1、表2和表3）；残胃吻合口粘膜LPO水平（1.32±0.24nmol/mg蛋白）显著高于胃体（0.96±0.17

表1 47例受检者胃粘膜（nmol/mg蛋白）和血清（nmol/ml）的LPO水平（$\bar{x}\pm s\bar{x}$）

Tab.1 LPO level in gastric mucosa (nmol/mg protein) and serum (nmol/ml) from 47 selected subjects

Groups	n	LPO level ($\bar{x}\pm s$)		
		mucosa from corpus (nmol/mg pr)	mucosa from anastomic stoma (nmol/mg pr)	serum (nmol/ml)
Controls	11	0.36±0.13	0.69±0.15***	3.35±0.68
PAFPG	11	0.57±0.10	0.92±0.17	3.81±0.96
B-I	11	1.01±0.23	1.35±0.22	3.95±0.58*
B-II	14	1.23±0.18**	1.60±0.32	4.63±1.21

Values are means±SEM * $n=10$, ** $n=13$, *** from mucosa in the antrum

表2 47例受检者胃粘膜（μg/mg蛋白）和血清（μg/ml）的SOD-1含量（$\bar{x}\pm s\bar{x}$）

Tab.2 SOD-1 level in gastric mucosa (μg/mg protein) and serum (μg/ml) from 47 selected subjects

Groups	n	SOD-1 level ($\bar{x}\pm s$)		
		mucosa from corpus (μg/mg pr)	mucosa from anastomic stoma (μg/mg pr)	Serum (μg/ml)
Controls	11	1.34±0.14	1.21±0.18+	0.42±0.03
PAFPG	11	1.28±0.20	1.20±0.21	0.40±0.11
B-I	11	1.11±0.32	1.04±0.26	0.39±0.10
B-II	14	0.71±0.12	0.88±0.31	0.37±0.07*

Values are means±SEM + from mucosa in the antrum * $n=13$

表3 各组不同部位的LPO和SOD-1含量均值比较*

Tab.3 Comparison between mean values of LPO and SOD-1 level of four selected groups*

Groups	LPO			CuZn-SOD-1		
	mucosa from corpus	mucosa from anastomic stoma	serum	mucosa from corpus	mucosa from anastomic stoma	serum
(1):(2)	NS	NS	+	NS	NS	NS
(1):(3)	+++	+++	++	++	+	NS
(1):(4)	+++	+++	+++	+++	+++	NS
(2):(3)	+	+	NS	+	+	NS
(2):(4)	+++	+++	+++	++	+++	NS
(3):(4)	NS	NS	+++	+++	+	NS

* NS: $P>0.05$ +: $P<0.05$ ++: $P<0.01$ +++: $P<0.001$

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nmol/mg蛋白）（$P<0.001$），但SOD-1含量吻合口（1.03±0.21μg/mg蛋白）与胃体（1.01±0.21μg/mg蛋白）无明显差别。

残胃吻合口粘膜中，LPO水平与胃内pH正相关（$n=36$；$r=+0.471$，$P<0.01$），SOD-1含量与胃内pH负相关（$n=36$；$r=-0.357$，$P<0.05$）；残胃体粘膜中的情况与其吻合口相似（图1、2）。残胃粘膜中LPO水平与SOD-1含量负相关（图3），但血清中LPO与SOD-1无关。

残胃吻合口和胃体粘膜病检，均为轻～中度慢性浅表性胃炎，未发现萎缩或肠化。

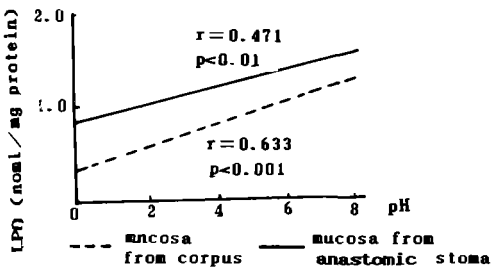


图1　36例残胃患者胃液pH与其胃粘膜LPO含量的关系

Fig.1 Correlation between pH of aspirates and LPO levels of gastric mucosa from 36 gastrectomized patients

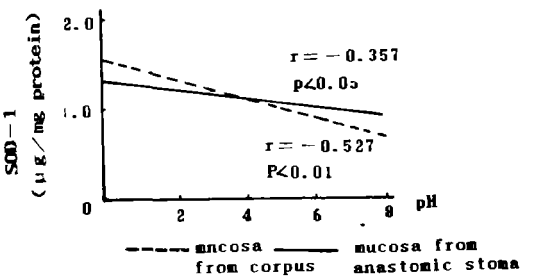


图2　36例残胃患者胃液pH与其胃粘膜SOD-1含量的关系

Fig.2 The relationship between pH of aspirates and SOD-1 levels of gastric mucosa from 36 stump-stomach patients

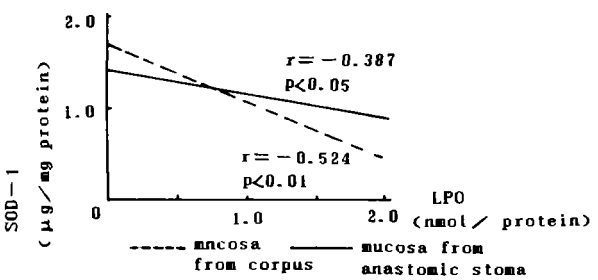


图3　36例残胃患者胃粘膜LPO与SOD-1含量的关系

Fig.3 Correlation between LPO and SOD-1 levels of gastric mucosa from 36 intact stomaches after gastric resection

3　讨　论

本文随访36例行不同胃大部切除术的残胃患者，进行了氧自由基反应与胃切除后消化道连续性重建方式的关系研究。发现胃切除患者血清和残胃粘膜的LPO水平升高，尤其是B-Ⅱ和B-Ⅰ，较PAFPG组明显升高，PAFPG组接近健康对照组；相反，SOD-1含量B-Ⅱ组和B-Ⅰ组明显低于PAFPG组，后者与对照组相似。本文还发现残胃吻合口和胃体粘膜的LPO与SOD-1明显负相关。提示B-Ⅱ和B-Ⅰ后残胃粘膜的O_2^-和OH·水平较高，所介导的氧自由基反应较活跃，而PAFPG后的自由基及其反应比较接近生理水平。与传统胃切除后残胃易发生碱性反流性胃炎等并发症的事实相符[10]。毕罗氏胃术后氧自由基反应增强的原因不仅与肠胃反流等胃肠动力学改变有关，也可能与附于残胃粘膜表面的粘蛋白减少有关。Parks等认为粘蛋白是胃肠道重要的生理性抗氧化剂，能有效地清除OH·[11]。

本研究胃镜检查发现，肠胃反流率PAFPG（0.0%）、B-Ⅰ（36.3%）和B-Ⅱ（64.0%）组依次明显升高（$P<0.05$），与氧自由基的变化相一致，但3个手术组残胃粘膜活检结果却无明显差别，提示残胃的氧自由基变化早于粘膜病理改变，有希望成为早期诊断残胃癌变

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的敏感指标。

氧自由基参与的某些急性胃粘膜损伤，如缺血再灌注损伤[12]或阿斯匹林性损伤[13]，依赖于胃腔的酸性条件，说明氧自由基与胃内pH有一定联系；O'neill等也认为pH影响着SOD的活性[14]。本研究表明，胃粘膜LPO含量随胃液pH的升高而增加，SOD-1含量随pH升高而降低，提示残胃内pH与其粘膜的LPO和SOD-1含量密切相关，其机理有待进一步探讨。

本文发现，残胃吻合口粘膜的LPO水平显著高于胃体，与残胃炎症、溃疡或癌前病变多见于其吻合缘的特征相吻合，说明OH·介导的脂质过氧化作用在残胃吻合口病变中可能起着某种作用。但残胃吻合口粘膜的SOD-1含量与胃体相似，可能与放免法仅测定SOD含量而未能反映其生物活性有关[8]。

总之，虽然本文显示胃内氧自由基反应受着胃内pH的影响且在残胃炎症中可能发挥着某种作用，但人类慢性胃疾患中氧自由基的种类、来源及其特殊作用有待深入研究。

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Level of lipid peroxides and cuprozinc superoxide dismutase in gastric mucosa and serum of gastrectomized patients

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Abstract The level of lipid peroxides (LPO) and copper-zinc containing superoxide dismutase (SOD-I) in the gastric mucosa and serum was determined in 141 samples from 25 patients after conventional subtotal gastrectomy (11 cases of Billroth I and 14 cases of Billroth II) and 11 patients after pylorus and antroseromuscular flap preserving gastrectomy (PAFPG). Those of 11 normal subjects were examined likewise to serve as control. It was found that:

1. The average LPO level was much higher and the average SOD-I level much lower in the gastric mucosa after conventional subtotal gastrectomy especially the Billroth type II than in those after PAFPG.
2. In 36 specimens of stump mucosa, the average LPO level was significantly higher in the tissue around the anastomotic ring than in that of the body of the stump; no marked difference of SOD-I level between the 2 was revealed.
3. The LPO value in the stump mucosa was positively correlated to and the SOD-I value negatively correlated to the pH value of gastric juice.

Thess findings suggest that the reaction of oxygen free radicals in the stump-mucosa may be influenced by the intragastric pH or by the type of digestive continuity reconstruction, and that the reaction of free radicals specially lipidperoxidation may play a role in the pathogenesis of the lesions in the anastomotic stoma.

Key words lipid peroxides; superoxide dismutases; gastrectomy; hydrogen-ion concentration; stomach

水痘并发传染性单核细胞增多症一例报告

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患儿，女，3岁。因出疹6d，发热、颈部肿痛2d于1991年6月1日入院。6天前发现全身皮肤散在稀疏的红色丘疹，轻痒，不发热。次日躯干出现水泡疹。曾服板兰根冲剂治疗。起病3日后部分皮疹结痂。入院前2日开始发热，体温38.5℃，伴咽痛，颈部两侧出现肿块，轻痛，无咳嗽等症状。所在幼儿园近期有水痘流行。入院时体温37.8℃，急性热病容。皮肤散在红色丘疹、水疱疹和结痂疹。水疱疹直径约3～5 mm，椭圆形，周围有红晕。皮疹以躯干居多，四肢稀少。双侧颈部淋巴结群及颌下淋巴结肿大，左侧显著，最大者2 cm×1.5cm，质稍硬，轻度压痛，局部皮肤不红。巩膜不黄。咽部充血，双侧扁桃体Ⅱ°肿大，无脓性分泌物。心肺无特殊发现。腹平软，肝肋下2 cm，质软轻压痛，脾侧卧肋下2 cm，质软无压痛。入院后共查血相3次，分别为：白细胞总数20×10⁹/L、13×10⁹/L、8.3×10⁹/L，嗜中性细胞0.39、0.34、0.18，淋巴细胞0.45、0.54、0.70，异型淋巴细胞0.13、0.12、0.12。肝功能：SB正常，ALT83u，ZnT6u。HBV感染标志(－)。血清嗜异性凝集试验阳性。经青霉素肌注、板兰根冲剂口服及龙胆紫外涂

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