

三叉神经痛的外科治疗进展研究

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收稿日期: 2023年1月16日; 录用日期: 2023年2月11日; 发布日期: 2023年2月20日

摘 要

三叉神经痛是在面部三叉神经分布区域内反复发作的一种短暂性神经痛, 严重影响患者的日常生活及精神状态。对于药物治疗无效时应尽早考虑手术治疗, 目前外科治疗手段大致分为开颅手术、经皮神经损伤及立体定向放射治疗3类, 各类手术方式的适应症及优缺点各有不同, 现本文将就这3类治疗方式的临床应用展开综述, 旨在为三叉神经痛的个体化手术治疗提供一定的科学依据。

关键词

三叉神经痛, 开颅手术, 经皮神经损伤术, 立体定向放射治疗

Progress in Surgical Treatment of Trigeminal Neuralgia

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Received: Jan. 16th, 2023; accepted: Feb. 11th, 2023; published: Feb. 20th, 2023

Abstract

Trigeminal neuralgia is a kind of transient neuralgia that occurs repeatedly in the distribution area of facial trigeminal nerve, which seriously affects the daily life and mental state of patients. Surgical treatment should be considered as soon as possible when drug treatment is ineffective. At present, surgical treatment methods are roughly divided into craniotomy, percutaneous nerve injury and stereotactic radiotherapy. The indications, advantages and disadvantages of various surgical methods are different. Now, this article will review the clinical application of these three types of surgical methods in order to provide certain scientific basis for the individualized surgical treatment of trigeminal neuralgia.

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Keywords

Trigeminal Neuralgia, Craniotomy, Percutaneous Nerve Injury, Stereotactic Radiotherapy

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1. 引言

三叉神经痛(Trigeminal neuralgia, TN)是在面部三叉神经分布区域内反复发作的一种短暂性神经痛。疼痛可由常见的日常活动而触发,如说话、洗脸亦或是微风拂面时,严重影响患者的日常生活及精神状态[1] [2]。尽管全球每年 10 万人中仅有 12.6~27 人罹患此病,但由于其特殊疼痛性质对患者生活质量的不良影响,研究三叉神经痛的个体化治疗具有重要的临床意义[3] [4]。

TN 分为由神经血管压迫(Neurovascular compression, NVC)所致的经典型 TN、由颅内肿瘤、脑动脉瘤、多发性硬化症等神经系统疾病所致的继发型 TN、无 NVC 及三叉神经根形态学变化的特发型 TN [5]。国际指南和国内专家共识指出,口服钠通道阻滞剂药物是 TN 的一线治疗方式,而当药物疗效不佳或严重的药物副作用导致患者无法耐受时,应考虑尽早行手术治疗[6] [7]。手术大致分为开颅手术、经皮神经损伤及立体定向放射治疗 3 类。各类手术方式的适应症及优缺点各有不同,现本文将就这 3 类治疗方式的临床应用展开叙述,旨在为 TN 的个体化手术治疗提供一定的科学依据。

2. 开颅手术

2.1. 微血管减压术(Microvascular decompression, MVD)

早在 1929 年, Walter Dandy 就已通过类似乳突后枕下入路的途径暴露三叉神经,并无意中使用了 MVD 治疗了第 1 个 TN 患者[8]。随后通过总结 250 例 TN 患者手术过程中三叉神经根的解剖特点提出,桥前池三叉神经根进入区的血管压迫是 TN 的病理生理机制[9]。经过二十世纪神经外科医学届的不断探讨, MVD 技术发展至今已成为了治疗经典型 TN 的一线手术方案。

临床医生首先应用磁共振成像检查(Magnetic resonance imaging, MRI)初步明确血管压迫位置,其次通过开颅、后颅窝检查确认压迫或与三叉神经粘连的责任血管,解除压迫后使用 Teflon 垫片或 Ivalon 海绵将其与神经根分离开[10]。也有报道称使用缝合线、生物胶制作 Teflon 吊索也能实现完全减压[11]。在静脉压迫三叉神经的情况下,也可以使用双极烧灼来分割静脉。

MVD 术后疼痛缓解率可达 80%~90%,治疗效果持续时间最长,通常为 10 年以上,70%的患者在术后 10 年可达到疾病完全缓解,无疼痛症状出现。另外 4%的患者偶尔会有疼痛,也不需要长期药物治疗[12] [13]。Holste 等人[14]通过对 46 项研究 3897 名 TN 患者进行荟萃分析后发现,术后 1.7 ± 1.3 年的随访时间中,76%的患者可无三叉神经痛症状,与疾病预后相关的因素包括症状持续时间 ≤ 5 年、动脉而不是静脉或其他因素所致的神经根压迫、小脑上动脉受累和 Burchiel I 级疼痛。但值得注意的是,因开颅手术需暴露 IV-XII 颅神经,5%~10%患者会出现三叉神经麻木和感觉障碍、1%~20%患者会出现听力损伤、3%~4%患者会出现脑脊液漏以及罕见的面部神经麻痹,该手术相关死亡率为 0.2% [12] [15] [16]。而且由于减压材料移位、责任血管遗漏、非动脉压迫、高龄和较长病程等原因,约 10%的患者会在术后 2 月左右出现复发。传统显微镜联合神经内镜、MVD 联合部分感觉根切断术、二次手术时使用医用胶充分

悬吊压迫血管等方法可降低复发率, 分别为 2.3%、1%、1.2% [17]。

2.2. 感觉根部分切断术(Partial sensory rhizotomy, PSR)、神经内松解术

在 MVD 术中未见任何责任血管压迫三叉神经根时, 可考虑使用感觉根部分切断术代替 MVD, 或与 MVD 联合治疗。在接近桥脑处切断感觉根后外侧的 3/4 神经纤维, 能使三叉神经整个分布区的痛觉消失, 而仍能保留部分触觉。PSR 的疗效较 MVD 稍差, 术后约 48%~86% 患者可达到完全无痛[18] [19]。除此之外, 还可考虑使用神经内松解术在三叉神经根进入区将神经纤维纵向分裂为 2~6 个束, 破坏神经纤维的髓鞘和部分轴突, 抑制疼痛信号的传导。其疼痛的有效缓解率也可达 72%~82.1% [20] [21]。上述其他手术方式的并发症发生率与 MVD 类似, 但其具体疗效还需进一步研究。因此当术中未发现明显的动脉压迫部位或二次 MVD 时, 可酌情考虑采用 PSR、神经内松解术治疗 TN。

3. 经皮神经损伤术

经皮损伤神经损伤术是通过卵圆孔穿刺定位三叉神经节, 采用机械压迫、射频热凝、酒精或甘油阻断等方法有选择性地损伤传导痛觉的神经纤维, 从而干扰疼痛传递达到治疗效果。靶向三叉神经的常用方法包括超声引导、X 光透视及 CT 导航。其中超声引导是经皮靶向三叉神经浅表分支的常用办法, X 光透视在临床中常为常见, CT 导航改善了穿刺路径的可视化、提高了手术效率。

3.1. 经皮穿刺球囊压迫术(Percutaneous balloon compression, PBC)

PBC 是一种经面部、卵圆孔穿刺途径将球囊导管置于 Meckel 腔, 通过注入对比剂充盈球囊压迫三叉神经半月节治疗三叉神经痛的技术, 目前主要适用于 MVD 复发及高龄等人群。

根据研究表明, PBC 术后疼痛缓解率约为 82%~97.1%, 疼痛缓解时间约为 18~20 个月[22]。PBC 术后复发时间平均为 11.8 月, 较 MVD 晚(9 个月) [23]。术后患者发生颅内感染, 术中大出血, 神经功能损害等并发症相对较少, 但 PBC 为神经损毁性手术, 从病因学角度来看, 从根本上并未解决三叉神经痛。此外, PBC 压迫三叉神经痛觉纤维的同时仍有损伤味觉及运动纤维、由于三叉神经心脏反射引起的血压和心率急性变化等可能, 术后患者出现面部麻木、咀嚼肌无力、味觉减退等并发症明显高于 MVD 等手术治疗[24] [25]。手术的最终疗效主要与术中球囊形态、压迫时间和球囊压力有关, 标准梨形组患者疼痛缓解率明显高于非梨形组, 这与术者的治疗经验以及术中所使用设备有较大关系[26]。目前有报道称在采用 CT 导航下球囊压迫治疗三叉神经痛有确切疗效, 可减轻患者的疼痛程度, 降低并发症发生率和复发率, 具有较高的应用意义, 另外机器人辅助下或神经导航技术精确识别卵圆孔所在位置, 也不乏为 PBC 术前技术应用的可选方式[27]。

3.2. 化学去神经法

自 19 世纪以来, 甘油、无水酒精、苯酚注射三叉神经节或分支就已用于 TN 的治疗。其作用机制尚不清楚, 目前普遍认为是化学药物导致了受损神经纤维中轴突鞘的选择性溶解, 阻断了疼痛信号的传导, 或是三叉神经节内突触电位的正常化导致疼痛减轻。Han 等人研究发现, 在眶下神经、眶上神经、上颌神经、下颌神经处注射无水酒精治疗 TN, 术后 1 年、2 年、3 年和 5 年的疼痛缓解概率分别为 86.2%、65.5%、52.5% 和 33.4%, 该疗法可以反复使用, 且疗效不会随着注射次数增加而降低[28]。由于无水酒精阻滞三叉神经疗法的并发症发生率约为 1%~33%, 包括轻微的短暂烧灼感、感觉障碍, 严重可致皮肤坏死、吞咽困难、面瘫等, 目前临床已较少使用。

神经鞘内注射苯酚也具有一定疗效, 研究表明约 87% 患者术后可达到疼痛明显缓解或完全缓解, 但长期接触苯酚具有严重的肾毒性、皮肤及胃肠道损害, 故其主要用于缓解晚期颅内恶性肿瘤所致 TN [29]

[30]。而在甘油注射去神经治疗中,相关研究表明术后疼痛缓解率约为70%~90%,20%~40%患者在术后20~60个月内出现复发[31][32]。综上所述,甘油较无水酒精、酚类物质在局部组织内滞留时间较长,对周围其他神经损害较小。

3.3. 射频消融

射频消融治疗疗效显著,局麻下即可进行,是治疗TN最常见的经皮手术,特别是在老年患者中。一般在X线、CT等透视辅助装置下置入电极,通过电刺激、热凝破坏三叉神经感觉纤维,达到镇痛效果。Kanpolat等人在针对使用射频消融术治疗的1600例患者术后25年的跟踪随访研究中发现,97.6%的患者术后无疼痛,7.7%的患者在术后6个月内出现复发,另外有17.4%的患者出现晚期疼痛复发[33]。射频消融术的并发症包括角膜反射减弱、咬肌无力、感觉异常、角膜炎和颅神经麻痹。极少部分患者会出现脑脊液泄漏、颈动脉海绵状瘘、脑膜炎和麻木性疼痛。

除射频热凝外,冷冻消融也在TN临床治疗中有所应用。其作用机制是在 -60°C 至 -140°C 之间,神经轴突受低温影响断裂。早在1976年Lloyd就已首次描述了阻断周围神经的冷冻疗法[34],之后也有大量研究陆续报道冷冻消融的临床疗效。Zakrzewska等人[35]发现在145名接受冷冻消融治疗的患者中,疼痛缓解时间仅为6个月,且平均复发时间为术后24个月。Bansal等人[36]反而在49例TN患者中发现,仅有4.08%的患者在术后18个月内复发,48.97%的患者术后36~40个月复发,考虑冷冻消融治疗是一种安全、经济的治疗手段,建议复发患者重复治疗。但关于冷冻循环的次数或温度是否会影响术后长期疗效,目前还缺乏系统的研究。而且与其他经皮技术相比,总体上无疼痛生存期较短,很少有医生推荐冷冻消融术作为TN患者的一线治疗选择。

4. 立体定向放射治疗

随着影像学、立体定向技术及计算机技术的不断发展,1971年瑞典神经外科教授Leksell[37]应用立体定向放射外科技术以伽玛线照射三叉神经半月节。但早期选择三叉神经半月节作为靶点,治疗效果并不理想。Lindquis等[38]选择三叉神经感觉根桥脑进入区作为照射靶点,其有效率得到较大提高,且没有任何并发症,目前得以大量推广应用。伽马刀手术(Gamma knife surgery, GKSS)是通过多条Y射线照射在靶区形成小范围的高剂量区(70~90 Gy)。有文献显示60~97 Gy是伽马刀治疗三叉神经痛的最佳照射剂量[39]。目前的II级证据表明,最小有效剂量为70 Gy,最大有效剂量为90 Gy。当剂量超过90 Gy时,会导致更多的并发症。GKS对三叉神经进入区感觉支传导通路进行破坏,达到治疗三叉神经痛的目的,而神经感觉支的破坏是缓慢渐进的,因此对比其他的外科治疗手段来说,伽马刀治疗具有起效慢、短期缓解率低等特点。

与其他经皮或开放手术方法不同,放射治疗并不能立即缓解疼痛。相关研究表明,患者疼痛症状一般在术后半年内能得到逐步缓解[40][41]。但GKS治疗复发率偏高,这可能与神经纤维的自我修复有关。GKS的优势在于非侵袭性、安全、适于任何年龄,任何具有基础疾病的且无法耐受的都可以接受GKS治疗,并且在经济方面大多数的患者能够接受,对于复发后还可进行二次GKS治疗等优势,对于继发型TN(较小肿瘤压迫),原发型TN血管压迫明显的患者效果更佳。其相对于MVD手术来说并发症较少,包括面部感觉减退、感觉异常等,但大多随着时间的推移可逐渐缓解。总之在高龄、基础疾病较多无法耐受手术、恐惧手术、药物控制不佳的TN患者中,GKS治疗不乏为一种不错的选择。

总的来说,TN患者手术治疗方式的选择主要是由其临床分型决定的。经典型、继发型TN患者治疗原则相同,MVD是首选治疗方案;对于没有明显NVC的TN患者,射频消融与MVD治疗均可考虑。如前所述,每种手术方式都有一定的优缺点,但关于哪些病人、何时应该接受手术还存在争议,未来的

研究应集中于使用独立评估手术结果的前瞻性研究,探索新药和新的外科治疗手段,开发更多联合治疗方案。

药物和手术治疗是 TN 众所周知的治疗方式,这些疗法大多数情况下都能控制疼痛,但随着时间的推移,临床疗效不是永久的,许多患者需要多种治疗方式联合控制疼痛。此外药物治疗及慢性疼痛可能会引起神经心理障碍。因此除了提供多学科外科医疗管理外,还建议为患者提供心理和护理支持。未来迫切需要开展对 TN 的病理生理学和预后的研究,并针对 TN 患者生活质量变化提出更加标准化的评估工具,以便对不同研究的结果进行更可靠的比较。

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