

人工关节假体周围感染的抗生素应用

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摘要

人工关节置换术已经改善了世界各地数百万人的生活。该手术的效果包括功能恢复和疼痛减轻。人工关节假体周围感染(Periprosthetic joint infection, PJI)目前仍然是人工关节翻修术最常见的原因之一。因PJI感染复发率较高, 故假体周围感染常伴随着长期反复的治疗, 对患者及其家属带来极大的痛苦与经济负担。同时假体周围感染的病原菌常为耐药菌且常伴有多种病原菌的混合感染, 故治疗难度较高。治疗感染抗生素的应用尤为重要, 因此本文将结合国内外最新的指南以及相关的研究成果, 对假体周围感染的抗生素应用进行总结和归纳, 对骨科医生治疗假体周围感染给予一定的帮助。

关键词

人工关节假体周围感染, 抗生素治疗

The Use of Antibiotics in Periprosthetic Joint Infection

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Abstract

Artificial joint replacement has improved the lives of millions of people around the world. The results of the procedure include functional recovery and pain reduction. Periprosthetic joint infection (PJI) remains one of the most common causes of revision surgery. Because of the high recurrence rate of PJI infection, periprosthetic infection is often accompanied by long-term repeated treatment, which brings great pain and economic burden to patients and their families. At the

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same time, the pathogens around the prosthesis infection are often drug-resistant bacteria and often accompanied by a variety of pathogens mixed with infection, so the treatment is relatively difficult. The application of antibiotics in the treatment of infection is particularly important. Therefore, this paper will combine the latest domestic and foreign guidelines and relevant research results to summarize and conclude the application of antibiotics in the treatment of periprostheses infection, so as to give certain help to orthopedic surgeons in the treatment of periprostheses infection.

Keywords

Periprosthetic Joint Infection, Antibiotic Therapy

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1. 前言

人工关节置换术是晚期重度骨关节炎最理想的治疗方式,随着人工关节置换术后患者的不断增加,人工关节置换术后并发症的发生人数也在逐年不断增加,其中人工关节假体周围感染是近几年导致人工关节置换术失败的主要原因。PJI 是人工关节置换术后最严重、最难以治疗的并发症,其整体发生率为 0.3%~1.9%,同时 PJI 的诊断以及治疗选择方面依然存在较大的争议[1] [2]。2013 年 PJI 国际感染共识建议假体取出后静脉抗生素治疗 2~6 周,但有许多研究表示应用 1 周抗生素也取得了良好的效果[3] [4]。同时在选择 I 期翻修手术还是 II 期翻修手术方面不同的专家也有不同的意见,哪种方式更加合适依然引起相关专家们的热烈讨论[5] [6]。

2. 假体周围感染的发病机制

手术后一年内发生的大多数 PJI 是通过手术时引入微生物而引发的,这是引发感染的第一种机制。这可以通过假体或假体周围组织的直接接触病原菌而发生。微生物一旦与植入物表面接触,微生物就在植入物表面定居。这一过程中的一个重要因素是在假体材料存在的情况下建立感染所需的微生物接种量低。感染从邻近部位的连续传播是引发感染的第二种机制。在术后早期,由于表面和深层筋膜平面未完全愈合,浅表手术部位感染可能传播到假体。然而,如果正常的组织平面在邻近位置由于外伤或手术而再次被破坏,则随后也可能发生连续扩散。最后,在人工关节假体的整个生命周期中,假体仍然存在血源性感染的风险。总的来说,由偏远感染部位引起的 PJI 是罕见的。如在 6101 例人工关节置换术中发生的 551 例偏远部位感染中,只有 7 例确诊为血源性假体周围感染[7]。

3. 假体周围感染的分类

PJI 有多种分类方案。根据感染的时间分为早发、迟发或迟发。早发性 PJI 发生在末次手术后 3 个月内。这些感染最常见于手术时术中污染引发,并且是由相对毒性较强的微生物引起的。迟发性 PJI 发生在 3 个月,但在 12 月前。这些感染通常也是在手术时获得的,但由毒性较低的微生物引起,因此明显的感染表现在最初的 3 个月内没有发生。术后 12 个月后发生的感染为晚发性 PJI,通常被认为是由于血源性感染引起[8] [9]。

4. 假体周围感染的病原菌

对于早期感染和迟发感染,金黄色葡萄球菌、凝固酶阴性葡萄球菌、链球菌和肠杆菌是最常见的微生物。急性晚期感染多为金黄色葡萄球菌,链球菌,肠杆菌,凝固酶阴性葡萄球菌,慢性晚期感染则为凝固酶阴性葡萄球菌,金黄色葡萄球菌,链球菌。金黄色葡萄球菌是一种重要的病原体。不仅是假体周围感染的主要原因之一,它还是侵入性感染的常见原因之一,包括医疗、外伤相关的血流感染,其随后可能导致假体周围感染[10][11]。凝固酶阴性葡萄球菌也是假体周围感染的主要原因之一,其中以表皮葡萄球菌最为常见[12],凝固酶阴性葡萄球菌主要通过其粘附假体材料并产生生物膜的能力导致假体周围感染[9]。凝固酶阴性葡萄球菌可以在人工关节置换术后任何时候引起 PJI,早发性 PJI 典型表现为伤口渗液、局部皮肤变化和疼痛,延迟性或迟发性 PJI 中疼痛可能是唯一的表现。Aggarwal 的研究中凝固酶阴性葡萄球菌引起的延迟性或迟发性 PJI 有 9% 的患者只出现疼痛这一临床症状。金黄色葡萄球菌和凝固酶阴性葡萄球菌导致超过四分之三的人工关节置换术感染[13][14]。

5. 假体周围感染的抗生素应用

5.1. 抗生素的选择

对临床确定感染为阴性或等待药敏结果的 PJI 患者应给予经验性抗菌治疗,其抗生素治疗方案应覆盖假体周围感染的多种常见病原体,如金黄色葡萄球菌和凝固酶阴性葡萄球菌、肠杆菌。万古霉素是一种常见的抗生素,多用于治疗培养阴性患者,一些研究表明环丙沙星联合利福平应用更加有效。有研究表明手术前单次应用抗生素不会影响术中留取的标本的培养阳性率[15]。

病原体一旦明确,应将抗生素从经验覆盖范围调整到病原体特异性覆盖范围以减少广谱抗生素的不必要的覆盖,并使副作用尽量减少。对于致病菌为葡萄球菌属者(主要为金黄色葡萄球菌和凝固酶阴性葡萄球菌),对甲氧西林敏感者静脉多应用 β -内酰胺类抗生素,苯唑西林或头孢唑啉是首选抗生素,口服多应用喹诺酮类与利福平,对甲氧西林耐药者静脉抗生素方案多为万古霉素、头孢他啶、替考拉宁或利奈唑胺,口服抗生素多为喹诺酮类与利福平联合应用。对链球菌感染者(主要为草绿色链球菌和 B 族链球菌),抗生素多应用 β -内酰胺类抗生素联合利福平或喹诺酮类联合利福平[16]。对肠杆菌感染者,常使用头孢曲松进行治疗[17]。对肠球菌感染者,氨苄西林可用于对氨苄西林敏感的肠球菌感染,对耐万古霉素的肠球菌多应用利奈唑胺治疗。对铜绿假单胞菌感染者,可以使用环丙沙星或者美罗培南进行抗生素治疗[18]。对于真菌感染常应用氟康唑或者两性霉素进行治疗。

5.2. 抗生素的给药方式及时间期限

II 期翻修依然是目前主要治疗 PJI 的手术方式,在第一次手术中,在采集微生物样本进行培养后,移除假体并进行彻底清创,随后放置载有高剂量抗生素的间隔物。根据培养结果使用抗生素治疗,通过检查明确感染被清除后,第二次进行手术植入新的假体[19][20][21][22]。间隔物植入术后根据 2013 年 PJI 国际感染共识建议假体取出后静脉抗生素治疗 2~6 周,完成静脉抗生素疗程且病人的临床症状好转时,可以改用口服抗生素进行治疗[23]。在美国,口服抗生素越来越多地用于治疗 PJI。一项研究观察了更长时间的抗生素应用,比较了 6 周和 12 周。这两组之间的结果没有差异[24]。最近,Benkabouche 等人发表了一项研究,其中他们将 123 名患者随机分为 4 周组和 6 周组,他们术后静脉注射抗生素的平均持续时间为 4 天(范围为 3.5 至 5 天),随后是口服抗生素的随机治疗持续时间。4 周治疗组中有 98% 的患者获得了治愈,而 6 周治疗组中有 94% 的患者获得了治愈[25]。有部分相关研究表明静脉使用 2 周抗生素治疗,最终也取得了较高的感染清除率[26]。目前关于 II 期翻修摘除假体后及假体 II 期再植后静脉抗生素

的治疗时间未达成共识[23]-[28]。

I 期翻修术后抗生素的应用同样未达成共识。Winkler 等人进行了髌关节置换手术后感染的相关研究, 他们发现在 I 期翻修术后两周内静脉注射抗生素的治疗成功率为 92% [29]。I 期翻修术后配合短程抗生素治疗效果良好, 延长疗程抗生素治疗对感染消除率无明显提高。

保留假体清创术患者抗生素的应用同样存在极大争议, 相关指南推荐: PJI 患者清创保留假体术后应静脉应用抗生素 4~6 周, 髌关节静脉应用抗生素后再口服敏感抗生素 3 个月, 膝关节则为口服 6 个月[4]。但大多数的研究结论是, 延长疗程抗生素治疗对感染消除率无明显提高[6]。

目前有相关研究表明 PJI 的治疗中人工关节翻修手术后仅行局部抗生素治疗也取得了良好的治疗效果。Whiteside 有研究表明局部给药的抗生素产生的峰值浓度比静脉给药后高许多个数量级, 其治疗作用持续 24 小时, 血清中也达到了治疗水平。局部高浓度的抗生素在治疗人工关节假体周围感染方面有明显的优势[30]。

6. 展望

PJI 很难治疗。应采用骨科医生、微生物专家和患者联合的方式, 以帮助获得更好的结果。尽管治疗 PJI 病患者的最佳方案仍有待确定, 但适当的手术和抗生素治疗仍然至关重要。需要根据患者的合并症、培养结果来考虑抗生素。大规模、高质量、多机构研究对于更准确地确定最佳治疗方法是有益的, 但使用目前的治疗方法产生成功率尚可以接受。考虑到未来几年越来越多的人将接受关节置换手术, 骨科医生应该预见到 PJI 的增加。需要在预防 PJI 方面取得进展, 以减少未来几年预期增加的 PJI 患者数量。

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