·文献综述·

# 地塞米松玻璃体内植入剂移位至前房的研究进展

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**摘要**
地塞米松玻璃体内植入剂(Ozurdex)不仅能治疗视网膜静脉阻塞继发的黄斑水肿、糖尿病性黄斑水肿和非感染性后葡萄膜炎,还能治疗内眼手术后黄斑水肿和其他炎症相关的眼底疾病继发的黄斑水肿。随着地塞米松玻璃体内植入剂广泛应用,不常见的并发症,如地塞米松玻璃体内植入剂移位至前房,逐渐受到重视。地塞米松玻璃体内植入剂移位至前房多见于悬韧带-晶状体囊膜复合体不完整、玻璃体切除术后的患眼。地塞米松玻璃体内植入剂移位至前房后多沉于下方房角,似前房积脓,可引起视力下降和眼痛,常并发角膜水肿和高眼压。合并角膜水肿的患眼应尽快复位或取出地塞米松玻璃体内植入剂,以降低角膜内皮失代偿风险。缩瞳和避免诱因,如俯卧、跳跃、长途飞行等,可以预防地塞米松玻璃体内植入剂移位至前房。文章主要综述了地塞米松玻璃体内植入剂移位至前房的研究进展,以期为地塞米松玻璃体内植入剂移位至前房的诊治和预防提供参考。
**关键词**:地塞米松玻璃体内植入剂;移位;前房;角膜水肿;黄斑水肿
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## Research progress on the migration of intravitreal dexamethasone implant into anterior chamber

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## Abstract
• Dexamethasone intravitreal implant (Ozurdex) is approved for the treatment of macular edema secondary to retinal vein occlusion, diabetic retinopathy, and non-infectious uveitis. It has also been reported to treat macular edema after intraocular surgery and macular edema secondary to other inflammation-related ocular fundus diseases. With the widespread application of dexamethasone intravitreal implant, uncommon complications such as migration of dexamethasone intravitreal implant into the anterior chamber are gradually receiving attention. Anterior chamber migration of dexamethasone intravitreal implant usually occurs in the eyes with an incomplete complex of suspensory ligament and lens capsule or after vitrectomy. After dexamethasone intravitreal implant migrates into the anterior chamber, it tends to sink to a lower angle, resembling hypopyon, causing vision impairment and eye pain, accompanied by corneal edema and intraocular hypertension. If corneal edema occurs, dexamethasone intravitreal implant should be repositioned or removed as soon as possible to reduce the risk of corneal endothelial decompensation. Miosis and avoiding predispositions, such as lying prone, jumping, or long flights, can prevent dexamethasone intravitreal implant from migrating into the anterior chamber. In this paper, the recent advances in anterior chamber migration of dexamethasone intravitreal implant are reviewed to provide a reference for the diagnosis, treatment, and prevention.
• KEYWORDS: dexamethasone intravitreal implant; migration; anterior chamber; corneal edema; macular edema

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## 0 引言

地塞米松玻璃体内植入剂(商品名 Ozurdex)是含 0.7 mg地塞米松、直径 0.46 mm、长 6 mm 的棒状聚乳酸-乙醇酸聚合物,通过预装推注器 22 G 针头注射入玻璃体腔,持续缓慢释放地塞米松长达 6 mo,可治疗视网膜静脉阻塞继发的黄斑水肿、糖尿病性黄斑水肿[1]、非感染性后葡萄膜炎[2]。泛美协作视网膜研究组调查 11 个拉丁美洲中心 468 例患者 764 次玻璃体内注射地塞米松玻璃体内植入剂治疗,发现地塞米松玻璃体内植入剂移位至前房发生了 12 次,按次计发生率 1.6%[3]。Betsch 等[4]调查 32 例地塞米松玻璃体内植入剂移位至前房患者的临床记录,发现 27 例(84.4%)确诊时角膜水肿,12 例(37.5%)经过复位或取出治疗后仍因角膜内皮失代偿需行角膜内皮移植治疗。

地塞米松玻璃体内植入剂移位至前房虽然不常见,但可引起角膜水肿,严重者因角膜内皮失代偿需行角膜内皮

移植。因此,地塞米松玻璃体内植入剂移位至前房引起了临床医师的重视。本文对地塞米松玻璃体内植入剂移位至前房的危险因素、临床表现、治疗、预防及同类产品进行综述。

## 1 危险因素

Khurana 等[5]研究发现,15 例地塞米松玻璃体内植入剂移位至前房患眼全部都曾经历玻璃体切除手术,其中 14 例没有晶状体囊袋,剩余 1 例囊袋完整、内装有人工晶状体但部分悬韧带离断。Gonçalves 等[3]研究发现,经历玻璃体切除术的患眼地塞米松玻璃体内植入剂移位至前房的发生率为 4.8%(7/147),而未经历的患眼发生率为 1.6%(5/321);经历白内障手术的患眼地塞米松玻璃体内植入剂移位至前房的发生率为 3.4%(12/350),而未经历的患眼发生率为 0.0%(0/118)。Röck 等[6]研究发现,在人工晶状体患眼中,经历玻璃体切除手术的患眼与未经历的患眼相比,发生地塞米松玻璃体内植入剂移位至前房的风险更高($OR$=50.4,95%$CI$:2.7-945.2);在经历玻璃体切除手术的患眼中,悬韧带-晶状体囊膜复合体不完整的患眼与完整的患眼相比,发生地塞米松玻璃体内植入剂移位至前房的风险更高($OR$=58.7,95%$CI$:2.9-1171.2)。

可活动的地塞米松玻璃体内植入剂和沟通前房与玻璃体腔的通道,是地塞米松玻璃体内植入剂移位至前房的必要条件。经历玻璃体切除手术的患眼缺少黏滞地塞米松玻璃体内植入剂的玻璃体纤维,因此地塞米松玻璃体内植入剂在玻璃体腔漂浮,容易受体位、房水循环等影响向前移位。晶状体、悬韧带和虹膜是前房与玻璃体腔的屏障,可以阻挡地塞米松玻璃体内植入剂移位至前房。晶状体、悬韧带和虹膜结构异常,如无晶状体[7]、后囊膜破裂[3]、悬韧带离断[8-9]、虹膜周切孔[10]、虹膜缺损[11]等,可以为地塞米松玻璃体内植入剂从玻璃体腔移位至前房提供通道。部分患眼地塞米松玻璃体内植入剂移位至前房的通道比较隐匿,需要临床医师仔细检查分析。Kocak 等[9]报道 1 例晶状体后囊膜完整且内装后房型人工晶状体患眼,地塞米松玻璃体内植入剂植入 5 wk 后被发现前移至完整囊袋内人工晶状体后方,推测细长的地塞米松玻璃体内植入剂通过悬韧带缝隙前移。

此外,面朝下俯卧位[12-13]、跳跃[8]、长途飞行[14]等诱发因素对地塞米松玻璃体内植入剂移位至前房的发生具有重要作用。Pacella 等[14]报道 1 例巩膜固定的人工晶状体眼因持续性黄斑水肿接受玻璃体注射地塞米松玻璃体内植入剂治疗,长途飞行后出现视力下降、眼痛,经检查发现地塞米松玻璃体内植入剂移位至前房,推测飞行过程中眼内压力受气压影响发生急剧变化,促使玻璃体腔地塞米松玻璃体内植入剂移位至前房。

## 2 临床表现

地塞米松玻璃体内植入剂完全进入前房后常沉于下方房角,容易被误认为前房积脓。地塞米松玻璃体内植入剂移位至前房患者最常见的症状是视力下降和眼痛。Betsch 等[4]调查 32 例地塞米松玻璃体内植入剂移位至前房患者的症状,发现 29 例(90.6%)诉视力下降,10 例(31.3%)诉眼痛,3 例(9.4%)诉眼内有“白线”,2 例(6.3%)未诉不适。

地塞米松玻璃体内植入剂移位至前房患者最常见的并发症是角膜水肿、高眼压。Gonçalves 等[3]调查 12 例地塞米松玻璃体内植入剂移位至前房患眼,发现 11 例(91.7%)确诊时角膜水肿,7 例(58.3%)确诊时眼压高。Betsch 等[4]调查 32 例地塞米松玻璃体内植入剂移位至前房患眼,发现 27 例(84.4%)确诊时角膜水肿。

Malclès 等[15]通过角膜内皮显微镜检查发现地塞米松玻璃体内植入剂移位至前房患眼角膜内皮细胞计数下降,推测地塞米松玻璃体内植入剂在前房可损伤角膜内皮细胞,进而引起角膜水肿和视力下降。有学者推测,角膜内皮细胞损伤可能是因为地塞米松玻璃体内植入剂成分(地塞米松、乳酸或乙醇酸)的化学毒性或与坚硬的地塞米松玻璃体内植入剂摩擦引起的机械创伤[5]。Chen 等[16]体外实验发现,高浓度地塞米松可以抑制牛角膜内皮细胞增殖,并诱导其凋亡和(或)坏死。然而,地塞米松前房内植入剂(商品名 Surodex)的安全性数据并不支持地塞米松玻璃体内植入剂成分毒害角膜内皮细胞。地塞米松前房内植入剂是含 60 μg 地塞米松、直径 0.5 mm、长 1.0 mm的棒状聚乳酸-乙醇酸聚合物,常被放置在 6 点位房角,可缓慢释放地塞米松约 7-10 d,适用于减轻白内障手术后前房炎症。2 项随机对照临床试验比较地塞米松前房内植入剂与 0.1%地塞米松滴眼液对白内障术后炎症的治疗效果,发现两组患眼在眼内炎症的主观评估和角膜内皮细胞计数方面无显著差异[17-18]。

长期使用糖皮质激素可引起小梁网组织形态改变,使房水流出阻力增加,进而引起眼压升高和眼胀痛[19]。高眼压是地塞米松玻璃体内植入剂的常见并发症[1-2]。Mathis 等[2]回顾性分析经地塞米松玻璃体内植入剂治疗的 152 例葡萄膜炎患者的医疗记录,发现 28.3%出现高眼压。有学者认为,玻璃体内糖皮质激素植入剂移位至前房后可能增加房水中糖皮质激素浓度,进而增加高眼压的发生率[20]。

## 3 治疗

地塞米松玻璃体内植入剂移位至前房患眼应根据具体情况接受个性化治疗。若患眼无角膜水肿,可随访观察。若患眼有角膜水肿,需尽快复位或取出,并根据角膜水肿消退情况酌情行角膜内皮移植治疗。高眼压多可用降眼压药物控制[21]。

**3.1 随访观察** 针对无角膜水肿的患眼,可考虑随访观察,等待地塞米松玻璃体内植入剂完全降解。Zafar 等[22]报道 1 例 74 岁男性患者在地塞米松玻璃体内植入剂植入 2 wk 后检查发现地塞米松玻璃体内植入剂嵌在虹膜与虹膜爪型人工晶状体之间且未接触角膜,无角膜水肿、高眼压;确诊 4 wk 后检查发现地塞米松玻璃体内植入剂明显降解;确诊 8 wk 后检查发现地塞米松玻璃体内植入剂完全降解。Eadie 等[23]报道 1 例 48 岁男性患者在地塞米松玻璃体内植入剂植入 3 mo 后检查发现地塞米松玻璃体内植入剂移位至前房,位于下方房角,无角膜水肿、高眼压;确诊 4 mo 后检查发现地塞米松玻璃体内植入剂明显降解。地塞米松玻璃体内植入剂移位至前房患眼未出现角膜水肿,原因可能是地塞米松玻璃体内植入剂未与角膜内皮接触造成机械损伤,或者地塞米松玻璃体内植入剂在降解过程中硬度下降,对接触的角膜内皮损伤减小。

**3.2 复位至玻璃体腔** 针对角膜水肿且晶状体囊袋缺如的患眼,可考虑将前房地塞米松玻璃体内植入剂复位至玻璃体腔。传统的非手术复位方法是散瞳后让患者保持仰卧位、头后仰,使前房地塞米松玻璃体内植入剂在重力作用下经瞳孔返回玻璃体腔。如地塞米松玻璃体内植入剂

黏附于下方房角,固定不动,可尝试轻轻叩下眼睑[12],或表面麻醉后湿棉签轻轻叩眼球[23],使地塞米松玻璃体内植入剂游离。Rivera-Pérez 等[24]为缩短巩膜固定的人工晶状体患眼复位时间,提出在地塞米松玻璃体内植入剂完全进入瞳孔区后,抬高患者头部并要求患者向下看,使地塞米松玻璃体内植入剂从虹膜与人工晶状体之间滑入玻璃体腔。Ahuja 等[25]提出诊室内急诊手术复位地塞米松玻璃体内植入剂,在裂隙灯显微镜下用 30 G 针头从周边角膜刺入前房,轻轻拨动下方房角的地塞米松玻璃体内植入剂,使其穿过瞳孔回到玻璃体腔。复位至玻璃体腔可以使地塞米松玻璃体内植入剂继续发挥治疗作用,但需要注意防范地塞米松玻璃体内植入剂再次移位至前房。

**3.3 手术取出** 针对角膜严重水肿、反复移位至前房或前房与玻璃体腔通道隐匿的患眼,需尽快取出前房地塞米松玻璃体内植入剂,以降低角膜内皮失代偿风险。传统的取出方法是前房填充黏弹剂后眼内镊夹取出地塞米松玻璃体内植入剂。手术难点是,降解中的地塞米松玻璃体内植入剂易碎裂,尤其是眼内镊夹持地塞米松玻璃体内植入剂时和经角膜切口取出地塞米松玻璃体内植入剂时。Stelton 等[26]提出,采用斜角镊沿地塞米松玻璃体内植入剂长轴夹持并保护地塞米松玻璃体内植入剂以避免地塞米松玻璃体内植入剂碎裂。此外,可以使用管状工具,如人工晶状体滑道(lens glide)[27]、人工晶状体植入舱(lens injector)[28]、静脉插管[29]、注射器针头[30-31]等,在前房内接引并保护地塞米松玻璃体内植入剂以避免地塞米松玻璃体内植入剂碎裂。Depla 等[31]描述使用 19 G 针头取出前房地塞米松玻璃体内植入剂的方法。手术过程如下:(1)角膜缘作 2 mm 切口,前房注入适量黏弹剂以维持前房并调整地塞米松玻璃体内植入剂位置至一端朝向角膜切口;(2)19 G 针头斜面向角膜,进入前房对准地塞米松玻璃体内植入剂一端,使地塞米松玻璃体内植入剂一端进入针管,且地塞米松玻璃体内植入剂长轴与针管呈一条直线;(3)轻轻拉注射器柱塞,地塞米松玻璃体内植入剂完全抽吸至针管内后取出;(4)冲洗清除前房内黏弹剂,2 mm角膜切口一般不需要缝合。此外,Stewart 等[32]提出无接触取出地塞米松玻璃体内植入剂的手术方法。手术过程如下:(1)缩小瞳孔,表面麻醉,在地塞米松玻璃体内植入剂对侧角膜缘作 2.75 mm 切口,酌情扩大至 3 mm;(2)前房注入黏弹剂充盈,地塞米松玻璃体内植入剂周围注射黏弹剂使其长轴指向切口,地塞米松玻璃体内植入剂近切口端下方注射黏弹剂使其抬高;(3)针管压迫角膜缘切口后唇使地塞米松玻璃体内植入剂随黏弹剂溢出;(4)冲洗前房剩余黏弹剂,10-0 线缝合角膜缘切口。地塞米松玻璃体内植入剂取出后,患眼黄斑水肿恶化[33],可考虑玻璃体内注射曲安奈德、阿柏西普等替代治疗[34-35]。

## 4 预防

**4.1 避免诱因** 研究报道的诱发因素包括面朝下俯卧位[12-13]、跳跃[8]、长途飞行[14]。地塞米松玻璃体内植入剂治疗的患者,尤其是悬韧带-晶状体囊膜复合体不完整、玻璃体切除术后的患者,应避免上述诱因,以预防地塞米松玻璃体内植入剂移位至前房。

**4.2 缩小玻璃体腔与前房的通道** 瞳孔是地塞米松玻璃体内植入剂移位至前房的常见通道。避免散瞳检查[36],甚至滴用毛果芸香碱滴眼液以缩小瞳孔[37-38],可以预防地塞米松玻璃体内植入剂移位至前房。瞳孔括约肌损伤致瞳孔变形超出人工晶状体光学面的患眼,需要采用瞳孔成形术使瞳孔缩小至人工晶状体光学面内,以预防地塞米松玻璃体内植入剂移位至前房[39]。虹膜周切孔是地塞米松玻璃体内植入剂移位至前房的潜在通道。虹膜周切孔过大的患眼,需要手术缝合以缩小周切孔[10]。

**4.3 限制地塞米松玻璃体内植入剂活动** 地塞米松玻璃体内植入剂产品说明书上推荐的注射方法是:(1)将针头斜面朝上背对巩膜(操作者能看到针头开口),长轴平行于角膜缘;(2)将针头缓慢斜行插入巩膜内约 1 mm 深;(3)将针头指向眼球中央刺穿巩膜进入玻璃体腔,直至硅胶套碰到结膜;(4)按压推进钮直到听到一声“咔”;(5)移出针头。Lee 等[40]提出一种改良注射方法,可以将注射的地塞米松玻璃体内植入剂滞留于玻璃体基底,以防其漂浮到视轴干扰中央视野或前移至前房。改良之处是在玻璃体腔进针之后、按压推进钮释放地塞米松玻璃体内植入剂之前添加一项操作,即是将推注器旋转 180°使针尖斜面向下朝向玻璃体基底。Lee 等[40]报道 1 例患者左眼地塞米松玻璃体内植入剂常规植入后数周发生地塞米松玻璃体内植入剂移位至前房,取出前房地塞米松玻璃体内植入剂后采用改良方法植入新的地塞米松玻璃体内植入剂,随访期间未再出现地塞米松玻璃体内植入剂移位。Mateo 等[41]提出将地塞米松玻璃体内植入剂用 10-0 不可吸收缝线固定于巩膜,以限制其活动。手术过程如下:(1)将预装的地塞米松玻璃体内植入剂注入无菌软管套中;(2)取出地塞米松玻璃体内植入剂并在其一端绑上带针的 10-0不可吸收缝线;(3)在 6:00 位角膜缘后 4 mm 睫状体平坦部作 23 G 巩膜切口,用镊子将带针线的地塞米松玻璃体内植入剂从巩膜切口小心塞入玻璃体腔;(4)用地塞米松玻璃体内植入剂上的针线缝合巩膜切口。Mateo 等[41]报道 1 例右眼前房型人工晶状体且未保留晶状体囊膜的患者经此方法植入地塞米松玻璃体内植入剂,术后 6 mo随访期间未出现地塞米松玻璃体内植入剂移位。上述两种方法限制地塞米松玻璃体内植入剂的有效性及安全性还有待进一步研究。

## 5 其他玻璃体内糖皮质激素植入剂

玻璃体内糖皮质激素植入剂除地塞米松玻璃体内植入剂外,还有氟轻松玻璃体内植入剂(商品名 Retisert、Iluvien、Yutiq)。三种植入剂移位至前房的危险因素与地塞米松玻璃体内植入剂相同,但临床表现有些许差异。

Retisert 由含 0.59 mg 醋酸氟轻松的硅胶储药器和缝合翼片组成,可在玻璃体腔持续释放醋酸氟轻松约30 mo,可治疗慢性非感染性后葡萄膜炎[42]。植入 Retisert 需要将硅胶储药器从睫状体扁平部切口推入玻璃体腔,然后用 10-0 缝线将缝合翼片固定于切口处。硅胶黏合剂连接硅胶储药器与缝合翼片,且黏合强度会随时间延长而降低。Retisert 储药器与缝合翼片自发分离并移位至前房,与地塞米松玻璃体内植入剂移位至前房一样引起角膜水肿、视力下降,但植入至移位的时间间隔(>3 a)更长。移位的 Retisert 储药器内醋酸氟轻松已完全释放,应尽快手术取出以免其继续损伤角膜内皮[43-45]。

Iluvien 和 Yutiq 均是直径 0.37 mm、长 3.5 mm 的浅棕色非生物可溶性玻璃体内植入剂,通过预装给药器 25 G 针头注入玻璃体腔,持续释放醋酸氟轻松 36 mo[46-47]。多名学者报道,Iluvien 或 Yutiq 移位至前房患眼确诊时角膜透明[48-51]。Gunzenhauser 等[52]报道 1 例 61 岁男性患者,

初次 Iluvien 植入 3 mo 后检查发现 Iluvien 移位至前房,角膜透明,眼压 18 mmHg,通过仰卧位复位;后续多次检查发现 Iluvien 移位至前房,都通过仰卧位复位,角膜透明;第二次 Iluvien 植入 6 mo(初次植入 36 mo)后检查发现两根 Iluvien 移位至前房,角膜水肿,仰卧位复位后角膜水肿消退。与地塞米松玻璃体内植入剂移位至前房相比,Iluvien 或 Yutiq 移位至前房患眼角膜状态更好,原因可能是其表层材料不会生物降解,始终保持光滑,对角膜内皮的机械损伤更小。Iluvien 或 Yutiq 移位至前房的患眼,多可随访观察或仰卧位复位,出现症状者可手术取出后重新植入玻璃体腔并缝合固定[19,49-52]。

## 6 总结与展望

在地塞米松玻璃体内植入剂植入前,应评估地塞米松玻璃体内植入剂移位至前房的风险。地塞米松玻璃体内植入剂移位至前房常见于悬韧带-晶状体囊膜复合体不完整、玻璃体切除术后的患眼。高危患者在地塞米松玻璃体内植入剂植入前应充分告知风险,并采取缩瞳、避免俯卧等措施以预防地塞米松玻璃体内植入剂移位至前房。地塞米松玻璃体内植入剂移位至前房患眼如出现角膜水肿,需尽快复位或取出,以降低内皮失代偿性角膜水肿的风险。氟轻松玻璃体内植入剂也存在移位至前房的风险,同样应引起临床医师重视。未来需更大样本研究改良植入方法预防地塞米松玻璃体内植入剂移位的有效性及安全性。

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