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早产儿胃食管反流：肠外营养策略的研究

TRANSPILORIC FEEDING IN GASTROESOPHAGEAL REFLUX IN NEONATOLOGY

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优化营养支持对危重儿童至关重要，早产儿极易受到长时间禁食的影响。在科学文献中有很多证据表明肠内营养的好处。由于分解代谢过程占主导地位，早产儿需要一个单独的方法来组织喂养，而在重症监护病房治疗需要多余的卡路里。及时引入肠内喂养有助于降低该人群的发病率和死亡率。胃食管反流在早产儿中极为常见。由于对肠内喂养的耐受性降低，医生通常更倾向于肠外营养。然而，使用肠外营养可能与代谢、感染和医源性并发症有关。在早产儿胃食管反流的治疗中，建议循序渐进的治疗方法。对于无临床并发症的患儿，应以保守治疗为主。重病患者对胃管营养的耐受性并不总是很好。对于复杂的胃食管反流的治疗，广泛的研究表明，使用经腔喂养在效果上与胃底折叠术相当。食管穿刺术可以作为治疗胃食管反流的一种策略，保守治疗难治性。

关键词： 肠内营养；经幽门喂养；早产儿；胃食管反流；营养支持。

Optimizing nutritional support is essential for critically ill children, and premature infants are particularly vulnerable to the effects of prolonged fasting. There is a lot of evidence in the scientific literature for the benefits of enteral nutrition. It is known that premature babies need an individual approach to nutrition due to the prevalence of catabolic processes, while treatment in the intensive care unit requires a surplus of calories. Timely introduction of enteral nutrition helps to reduce morbidity and mortality in this population. Gastroesophageal reflux is common in preterm infants. When there is a decrease in tolerance to enteral feeding, doctors usually prefer parenteral nutrition. However, its use can be associated with metabolic, infectious and iatrogenic complications. A step-by-step therapeutic approach is recommended in the treatment of GER in preterm infants. Conservative treatment should be considered as first-line therapy in children without clinical complications. Feeding through a gastric tube is not always well tolerated by seriously ill people patients. As for the treatment of complicated GER, extensive studies show that the use of transpiloric feeding is comparable in effectiveness to fundoplication. Transpiloric feeding tube can be justified as a strategy for treating GER that is refractory to conservative therapy.

Keywords: enteral nutrition; transpiloric feeding; premature babies; gastroesophageal reflux; nutritional support.

绪论

早产是婴儿发病和死亡的主要原因。在婴儿死亡率的结构中，40%下降在新生儿早期，30%下降在新生儿后期[1,2,6]。在重症监护室为重症患者的护理提供营养支持似乎是麻醉师、复苏专家和新生儿医师面临的一项极其重要和非常困难的任务[5,7,9]。对于需要营养支持的患者，可以通过肠内或肠外提供早期喂养。根据欧洲的建议，肠内营养是胃肠道功能正常的患者首选的喂养方法。胃食管反流在早产儿中很常见。在2006年（加拿大蒙特利尔）的世界胃肠病学大会上，胃食管反流病的定义被提出为一种将胃内容物扔进食道引起令人不安的症状和/或导致相应并发症的情况[50]。经证实，确诊为

胃食管反流的新生儿比无胃食管反流的婴儿有更长的住院治疗时间[34]。早产儿胃食管反流的原因是存在胃窦运动功能减退[14]，食管下括约肌张力改变，胃排空延迟[34,41,52]。大量的胃残余量常常导致喂养中断，迫使使用肠外营养。十二指肠蠕动活动的减少可能不如胃蠕动违逆那么显著。将探针置于幽门外理论上可以克服胃食管反流的风险，因为幽门起保护屏障的作用，排除内容物反流回胃[33]。危重病人的喂养方法，以及提供肠内营养的最佳方式，仍然是讨论的主题[10]。幽门后喂养与胃残余容积显著减少有关，可以保证充足的营养供应。它被成功地用于维持肠内营养的患者，否则需要肠外营养[11]。

喂养早产儿的问题

在怀孕34周前出生的儿童中，胃食管反流的发生率约为22%[16,32]。对于早产儿，胃食管反流应该被认为是一种病理现象，可以由许多生理因素促成。首先，它们包括平躺仰卧的姿势，这加强了胃液的迁移[46]。此外，导致胃食管反流的因素包括食管运动不成熟，胃排空延迟，给反流的发生更多的时间[14]。较短的食管下括约肌位于横膈膜上方而非下方，对胃内容物的屏障效果较差[42]。出生后6—12个月，食管延长，食管下括约肌深入腹腔，增强屏障作用。在发育过程中，食管下括约肌发展成熟，导致暂时性放松的减少[28]。同时，婴儿喂养的性质导致胃食管反流的频率增加。早产儿的饮食和食物的液体稠度有利于胃食管反流。此外，为了达到正常的生长，早产儿应该比大一些的孩子获得更多的卡路里。对必要热量的需求给胃带来了很大的负担。在文献中，我们可以找到一些支持这一理论的证据，即胃排空延迟导致食管下括约肌松弛的增加，导致反流[21]。其他数据表明，婴儿反流主要是下食管括约肌功能障碍的结果，而不是排空胃的延迟[30]。也有外部因素有助于发展胃食管反流在婴儿。

一些药物，如茶碱和咖啡因，经常用于治疗早产儿呼吸暂停和支气管肺发育不良，有一些胃肠道的副作用。甲基黄嘌呤导致平滑肌松弛，胃分泌增加，可能与反流发作的增加有关。鼻胃肠管常用于喂养吸吮和吞咽反射减少或消失的婴儿。然而，有证据表明，安装鼻胃肠管的胃食管反流发作增加[9]。此外，重症监护病房常见的一些临床条件和综合征也增加了婴儿发生胃食管反流的风险。呼吸暂停、胃食管反流和支气管肺发育不良之间的关系仍然存在争议[18,27,29]。然而，在某些情况下，胃食管反流可能与并发症相关，如喂养问题、生长迟缓、食管炎和误吸等[20,48]。胃食管反流患者的保守治疗仍然是一个有争议的话题。一种非药物的方法，如改变身体位置[21]，改变喂养方式，以及使用抗反流混合物喂养，目前被认为是治疗早产儿的推荐策略[22]。使用胃酸分泌抑制剂，如β_2-受体阻滞剂和质子泵抑制剂，与坏死性小肠结肠炎和感染的病例数量增加有关[44]。有证据表明口服多潘立酮可延长Q-T间隔[16]。因此，在开始药物治疗之前，应该仔细评估风险和收益的前景。

胃食管反流通常是根据一些临床症状的发展而怀疑的，但也可以通过特殊

的诊断方法来确诊。食道24小时ph监测通常被认为是标准的诊断方法[21]，也允许检测胃酸反流的发作。然而，这种方法的一个显著的局限性是它不能检测中性回流。因此，由于胃液的酸度取决于年龄，混合饲料会缓冲胃内容物的pH值，因此，pH测定在早产儿中使用可能是错误的[42,46]。

另一种诊断胃食管反流的方法是监测多重腔内阻抗。该方法通过几个腔内电极分析食管电阻抗的变化[19,21]。由于其检测非酸反流的特异能力，腔内阻抗监测被认为是一个敏感的诊断工具，特别是在餐后有用[25]。

在治疗早产儿胃食管反流，一个循序渐进的治疗方法被推荐。对于无临床并发症的患儿，应以保守治疗为主[35]。基于现有的数据，体位可以被认为是一种经过充分验证的、安全的治疗早产儿无并发症的胃食管反流的方法。胃食管反流的表现在左侧卧位和抬高的头端观察到减少，而在背面和右侧的位置引起反流[13]。此外，通过改变饲料，如降低摄食率或使用水解混合液，也可获得一定的好处[26]。研究发现，抗反流混合物对早产儿胃食管反流的治疗无效，且用于增稠食物团块的口香糖使一些营养物质难以吸收[45,46]。有必要避免牛奶混合物的增稠剂与坏死性小肠结肠炎的发展之间可能存在的联系[12]。

根据许多专家的说法，喂养早产儿的目标应该是达到接近同胎龄正常胎儿生长速度的追赶增长率。大多数出生时体重极低或极低的早产儿得不到足够的营养以保证正常的发育速度，因此在住院期间发育迟缓。在出生后限制营养“直到婴儿变得稳定”忽略了没有营养的婴儿进入代谢分解状态的理解。分解代谢不能促进正常的生长、发育，甚至不能促进恢复。在这一阶段，重要的是确定一项改善早产儿营养状况的战略，以消除与营养摄入不足有关的生长不良的负面后果。

肠外喂养和肠内营养的缺乏有许多不良后果。随着时间的推移，肠外营养与生物多样性的显著丧失和肠道微生物定植性质的变化有关[24]。在动物模型上进行的研究表明，延长肠外营养有助于肠道细菌定植的改变，微生物群的改变和坏死性小肠结肠炎的发展[23]。

在1970–1980年对早产儿进行的九项经三通喂养和胃管喂养的随机对照试验中，得出的结论是，在“喂养不耐受”或生长方面没有改善的证据，但发现胃肠道疾病和死亡的风险增加了。然而，证明死亡风险增加的研究具有不平等的基线特征，这可以解释比较组的差异：经腹喂养组的平均胎龄为27.7周，而胃喂养组的平均胎龄为28.5周。在采用经幽门喂养的一组中，儿童的阿普加评分最初很低，这被认为是一个非常不利的标准[31]。将本研究从Cochrane分析中排除后，这些组之间在死亡率、体重增加、身高、头围、坏死性小肠结肠炎和肠道穿孔方面没有发现显著差异。本研究评估了将经幽门喂养作为改善生长和肠内负荷耐受的初始策略，而未将经幽门喂养作为治疗危重早产儿胃食管反流的方法。

对于儿童合并胃食管反流的治疗，广泛的研究表明，经幽门喂养与胃底折叠术的疗效相当[17,49]。由于经幽门喂养或胃底折叠术不影响吞咽功能，患有严重神经功能障碍的儿童因吞咽功能障碍而导致吸入性肺炎可能持续存在。对有呼吸暂停和心动过缓的新生儿进行的研究表明，与胃喂养相比，经幽门喂养可能在降低呼吸暂停和心动过缓的频率方面有一些好处[36,39]。误吸是公认的肺损伤因素，在早产儿中广泛存在，有助于支气管肺疾病的发展[27,52]。经幽门喂养已知可降低误吸风险，对早产儿是安全的[37,47]。在体重极低的婴儿中，早期经幽门喂养可降低因支气管肺发育不良死亡的风险[51]。

在2020年进行的一项研究中，与胃喂养相比，经幽门喂养期间低氧血症的频率没有增加[29]。难治性胃轻瘫可能是上腹腔手术后迷走神经受损所致。在这些研究中，我们发现对于术后胃瘫患者，经幽门探针是一种安全、有效和微创的选择[33]。经幽门喂养不会导致婴儿的激素水平变化[40]。在幽门后喂养过程中肠壁穿孔的风险很小[15,38,43]。因此，经幽门营养是一种有效的危重患者喂养策略，消除了肠外营养并发症，降低了误吸风险。

尽早对危重患儿进行幽门后喂养，可以使开始有效的肠内营养，减少可能的胃肠道并发症，这最终有助于优化儿童的治疗质量[8]。根据各种来源，在幽门后喂养过程中使用了半元素无乳糖等渗摩尔混合物[3,4]。根据文献，缺乏证据的基础上的可能性，使用母乳作为底物喂养，在一定程度上限制了泛光营养的治疗潜力。在危重新生儿中安装后幽门管的适应症有：当滞流量≥6 ml/天时，不能进行胃肠内营养[3]；严重胃食管反流并有误吸风险；无创人工肺通气时发生咽气、胃胀、肠内喂养不耐受；胃动力异常或胃麻痹[4]。

结论

基于上述分析，在早产儿中使用幽门后喂养，如果胃喂养是不可能的，将使用肠外营养和不进行肠内喂养相关并发症的风险降到最低。经幽门喂养可减少需要人工肺通气的早产儿的误吸频率。经经幽门管喂食可作为治疗上消化道麻痹引起的肠内机能不全的一种策略。在新生儿重症监护中，经幽门喂养的方法被低估和很少使用。

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