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· 综述 ·

椅旁紫外线光功能化技术提高钛种植体生物活性的研究进展

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【摘要】 钛及钛合金因其良好的生物相容性广泛应用于医学领域中。但钛表面的生物活性会随暴露时间的增加而逐渐下降,影响其最终的骨结合效能。作为一种有效的表面改性方法,紫外线光功能化技术不改变成品种植体的表面形貌,适合多数品牌的成品种植体表面处理。本文从紫外线光功能化技术对钛表面特性、细胞生物学行为、种植体骨结合的影响及临床应用现状等方面对紫外线光功能化技术的研究进展作一综述。目前研究表明,紫外线光功能化后的钛表面表现为超亲水性,钛表面的生物活性提高,从而加速和增强骨形成,获得更好更快的骨结合,提高种植手术的成功率,适合椅旁操作,是一种有潜力的椅旁临床新技术。

【关键词】 钛种植体; 表面处理; 椅旁操作; 紫外线; 光功能化; 亲水性; 碳氢化合物; 生物活性; 骨结合

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Research progress on enhancing biological activity of titanium implants by chairside ultraviolet photofunctionalization ZHANG Huaying, ZHAO Yuwei, YU Haiyang. State Key Laboratory of Oral Diseases & National Clinical Research Center for Oral Disease & Department of Prosthodontics, West China Hospital of Stomatology, Sichuan University, Chengdu 610041, China

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【Abstract】 Excellent mechanical properties and biocompatibility resulted in titanium and titanium alloys being widely used in the medical field. However, the biological activity of titanium surface will gradually fade with increasing exposure time, which affects its final osseointegration. As an effective surface modification method, ultraviolet (UV) photofunctionalization does not change the surface morphology of implants and is a suitable surface treatment for many brands of implants. This article summarizes the research progress on the effect of UV photofunctionalization technology on the characteristics of titanium surfaces, biological activity and implant osseointegration, as well as its current clinical applications. Studies have shown that the superhydrophilicity of the titanium surface and improved biological activity endowed by UV photofunctionalization can accelerate and enhance bone formation, resulting in a higher success rate of implant surgery. Therefore, UV photofunctionalization has great potential for clinical chairside applications.

【Key words】 titanium implant; surface modification; chairside operation; ultraviolet light; photofunctionalization; hydrophilic; hydrocarbon; biological activity; osseointegration

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目前临床种植体-骨结合率(bone-implant contact, BIC)为40%~70%^[1]。对于骨质疏松或糖尿病等危险系数较高的患者来说,采用喷砂、微弧氧化、等离子喷涂、陶瓷化处理等表面改性方法提高骨结合的效果是可选的方案^[2-3]。这些表面处理技术都是应用于种植体生产阶段,而对生产定型后的成品种植体无法进行上述常规表面处理。由于术前设计与术中患者实际情况不符、骨质变化、多颗种植、导板误差等原因,有时会因对成品种植体增加攻丝、更改方案内容等而意外延长种植体暴露时间,而部分品牌种植体本身就无抗氧化包装,文献报道钛种植体一旦暴露在空气中就会发生表面钝化,钛表面的生物活性会随暴露时间的增加而逐渐下降,保存4周后的钛表面即可充分老化^[4]。因此,在椅旁对成品种植体选择进行无损的表面活化,也是一个可行的方案。紫外线(ultraviolet, UV)介导的光功能化技术已被认为是一种有效的表面改性方法,UV光功能化可以重新获得活性表面,利于实现钛种植体更好更快的骨结合,提高种植体的稳定性,实现更高、更均匀的BIC,提高种植手术的成功率,适合椅旁使用,应用方便^[5]。为了全面了解UV光功能化对钛种植体生物活性的影响,本文对椅旁UV光功能化种植体的研究进展作一综述。

1 UV光功能化技术的活化机制

1997年,Wang等^[6]证实UV光催化可以使TiO₂膜表面产生超亲水性,此后UV照射作为一种新的表面处理技术用于提高种植体生物活性。而UV光功能化概念上是指UV照射后钛表面物理化学性质的变化和生物学能力的提高。现有研究表明UV光功能化使TiO₂氧化膜产生超亲水性表面的机制主要有两个:①亲水性—由于TiO₂介导的光功能化去除了疏水层的碳氢化合物或其他含碳物质,导致水与清洁的TiO₂表面互相吸引;②UV照射将TiO₂表面电子从价带激发到导带,Ti⁴⁺离子转化为Ti³⁺离子,从而产生氧空位,氧空位具有强氧化性,可以把吸附在TiO₂表面的OH⁻和H₂O分子氧化成·OH自由基,·OH自由基可以将TiO₂表面的碳氢化合物氧化成CO₂和H₂O^[6-7]。UV处理通过改变钛表面的物理化学性质,将钛表面的疏水性转变为超亲水性。该方法已大量应用于环境工程

和微生物学等领域^[8-11]。

2 UV光功能化技术对钛表面特性的影响

钛表面的生物活性会随着暴露时间的推移而下降,新鲜制备的纯钛表面为超亲水性,而老化钛表面形成一层TiO₂氧化膜,表现为疏水性^[12],经UV光功能化后可形成具有0°接触角的高度亲水亲油表面^[13-14]。X射线光电子能谱分析结果表明,UV光功能化技术可使钛表面碳元素含量明显下降,由35%~55%^[15-18]降至低于20%,与新鲜制备的钛表面相当^[19-20](表1)。无论紫外线的持续时间和强度如何,总能量为2 000 mJ/cm²是实现最高生物活性所需的最小能量^[21]。这些研究数据表明,UV光功能化技术可增加钛表面的表面能、增加亲水性、降低碳氢化合物含量,且不会改变表面形貌,这种变化对于后续的细胞增殖、分化和骨结合能力都至关重要。

3 UV光功能化技术对细胞生物学行为的影响

钛表面生物活性的下降也称为生物老化^[19, 22]。保存4周后的钛表面生物活性明显下降,早期减弱的生物学过程对随后成骨细胞的功能表达会产生不利影响^[4]。老化钛表面带负电,不会主动与带负电的细胞相互作用,而是需要离子桥(特别是二价阳离子)来吸引细胞^[4, 23-24]。UV光功能化的钛表面带正电,可作为细胞黏附的化学吸引剂,与带负电的细胞相互作用^[4]。多项研究表明,亲水性程度和生物学潜能之间没有明确的相关性^[4, 22, 25]。Iwasa等^[25]通过去除表面电荷或用阴离子处理来改变钛表面的静电状态,电荷中和前后钛表面均保持超亲水性,但电荷中和前钛表面的细胞黏附明显增强。这项研究证实在调节生物活性方面,UV光功能化钛表面的静电状态是决定钛表面生物活性(尤其是细胞黏附能力)的关键因素。UV光功能化钛表面生物活性提高表现为蛋白吸附能力增强,早期细胞黏附增加至老化钛表面的2~4倍,细胞增殖提高2倍,成骨细胞碱性磷酸酶活性和矿化结节面积提高2倍^[19, 26-28],促进细胞骨架发育^[29](表1)。

UV光功能化使钛表面带正电荷,将更多的带负电荷的蛋白质和成骨细胞带到钛表面,碳氢化合物的减少有助于细胞黏附,促进细胞增殖,从而加速和增强骨形成^[28, 30]。同时,UV光功能化可以

促进磷灰石在钛表面的沉积,从而进一步增加成骨细胞的增殖和分化。

4 UV 光功能化技术对种植体骨结合的影响

近年来,关于UV光功能化种植体的体内研究成为热点。很多种植体病例因较低的BIC或种植体-骨界面的破坏性改变而失败^[31]。研究表明,UV光功能化的种植体与骨之间几乎没有软组织介入,种植体周围有大量的新生骨生成,在愈合第4周时BIC即可达到最大化(近100%),经UV

光功能化的种植体在3周和8周时具有更高的骨密度和更多的骨组织附着^[22, 32-33],种植体周软组织的生物封闭性能增强^[34]。种植体生物力学测试表明,UV光功能化技术使种植体稳定性提高4倍^[22]。UV光功能化种植体可降低早期失败的风险,甚至在极差的条件下也可以保证更快、稳定的骨结合^[35]。已有学者证实UV光功能化的种植体在2型糖尿病大鼠及骨质疏松大鼠体内骨结合良好,可达到或高于正常的骨结合水平^[36],实现快速的骨结合(表1)。

表1 UV光功能化前后钛表面的变化

Table 1 Changes in titanium surface before and after UV photofunctionalization

	Before UV photofunctionalization (aging titanium)	After UV photofunctionalization
Characteristics of titanium surface	Hydrophobic and negatively charged surface with average carbon content of 35%-55% ^[15-18]	Super - hydrophilic, super - lipophilic and positively charged surface with carbon content of less than 20% and more hydroxyl ^[19-20]
Biological activity	Early cell adhesion was reduced to 1/4 to 1/2 of fresh prepared titanium surface, and cell proliferation was reduced by half. The cell shape of osteoblasts was round and the formation of cytoskeleton was inhibited. The alkaline phosphatase activity and mineralization were reduced by half, while biological activity of titanium surface also decreased ^[19]	Cell adhesion and proliferation were enhanced. The cell shape of osteoblasts was gradually stretched, multi-angled and significantly larger in volume. Alkaline phosphatase activity and mineralization of osteoblasts was enhanced, and osteoblast gene expression was up-regulated. Platelet adhesion and activation improved. Biological activity increased. No cytotoxicity
Implant osseointegration	BIC was 40%-70% ^[1] , early success rate was 28.6% ^[35] and the healing time was long	BIC significantly improved to more than 90% ^[4] . At early healing stage, implant stability increased by 4 times ^[22] and accelerated osseointegration

UV: ultraviolet; BIC: bone-implant contact

此外,UV光功能化技术可增强种植体的机械固位。Ishijima等^[37]评估了UV光功能化对老年大鼠种植体骨结合的影响。愈合两周后,UV光功能化的微型种植体具有更高的旋出力矩。UV光功能化技术是提高BIC、促进骨结合过程、增强种植体稳定性的一个可行方法,在基础研究和临床研究中均具有重要价值。

5 椅旁UV光功能化技术处理种植体的临床应用现状

目前临床上可用的亲水性种植体都储存于特定的溶液中^[1],UV光功能化或将其保存在介质中均可以诱导或保持种植体表面的亲水性,促进骨愈合过程并实现早期骨整合。UV光功能化种植体与这些种植体之间的区别在于:UV光功能化种植体表面是干燥、清洁的,而不是湿润的或伴有离子、分子的表面,储存在介质中可导致种植体表面

异物沉积,并且没有消除钛表面的碳氢化合物。此外,介质储存的方法在促进成骨细胞黏附和扩散方面的作用不如UV光功能化^[38]。因此UV光功能化技术是提高种植体表面生物活性更安全的方法。

Funato等^[39]报告了第一例UV光功能化种植体的临床研究,在2.5年的随访期内,UV光功能化种植体组(222颗)的种植体稳定系数(implant stability quotient, ISQ)每月增长量为2.0~8.7,而未经处理种植体组(168颗)的ISQ每月增长量仅为-1.8~2.8。UV光功能化种植体所需的平均愈合时间为3.2个月,而常规种植体约为6.5个月。UV光功能化种植体和常规种植体的成功率分别为97.6%和96.3%。

Hirota等^[40]研究发现,在初始稳定性极低和/或骨量不足的情况下,UV光功能化种植体仍能实现更快、更高的骨结合。在常规和复杂(骨增量、即

刻种植等)情况下,UV光功能化种植体的7年成功率为100%^[40],但对于口腔癌患者,由于口腔癌相关的治疗导致颌骨受到病理生理上的损害,颌骨切除后使用腓骨重建部位的骨质差,不易产生骨结合。使用颗粒松质骨和骨髓进行颌骨重建部位的种植体也极易发生种植体周围炎,即便是使用UV光功能化种植体,其成功率也仅为22.2%^[41]。这表明UV光功能化不是一种在任何情况下都能实现成功骨结合的全能技术,对于口腔癌患者要慎重选择可靠的种植治疗。

UV光功能化可增强机械加工和喷砂酸蚀种植体表面的骨结合能力,显著降低早期种植失败的风险^[42],该技术有望推广至其他表面类型的钛种植体。

6 小 结

综上,UV光功能化种植体的表面处理方法可在牙科、面部和整形外科等领域的植入治疗中广泛应用。UV光功能化增强骨结合归因于超亲水性的产生、表面碳氢化合物的显著减少以及钛表面静电状态的改善。这些表面性质的变化导致成骨细胞的增殖、黏附、分化和整体表达增加。但生物活性增强的基础机制、超亲水性和碳氢化合物去除等相互作用的机制还亟待进一步探索。因此,还需要进一步的研究来充分了解UV光功能化的作用。

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