·综　　述·

垂体腺瘤经鼻蝶入路术后并发DSH的危险因素

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【摘要】经鼻蝶入路神经内镜手术是治疗垂体腺瘤的手术方式之一，迟发性低钠血症（DSH）是术后常见并发症，发生率在3.6%~19.8%。尽管可以通过检测血清钠离子浓度明确诊断，但病人通常缺乏典型的临床症状，难以预测起病时间，易误诊、漏诊，从而增加病人的死亡风险。近年来，很多研究分析DSH的危险因素并进行归纳、总结，以改善DSH对垂体腺瘤病人术后预后的影响。本文就垂体腺瘤经鼻蝶入路神经内镜术后DSH的危险因素的研究进展进行综述，为临床提供参考。

【关键词】垂体腺瘤；经鼻蝶入路；神经内镜手术；迟发性低钠血症；危险因素

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Risk factors for delayed hyponatremia in patients with pituitary adenomas after transsphenoidal endoscopic surgery

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【**Abstract**】Transsphenoidal endoscopic surgery is a surgical method commonly used to treat pituitary adenomas. Delayed hyponatremia (DSH) is a frequent postoperative complication, with an incidence rate ranging from 3.6% to 19.8%. Although the diagnosis can be made by measuring serum sodium concentration, patients often lack typical clinical symptoms, making it challenging to predict the onset time and increasing the risk of misdiagnosis or missed diagnosis, ultimately leading to an increased risk of mortality. In recent years, numerous studies have analyzed and summarized the risk factors associated with DSH in order to improve its impact on the prognosis of patients with pituitary adenomas. This article provides a review of research progress on the risk factors for DSH following transsphenoidal endoscopic surgery for patients with pituitary adenomas, offering valuable insights for clinical practice.

【**Key words**】Pituitary adenoma; Transsphenoidal endoscopic surgery; Delayed hyponatremia; Risk factors

目前，经鼻蝶入路手术是垂体腺瘤的经典术式，但术后并发症仍是个值得关注的问题。迟发性低钠血症（delayed symptomatic hyponatremia，DSH）是垂体腺瘤经鼻蝶入路术后住院时间延长和再入院的常见原因[1]，发生率在3.6%~19.8%，多在术后4~12 d出现，术后7~8 d达峰值[2,3]。多种因素与DSH有关，然而尚未达成共识[4]。本文就垂体腺瘤经鼻蝶入路术后并发DSH的危险因素的研究进展进行综述。

1 发病机制

DSH的发生机制尚未得到共识，多推测是手术操作导致垂体后叶神经元释放的抗利尿激素（antidiuretic hormone，ADH）发生变化。DSH通常由抗利尿激素分泌失调综合征（syndrome of inappropriate antidiuretic hormone secretion，SIADH）引起，很少是由脑性耗盐综合征导致[3]。术后SIADH是垂体损伤导致下丘脑神经元不受控制地释放精氨酸加压素（arginine vasopressin，AVP），相对过量的AVP会导致尿液浓缩，增加尿钠排出；另一方面，由于细胞外液增加，心房利钠肽分泌增多，进一步增加尿钠排除[5]。

2 诊断

低钠血症的诊断标准为血钠<135 mmol/L，分为轻度（血钠131~135 mmol/L）、中度（血钠126~130 mmol/L）、重度（血钠≤125 mmol/L）。垂体腺瘤病人大多在术后72 h出院，如果没有预先告知低钠血症的相应症状和立即就医的必要性，可导致严重的后果[6]。DSH的症状可隐匿，或出现头痛、恶心、呕吐、嗜睡、躁动、神志不清等，症状严重情况下，不及时识别和治疗，可能会导致癫痫发作、昏迷，甚至死亡。有研究建议垂体腺瘤术后7 d常规进行血钠检测[7]。更多学者将注意力转移到危险因素的评估。

3 危险因素

Cote等[2]进行荟萃分析指出年龄、性别、肿瘤大小、血钠下降程度、库欣病是DSH潜在的预测指标，

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围手术期限制液体量以及补钠治疗等措施可以降低术后潜在的严重低钠血症的发生率。

3.1 一般指标 年龄、性别、肿瘤大小、肿瘤性质等因素与DSH的关系，意见尚不统一。Lee等[8]进行荟萃分析发现只有年龄是危险因素。彭雍等[9]研究认为性别及肿瘤相关指标作为危险因素无临床意义，ADH分泌调节功能下降存在临床意义。有研究显示，术后血钠水平较低以及手术时间长与DSH显著相关[10,11]。Tanaka等[12]认为高血压病人术后DSH的发生率较低。Cole等[13]发现术后运动量下降与DSH有关。

3.2 垂体功能减退 Tomita等[14]通过比较发现，DSH术后第二天的血钠水平显著低于正常无并发症的病人，并且DSH病人术前促甲状腺激素水平普遍升高，使用ACEI/ARB降压药物较多，而血清游离甲状腺素无明显差异。术前甲状腺功能减退及术前术后血钠差异大是DSH的独立预测因素[15]。Huang等[16]认为术前血清催乳素水平在预测无功能腺瘤发生DSH方面有一定的价值。代永庆等[17]发现术前存在垂体功能减退是发生DSH的独立危险因素，术后促肾上腺皮质激素（adrenocorticotropic hormone，ACTH）异常以及肿瘤腔高度显著变化同样是独立危险因素。Hong等[18]研究认为ACTH异常可能是DSH的主要原因。

3.3 垂体柄损害及鞍膈下陷程度 垂体柄作为连接垂体及下丘脑的存在，其异常可出现腺垂体功能减退或尿崩症等不良后果，那么手术所致垂体柄异常是否与DSH有关？临床发现，术中应该尽量减少对垂体的牵拉、挤压和损伤，注意保护垂体柄的供血，避免ADH分泌异常所致的DSH。研究发现肿瘤上下径较大导致肿瘤切除后鞍膈下陷越明显，术后发生DSH的概率越大，并且发现垂体腺瘤向上生长的趋势越快，垂体柄偏斜角越大，肿瘤切除后，垂体柄会急剧改变其原来的位置或形状，导致垂体柄受损，证实手术前后垂体柄偏角差异是DSH的独立预测因素[15,18,19]。代永庆等[17]认为肿瘤腔高度显著变化与DSH的发生密切相关，因为手术前后瘤腔高度的差异反映了肿瘤切除后鞍膈、瘤囊、蛛网膜或扁平垂体组织在垂体腺瘤上方的下沉深度，垂体柄易受损，进一步导致SIADH。

3.4 特定的计算方法 与其验证某一种或几种特定因素作为评估DSH的发生几率，不如通过计算机将DSH病人的激素水平、垂体MRI及一般观察数据进行综合分析，计算出DSH的发生几率，从而识别更有可能需要治疗的病人。Patel等[20]回顾性分析300例经鼻蝶入路手术治疗的垂体腺瘤的临床资料，以年龄、性别、手术时间、住院时间、术前血钠水平、出院用药、肿瘤大小等因素使用ROC曲线分析，开发了一个对有DSH风险的病人进行分层的评分系统。有学者选择使用机器学习技术进行预测建模，发现综合评估病人激素水平、手术前后垂体MRI以及术后血清钠等，较传统评估方法可降低发病率并提高安全性[21]。另有学者通过前瞻性研究验证了包含术后可测垂体柄长度、垂体柄偏离角度、术后尿崩症、鞍膈下陷深度和术后第二天血钠水平等预测因素的列线图来评估DSH风险[4,22]。李峰达等[23]使用XGboost算法建立包含垂体腺瘤病理、Knosp分级、腺瘤血供、切除程度、术前垂体激素水平、基础疾病病史等的预测模型，并基于SHAP算法对术后发生DSH的影响因素进行解释分析，认为有助于降低并发症发生率及改善病人的预后。另外，出院后，对病人进行出入量、体重及自我感觉的问卷调查可作为简便可行的预测方式[24]。然而，由于纳入病人数量较少，且有地域差异等问题，系统性评估工具并未普及，但是通过计算概率来评估DSH的发生率是一种新颖且可靠的研究方向。

4 治 疗

目前，尚无用于预防和管理垂体腺瘤经鼻蝶入路切除术常见并发症的标准化操作指南[25]，术后液体限制是预防DSH的有效方法[26,27]。采用较短干预时间的方法（POD 4-8）实施1 000 ml液体限制是一种非常成功且简单的策略，能够消除100%的DSH[7]。口服补钠为DSH的主要治疗方法，糖皮质激素及血管加压素V2受体拮抗剂（托伐普坦等）可辅助纠正低钠血症[28]。

综上所述，垂体腺瘤经鼻蝶入路切除术后并发DSH是再入院的常见原因。病人垂体激素水平、垂体柄改变以及鞍膈下陷程度等指标与其密切相关，值得更多的研究。文献报道的评估计算方法，由于地域等差异，并未达成共识，制定符合我国国人的计算方式是可行的方法。术后液体限制是预防及治疗DSH的有效方法。

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