

Research Progress on the Diagnostic Indexes Related to Neonatal Asphyxia

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Abstract

Neonatal hypoxic asphyxia is the most common emergency after birth and is one of the main causes of perinatal neonatal death and disability. Because of the urgency of the situation, the clinician needs first treatment, then diagnosis, which makes the doctor in a passive position. Now, with the release of the two-child policy leading to an increase in the number of births, the multiple factors of modern life leading to an increase in complex pregnancy, both directly increase the workload of obstetricians and birth attendants, will undoubtedly aggravate this situation. Even though there are many indicators of neonatal asphyxia available to clinicians, clinical neonatal asphyxia still occurs. This is because the fetus and mother, in order to improve the predictability of neonatal asphyxia and to provide timely clinical intervention, it is necessary not only to reduce the mortality, but also to reduce the rate of perinatal neonatal disability and improve the quality of life. This paper reviews the clinical indicators for predicting the significance of neonatal hypoxic asphyxia in order to provide reference for clinical diagnosis and treatment.

Keywords

neonatal asphyxia; hypoxia; acidosis

关于新生儿窒息相关诊断指标的研究进展

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摘要

新生儿缺氧窒息是出生后最常见的紧急状况,是导致围产期新生儿死亡和致残的主要原因之一。由于情况的紧急,临床医师需先救治,后诊断,这使医生处在被动的地位。而今随着二胎政策的放开导致分娩人数增多,现代生活的多元因素导致复杂妊娠增多,都直接使产科医生与产房助产师的工作量增大,毋庸置疑会加剧此种情况。即便目前有很多提示新生儿窒息的指标可供临床医师使用,但临床新生儿的窒息仍时有发生。这是由于胎儿与母体的循环系统相互联系,缺氧信号并非十分明显,新生儿的病情变化指标与成人有异,所以对医生及时、准确发现新生儿的缺氧窒息信号有了更高的要求,以提高新生儿窒息的预见性,及时的给予临床干预,不仅要降低围产期新生儿的死亡率,而且要降低围产期新生儿的致残率,提高生活质量。论文针对预测新生儿缺氧窒息意义的临床指标做一综述,以期临床诊断治疗提供参考。

关键词

新生儿窒息; 缺氧; 酸中毒

1 引言

要做到在窒息发生前给予干预,必须要充分了解新生儿窒息的变化机制。新生儿窒息的病理变化为:缺氧→酸中毒→机体应激性代偿→失代偿→脏器损伤,即新生儿窒息是宫内缺氧的延续与表现。当胎盘的血液供应被各种产前与产时的因素阻断,胎儿即可发生宫内缺氧。而酸中毒是缺氧引起脏器损害的第一步。氧是体内代谢不可或缺的物质,当氧合不足,体内会发生无氧代谢,产生大量的有机酸,而有机酸

需通过母体排出体外,排出速度慢,易发生胎儿体内的酸滞留。体内滞留的酸会对机体产生损害。机体有一定的代偿能力,在一定限度内,可保护机体免受伤害,或发生可逆性伤害,目前多认同胎儿的潜水反射,即当发生缺氧时,胎儿全身血流重新分布,以确保脑、心等重要器官的血流供应,此时机体处于应激性代偿状态^[1]。当缺氧条件持续存在,达到代偿的极限值后,进入引起脏器不可逆损害的失代偿阶段。缺氧引起的酸中毒是新生儿窒息的起始,对新生儿窒息的诊断与

治疗都以此为基础。临床上也多认为,新生儿的不良结局与发生的酸中毒严重程度存在平行关系^[2]。

2 新生儿窒息的筛查预测手段、指标

有许多情况与围产期窒息有关。然而很多时候,婴儿可能是“沉默”的,没有发生前哨事件^[3]。在这种情况下,要做到早期认识和及时处理,就必须提高标准指南的有效性和一致性。目前新生儿窒息的筛查标准仍然是主客观标准的复杂结合,以下将对新生儿窒息的筛查预测手段、指标进行阐述。

2.1 Apgar 评分

1953年提出的Apgar评分至今仍在被广泛使用。它是指评估新生儿娩出后的即时状态,以肌张力、脉搏、对刺激的反应、肤色、呼吸为标准进行评分,每项2分。Apgar评分因其简便、直观、实用的优点在临床上保留至今。但不能独用Apgar评分对新生儿下缺氧窒息的诊断或排除缺氧窒息状态已被广泛接受,因为其有不可忽视的缺点。例如,陈自励提出,将总分10分平分为五等分不合理,因为呼吸和心率是生命体征最重要的指标,显然比肤色等重要,因呼吸和心率扣4分和因其余项目扣4分的意义,不可等量齐观^[4]。虞人杰等人也认同此观点^[5]。Hogan Linda也指出,单用Apgar评分诊断窒息显然是不妥的^[6]。

2.2 脐动脉血气分析

脐动脉血气分析在临床中越来越受到重视,其对新生儿缺氧窒息的诊断与识别起到了很大的作用。国际对其的应用早于国内,中华医学会围产医学分会新生儿复苏学组、中国医师协会新生儿专业委员会、美国妇产科学会(American College of Obstetricians and Gynecologists, ACOG)、美国儿科学会(American Academy of Pediatrics, AAP)等组织均强调了其在围产期窒息诊断中的不可替代的作用^[5,7-11]。1958年的James等人是最早认识到脐带血气体分析可以提示胎儿出现缺氧应激^[12]。White CR认为脐动脉血气分析是更客观,更具特征性的指标,可以准确提示胎儿有无缺氧、酸中毒及其严重程度^[13]。

脐动脉血气分析包括PH值、PaO₂、PaCO₂、HCO₃⁻、BE、CO₂CP、阴离子间隙等。而在以上指标中,最重要的就是PH值,因为相对于其他指标,PH最为稳定,作为生化指标,也最为敏感。Malin GL等对481 753名婴儿进行了脐动脉血

气分析和预后追踪,得出脐动脉PH值低与新生儿死亡率和发病率等不良结局密切相关的结论^[14]。陈自励等也对临床中PH值的应用做了很多的研究,认为PH值在诊断新生儿窒息及预测新生儿不良预后中起重要作用^[15]。中国第九版《妇产科学》教科书将脐动脉血气PH < 7.15加入中国新生儿窒息标准。将其作为诊断窒息的金标准之一,足以说明它的重要性与可行性。

而其余标准也有一定的参考价值,但产妇在分娩时,由于宫缩产生的疼痛使母体过度换气,也会因为疼痛而屏气,进而直接影响PaO₂、PaCO₂的值,且变化幅度较大,往往只能反映短暂的瞬时的变化,稳定性差。且缺氧变化若在机体自调系统范围内,即使其余指标发生了变化,也不会引起恶性结局的新生儿缺氧窒息,而此时PH则多保持稳定。

2.2.1 乳酸

机体缺氧后无氧代谢产生的有机酸多为乳酸,乳酸的产生多引起代谢性酸中毒。乳酸的诊断价值也受到了广泛关注。Ramanah R比较了乳酸值、脐带血气pH值、乳酸值和Apgar评分,发现脐带血pH值和乳酸值有显著相关性,可预测缺氧^[16]。Gerris等人对2554例单胎分娩的脐带动脉血样本进行了描述性研究,发现乳酸与pH值之间存在显著的相关性,脐血中的乳酸可能比pH值更直接、更准确地反映胎儿在分娩时的窒息情况^[17]。Fiala Małgorzata和Wiberg Nana认为,乳酸可能比pH值更能预测新生儿发病率,或至少具有同等重要性^[18-19]。Ruta Einikyte对901例37周出生的新生儿进行了测定,发现脐带动脉乳酸和pH值预测短期新生儿结局的效果相似^[20]。Murray DM指出,在缺氧缺血性脑病患者中,乳酸恢复正常的时间与脑电图分级和癫痫发作相关^[21]。Vibeke Ramsgaard Eriksen指出,乳酸的消失率可能更能反映出窒息的程度^[22]。中国一些报道也显示,窒息新生儿的动脉血乳酸水平与窒息程度有着较高的相关性,并指出新生儿分娩6h内的乳酸清除率与多脏器损害呈反比关系^[23]。

2.2.2 乳酸脱氢酶(LDH)

机体功能障碍导致细胞损伤,细胞内的一些酶类被释放入血,如LDH。体内大多数组织细胞内均含有LDH,因此将LDH作为作为来源不明的细胞损伤的标志物更为优越。Mathias Karlsson的研究中发现LDH不仅对HIE具有高敏感性和特异性,而且对癫痫发作有良好的预测价值^[24]。Mukesh

Choudhary 在研究中提出, 72 小时 LDH 值的变化可以用于区分窒息新生儿和非窒息新生儿, 并可确定窒息严重程度^[25]。类似地, Karlsson Mathias 报道了窒息新生儿中 LDH 的平均值升高^[26]。Naina Kumara 指出 LDH 可以作为新生儿整体预后较好的预测因子^[27]。一些研究明确指出, LDH 值与一些新生儿并发症呈现明显的相关性, 如新生儿窒息^[28、29、30、31], 呼吸窘迫^[32], 重症入院率^[33], 坏死性小肠结肠炎^[34], 新生儿缺血缺氧性脑病^[35]等。就单一新生儿缺血缺氧性脑病来说, 也有研究表示 LDH 随着 HIE 的程度和分期加重而出现明显的升高趋势^[36]。在 Reddy S 的研究中, 得出了与 Mukesh Choudhary 一样的结论, 即在新生儿娩出 72 小时内, LDH 值在区分有无新生儿窒息方面较为准确^[37]。在检测 LDH 值与呼吸窘迫综合征的相关性的研究中发现, 脐带血 LDH 水平是新生儿短暂性呼吸过速所需氧量和呼吸支持量的最佳预测因子之一^[32]。也有研究表明脐血 LDH 值与 PH 值之间存在相近的预测价值^[38]。

2.2.3 肌钙蛋白

新生儿窒息死亡的原因中, 心肌损伤占较高的比例。而在成人人群中, 肌钙蛋白, 如肌钙蛋白 I (cTnI) 和肌钙蛋白 T (cTnT), 作为心肌损伤的金标准生物标志物, 在成人患者中使用。一些研究认为, 在胎儿发生缺氧时, 肌钙蛋白同样也可以作为心肌损伤的标志物。例如, Ana Mrkaic 提出, cTnI 是胎儿肌细胞损伤最敏感的标志物^[39]。Gaze David C 将所采集的脐动脉血标本进行分析, 结果显示缺氧患儿脐带血 cTnI 水平明显高于对照组, 非存活者脐带血 cTnI 水平显著高于存活者。由此提出, 脐带 cTnI 的显著升高是预测新生儿缺氧缺血性脑病严重程度和死亡率的良好早期指标^[40]。Liu Xun 在研究中指出新生儿缺氧缺血性脑病新生儿出生后的 cTnI 升高, 且与 HIE 严重程度呈正相关^[41]。Shastri 等人的研究结果也大致相同, 即 cTnI 在窒息患者中是一种敏感的心脏标志物^[42]。Mahajan 等人强调, 一系列 cTnI 水平的上升或下降有力地支持了心脏损伤演变的全貌^[43]。Zhou 等人的一项研究表明, 24 小时 cTnI 水平对新生儿窒息的死亡率有显著的预测价值^[44]。Simovic 等人发现 cTnI 在预测围产期窒息后死亡率方面的敏感性和特异性都稍高一些^[45]。而 Kanik 等人报告说, cTnI 在预测足月新生儿缺氧缺血性脑病的死亡率方面具有低敏感性和高特异性^[46]。Shiva Rafati 提出, cTnI 可被认为是宫内缺氧

的标志^[47]。

而关于 cTnT 的临床应用, 也有类似的一些报道。Clark S J 提出, cTnT 升高与新生儿呼吸窘迫综合征的高死亡率之间存在相关性^[48]。Güneş Tamer 认为 cTnT 对于窒息相关的心脏变化是一个良好的决定因素^[49]。但是, 有一些研究者认为 cTnT 水平可能会受到复苏过程中肾上腺素的影响, 在早产儿中可能有很小或没有临床应用价值^[50]。

少数研究者也检测了 hs-cTnI 在分娩窒息中的诊断作用。Jiang Li 等人提出, 心肌损伤组 hs-cTnI 水平明显高于非心肌损伤组, 从而得出 hs-cTnI 是早期预测新生儿窒息心肌损伤的一个有用的生物标志物^[51]。这与之前的一些报道存在一致性^[52-53]。

新生儿窒息的发生发展为级联效应, 在不同的环节, 针对不同的器官, 多种指标均发生相应的变化。要做到早期诊断, 正确评估, 及时防治, 并不是要替换诊断标志, 而是要多种诊断相结合, 互相协助。随着医疗水平的发展, 生物标志物研究的不断深入, 一些新的生物标志物会不断涌现, 提高诊断的特异度和敏感度, 更好、更系统的指导临床抢救及判断预后。

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