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神经内镜垂体腺瘤术后延迟性低钠血症的临床研究

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摘　要

垂体腺瘤是最常见的鞍部病变，约占颅内肿瘤的10%~15%，在颅内肿瘤中仅次于胶质瘤和脑膜瘤。垂体腺瘤来源于垂体前叶的肿瘤，大部分为良性，极少数为恶性。垂体腺瘤特指起源于垂体前叶的肿瘤，多为良性，极少发生恶变。垂体瘤可通过异常分泌激素及压迫正常的神经组织而影响病人的生活质量及寿命。一般的治疗措施包括手术切除、药物治疗及放射治疗，目前除少数对药物反应良好的垂体瘤患者外，多数患者均需接受外科手术，以彻底切除无功能性腺瘤或控制有功能性腺瘤对激素水平的影响。传统开颅手术因手术时间长，创伤较大，并且容易损伤正常脑组织，目前逐步被经鼻蝶手术取代。然而，经鼻内镜手术通道狭小、操作复杂，患者出现术后并发症风险较高，如脑脊液鼻漏、电解质平衡紊乱、尿崩症及颅内感染等。本文就神经内镜垂体腺瘤的术后出现延迟性低钠血症作一概述。

关键词

垂体腺瘤，延迟性低钠血症，神经内镜

Clinical Study of Delayed Hyponatremia after Neuroendoscopic Surgery for Pituitary Adenoma

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Abstract

Pituitary adenoma is the most common saddle lesion, accounting for 10%~15% of intracranial

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tumors, second only to glioma and meningioma in intracranial tumors. Pituitary adenomas originate from tumors in the anterior pituitary, most of which are benign, and a few are malignant. Pituitary adenoma refers to the tumor originating from the anterior pituitary, which is mostly benign and rarely malignant. Pituitary tumors can affect the quality of life and life span of patients through abnormal hormone secretion and compression of normal nerve tissue. The general treatment measures include surgical resection, drug treatment and radiotherapy. At present, except for a few patients with pituitary adenoma who have good drug response, most patients need to undergo surgery to completely remove non-functional adenoma or control the effect of functional adenoma on hormone level. Traditional craniotomy has been gradually replaced by transsphenoidal surgery due to its long operation time, large trauma and easy damage to normal brain tissue. However, due to the narrow channel and complex operation of transnasal endoscopic surgery, patients have a high risk of postoperative complications, such as cerebrospinal fluid rhinorrhea, electrolyte imbalance, diabetes insipidus and intracranial infection. This article summarizes the delayed hyponatremia after neuroendoscopic surgery for pituitary adenoma.

Keywords

Pituitary Tumor, Delayed Hyponatremia, Neuroendoscopy

1. 引言

垂体瘤是颅内常见的良性肿瘤，其发病率约为 1/10 万，在颅内肿瘤中仅次于胶质瘤和脑膜瘤[1]。手术是垂体瘤的主要治疗方式，随着高清神经内镜技术的发展，经鼻蝶入路的神经内镜手术已成为垂体瘤手术的首选方式[2] [3]。尽管神经内镜手术具有微创、安全、有效的特点，但术后仍有各种并发症的可能性，其中延迟性低钠血症是术后病人再入院的常见原因。因此，早期预防和有效管理延迟性低钠血症具有重要的临床意义。本研究旨在探讨垂体瘤术后延迟性低钠血症的危险因素并提出有效的预防管理措施，为临床诊疗提供重要参考价值。

2. 垂体瘤的分类

1) 依据垂体瘤的大小可将垂体瘤分为微腺瘤(直径 < 1.0 cm)、大腺瘤(直径 ≥ 1.0 cm)和巨腺瘤(>3.0 cm)。

2) 依据垂体瘤细胞的免疫表型和分化来源谱系可分为生长激素细胞腺瘤、泌乳素细胞腺瘤、促甲状腺激素细胞腺瘤、促肾上腺皮质激素细胞腺瘤、促性腺激素细胞腺瘤、零细胞腺瘤、多激素与双激素细胞腺瘤[4]。

3) 术前经影像学(MRI)证实侵袭蝶窦、包绕颈内动脉或海绵窦的为侵袭性垂体瘤(Knosp1~4 级)；反之为非侵袭性腺瘤(Knosp 0 级)。

3. 垂体瘤的治疗方法

垂体瘤的治疗包括手术切除治疗、药物治疗和放射治疗。除对药物反应良好的泌乳素腺瘤外，其它类型的垂体腺瘤均首选手术方案[5] [6]。但需注意的是，常用于治疗 PRL (Prolactin)腺瘤的药物为多巴胺

受体激动剂，DA 虽能控制 PRL 腺瘤的激素水平，多不能治愈，需定期复查，并且可能使肿瘤的纤维组织增生从而给手术带来困难[7]。

3.1. 药物治疗

① 降低功能性腺瘤过多分泌的激素水平，改善症状。② 缩小肿瘤体积、限制肿瘤的生长。③ 对于无内分泌功能的腺瘤，一般发现时均肿瘤体积均较大，因长期压迫垂体，引起垂体功能降低，需补充外源性激素替代治疗。

3.2. 放射治疗

放疗可作为药物控制不佳，不能耐受手术，或术后残留/复发及手术切除困难腺瘤的治疗方案。垂体瘤的放射治疗包括一般放射治疗(CFRT)、立体定向放射外科(SRS)。SRS 可以一次/数次给予较高的放射剂量一般放射治疗，并且与一般放疗相比，SRS 可使激素水平下降更快、并发症更少，从而逐步取代了一般放射治疗；但对于大的、靠近视交叉的浸润性腺瘤，CFRT 仍有其优势[8] [9]放疗剂量的选择对预后至关重要，目前对于最佳的放疗剂量尚无确切定论[10]。放疗后并发症也不容忽视，常见的并发症有垂体功能减退，需补充外源性激素[11]。

3.3. 手术治疗

手术治疗可以迅速消除肿瘤的异常激素释放和占位效应，解除肿瘤对视交叉或神经的压迫，从而保护视力和神经的功能。手术可以概括分为 2 种：传统开颅术、经蝶窦手术。1) 传统开颅术：最早可追溯到 1889 年，Horsley 实施了第一台开颅垂体瘤手术，经过多年的研究与发展，目前主要有经额下入路、纵裂入路及翼点入路等。随着经鼻蝶手术的出现，开颅切除术逐渐被经蝶手术取代，但对于① 巨大的“哑铃型”腺瘤。② 侵犯颅前窝、颅中窝或颅后窝的肿瘤。③ 伴有颈内动脉或大脑前动脉动脉瘤。④ 术前检查提示质地硬的肿瘤[12]，开颅手术仍是较好的选择。2) 经蝶窦手术：最早由 Schloffer 于 1907 年提出并实施[13]，随着“微创”理念在医学上的提出以及高科技技术在临床中的应用，如神经导航，术中核磁，显微镜及内镜的出现等，使该术式发展迅速，目前绝大部分垂体瘤，及部分既往需开颅手术的病人都可首选此种术式。经鼻蝶术式安全、有效，并可选择性切除微腺瘤，无需牵拉脑组织，对正常垂体创伤小，并且缩短了病人住院时间等优点[14]。目前主要有显微镜下经鼻蝶入路和内镜辅助下经鼻蝶入路两种方式。有报道称，与显微镜下经蝶窦手术相比，内镜下手术治疗有更高的治愈率、缓解率和较少的术后并发症[15] [16] [17]。因此，经鼻蝶手术常成为首选入路。

4. 延迟性低钠血症的诊断标准[18]

术后 3 d 出现的血钠低于 135 mmol/L 为延迟性低钠血症。根据血钠水平分为：轻度低钠血症(Na：131~135 mmol/L)；中度低钠血(Na：126~130 mmol/L)；重度低钠血症，(Na：≤125 mmol/L)。

5. 低钠血症的症状

低钠血症患者可有多种临床表现，从无症状到轻度(头痛、恶心、呕吐)或严重症状。严重的低钠血症可导致意识水平的改变、脑水肿、癫痫发作，甚至死亡[19] [20]。

6. 延迟性低钠血症的原因与机制

部分研究表明，发生延迟性低钠血症的原因是对下丘脑－神经垂体系统的医源性损伤，导致抗利尿激素(ADH)的不受控制的释放[21] [22]。

据报道称，低钠血症与性别、年龄、肿瘤大小、垂体功能低下、一过性尿崩或是否为库欣病有关[23]-[29]，还有人认为微腺瘤更容易发生低钠血症，因为术中需要探查更广的范围来寻找和切除病变[30]。另一份研究认为低钠血症与身高体重指数(BMI)呈正相关[29]。还有一篇文献表明，经鼻蝶术中垂体柄受损是引起水、电解质失衡的主要原因[31]。

延迟性低钠血症的产生机制，一般认为是抗利尿激素分泌异常综合征(SIADH)或脑性盐耗综合征(CSW)造成的。SIADH 又称为 Schwartz-Bartter 综合征，SIADH 的主要临床表现是由于下丘脑神经垂体系统损伤后，抗利尿激素分泌物(ADH)不受控制地释放，导致延迟性低钠血症，导致水潴留。ADH 的主要作用为增加远端肾小管细胞的通透性，增加水的重吸收，稀释血液，浓缩尿液。正常情况下刺激 ADH 分泌的最强的生理刺激为血浆渗透压的增高，只要血浆渗透压较正常变化超过±2%，ADH 的分泌就会有相应的变化，其次为血管内容物的降低。ADH 的过量分泌，导致体内潴留过多的液体，造成稀释性低钠血症。主要的实验室指标为低血钠、血浆渗透压降低，但尿钠高。临床可行补水试验来确定是否为 SIADH。治疗主要为限制限制液体摄入，必要时给予药物治疗。而 CS 定义为颅内病变引起钠经肾丢失，造成的低钠血症及全身血容量不足的症状，可出现在多种颅内疾病中，报道最多的为蛛网膜下腔出血，外伤及颅内感染，具体产生的机制不详，有文献表明可能与脑组织释放的利尿肽(BNP)有关[32]，还有研究结果显示可能因交感神经系统功能紊乱，不能促进肾素的释放及钠的重吸收所致[33]。临床中应予以鉴别 SIADH 和 CSW，两者的临床表现及实验室检查甚至可以相同，其中细胞外液量和盐平衡最重要，但两者的治疗措施完全不同。SIADH 主要为限制液体的摄入，而 CSW 则需要及时补液和钠盐。另外，若术后病人垂体功能低下，肾上腺功能不全，也可导致低钠血症的出现[34]，治疗前先明确患者的激素水平，有文献称氢化可的松可以促进肾脏对钠的吸收。但需要强调的是，补充钠盐速度不能过快，过快则可能导致渗透性脱髓鞘综合征，即脑桥及周围组织、大脑皮层的白质脱髓鞘引起的综合征，临床表现为精神状态的改变，脑神经功能损伤、隐匿性四肢无力等。

7. 延迟性低钠血症的危害

延迟性低钠血症经常被临床医生忽视。但这是重新入院的主要原因[35] [36]。

延迟性低钠血症的管理具有挑战性，因为对其发生的预测因素的了解有限。此外，其临床治疗方法是复杂且大多数的治疗需要在重症监护病房进行密切观察和频繁的实验室检测，从而导致高昂的医院费用[37]。

8. 延迟性低钠血症的危险因素

既往研究报道，年龄较大、术后 1~2 天钠浓度低、手术时间长、BMI 低、年龄较小、鞍膈膜的下降、术前血钠含量低是迟发性低钠血症的预测因素[20] [38] [39]。此外，由于对抗利尿激素反应的性别差异，女性比男性更容易发生术后迟发性低钠血症[40]。另一项研究报道，肿瘤越大，手术中垂体柄的破坏就越多，术后发生延迟性低钠血症的可能性就越高[41]。Jahangiri 报道，术前垂体功能低下是手术中垂体柄和垂体后叶机械操作的标志，因此是术后低钠血症发生的潜在危险因素。术前甲状腺功能减退是术后迟发性低钠血症的独立预测因素。甲状腺功能减退可通过增加 ADH 水平和肾内机制引起低钠血症[19]。低甲状腺素水平会导致心排血量减少，刺激颈动脉窦内的压力感受器，并释放抗利尿激素。此外，低甲状腺素水平还可以通过减少流向远端肾小管和收集管的原始尿量来降低肾小球滤过率和游离水的排泄[42]。因此，对于术前甲状腺功能减退的患者，可采用适当的补充甲状腺素，以减少术后低钠血症的发生。

9. 延迟性低钠血症的管理

延迟性低钠血症的患者均进行限水治疗，根据低钠血症程度的不同，治疗计划也有差异。轻度低钠

血症，给予限制液体入量及口服钠盐，多数可以纠正。中重度延迟性低钠血症，除了静脉补充钠之外，还可以给予少量激素及利尿剂纠正。

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