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全膝关节置换术在膝关节骨性关节炎治疗中的应用效果及对血清 SOD、NO、TNF- α 水平的影响 *

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摘要 目的:研究全膝关节置换术(TKA)治疗膝关节骨性关节炎(KOA)的临床疗效及对血清超氧化物歧化酶(SOD)、一氧化氮(NO)、肿瘤坏死因子 α (TNF- α)水平的影响。**方法:**选取我院2014年8月到2016年1月收治的KOA患者94例,采用随机数字法将其分为对照组和观察组,每组各47例。对照组患者接受传统保守药物治疗,观察组患者接受TKA治疗,术后随访1年。比较两组患者的治疗效果,治疗前后膝关节评分(AKS)评分、视觉模拟评分法(VAS)评分及血清SOD、NO、TNF- α 水平的变化。**结果:**治疗后,观察组的治疗效果优良率(93.61%)明显高于对照组(65.96%)($P=0.00$);治疗后随访1年,观察组的VAS评分明显低于对照组($P<0.01$),AKS中膝评分和功能评分均明显高于对照组($P<0.01$),血清SOD水平明显高于对照组($P<0.01$),血清NO和TNF- α 水平均明显低于对照组($P<0.01$)。**结论:**TKA治疗KOA患者的手术效果显著优于传统保守药物治疗,其能明显降低膝关节疼痛感,促进膝关节功能恢复,其机制可能与升高血清SOD水平,降低血清NO和TNF- α 水平有关。

关键词:全膝关节置换术;膝关节骨性关节炎;临床疗效;超氧化物歧化酶;一氧化氮;肿瘤坏死因子- α

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Application of Total Knee Arthroplasty for the Treatment of Knee Osteoarthritis and Its Influence on the Serum SOD, NO, TNF- α Levels*

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ABSTRACT Objective: To study the clinical efficacy of total knee arthroplasty (TKA) in the treatment of knee osteoarthritis (KOA) and its effect on the serum Superoxide dismutase (SOD), nitric oxide (NO), tumor necrosis factor (TNF- α) levels. **Methods:** 94 patients with KOA who admitted to our hospital from August 2014 to January 2016 were selected, they were divided into the control group and the observation group with 47 cases in each group by the random number method. Patients in the control group were treated with traditional conservative medicine, while patients in the observation group were treated with TKA and followed up for 1 year. The therapeutic effects, changes of knee joint score (AKS), visual analogue score (VAS) and serum SOD, NO and TNF- α levels before and after treatment were compared between two groups. **Results:** After treatment, the excellent and good rate of observation group (93.61%) was significantly higher than that in the the control group (65.96%)($P=0.00$). After 1 year of follow-up, the VAS score of observation group was significantly lower than that of the control group ($P<0.01$), the knee score and functional score of AKS were significantly higher than those of the control group ($P<0.01$), the serum SOD level was significantly higher than that of the control group ($P<0.01$), and serum NO and TNF- α levels were significantly lower than those of the control group ($P<0.01$). **Conclusion:** The operative effect of TKA on KOA patients is significantly better than that of traditional conservative medicine, which can significantly reduce the pain sensation of knee joint and promote the recovery of knee joint function. The mechanism may be related to the increase of serum SOD level and the decrease of serum NO and TNF- α levels.

Key words: Total knee replacement; Osteoarthritis of the knee; Clinical efficacy; Superoxide dismutase; Nitric oxide; Tumor necrosis factor alpha

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前言

膝关节骨性关节炎(KOA)是常见的慢性骨关节疾病,以膝关节软骨变性和继发性骨质增生为主要病理改变。KOA好发

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于 60 岁以上老年人群,我国整体患病率约为 8.1%^[12],女性发病率略高,且近年来随着人口老龄化加重,其发病率呈逐年上升之势。KOA 早期临床症状不明显,随着病情进展可出现膝关节疼痛、活动障碍等症状,晚期则可导致关节骨性增粗、肿胀、畸形甚至肌肉萎缩,对患者正常生活及功能造成严重影响^[3-5]。如何提高 KOA 治疗疗效,改善患者生活质量是临床关注重点^[6-8]。

早期 KOA 多既往采用保守药物治疗,虽能不同程度改善疾病症状,但对晚期及病情严重患者疗效欠佳。最新研究显示^[4]膝关节置换术(TKA)能够有效改善 KOA 患者疼痛、炎症反应等症状,矫正膝关节畸形和提高其稳定性,促进膝关节功能恢复,提高患者的生活质量,其手术效果优良率高达 90.0%以上^[9-11],已成为重度 KOA 重要的治疗手段,为晚期症状严重患者提供了治愈可能。且随着外科技术及医疗器械发展,各种性能较优的生物型人工膝关节假体出现,使得 TKA 治疗效果得到进一步提升^[12,13]。本研究主要探讨了全膝关节置换术治疗膝关节骨性关节炎的临床疗效及其可能机制,结果报道如下。

1 资料与方法

1.1 一般资料

选择 2014 年 2 月到 2016 年 2 月于我院进行治疗的 KOA 患者 94 例进行研究,纳入标准^①:符合膝关节骨性关节炎诊断标准,且病情程度为中、重度;②前 1 个月内无服用激素、免疫抑制剂等药物治疗;③符合手术指征。排除标准:④感染性关节炎;⑤合并代谢性骨病、严重骨质疏松、严重创伤或外科手术史等因素导致关节功能障碍疾病者;⑥对本研究药物过敏或不符合手术指征者;⑦妊娠期或哺乳期妇女;⑧治疗后随访资料不全或拒绝随访者。

采用简单随机分组法将所有患者分为两组,每组各 47 例。对照组患者男 23 例、女性 24 例,年龄在 46~77 岁,平均年龄为(65.23±5.61)岁,病程在 2~15 年,平均病程为(6.85±1.96)年,病变部位:左膝 24 例、右膝 17 例、双膝 6 例;观察组患者男性 21 例、女性 26 例,年龄在 45~78 岁,平均年龄为(65.14±5.53)岁,病程在 2~16 年,平均病程为(6.78±1.83)年,病变部位:左膝 22 例、右膝 18 例、双膝 7 例。两组患者临床资料比较无显著性差异($P>0.05$),具有可比性。

1.2 治疗方法

对照组患者采用止痛药、非甾体抗炎药、糖皮质激素等。观

察组患者则接受 TKA 治疗,手术步骤:(1)术前准备:分别于术前 3 d 和 14 d 给予抗凝药物、抗生素及抗感染药物治疗,结合膝关节正侧位 X 片评估患者病情,制定相应手术方案;(2)手术方法:取患者仰卧位于手术床,行联合阻滞麻醉,同时常规消毒铺巾后,将止血带绑于大腿上端,取患者膝正中切口并做长 15 cm 左右切口,依次切开皮肤和浅层深筋膜,经髌骨内侧切开关节囊并暴露关节腔,手术清除髌上囊、滑膜、磨损半月板、脂肪垫、交叉韧带。术后根据患者病情及器械情况,适当松解关节周围软组织、后侧关节囊,修整髌骨、股骨以及胫骨截骨,同时矫正关节畸形、力线角度,并测量伸屈膝关节时间隙,指导选取合适膝关节假体植入,并注入骨水泥进行固定。随后松绑止血带,采用电凝方法止血,常规留置引流管后,逐层缝合切口,将消毒敷料覆盖于切口处,并给予绷带加压包扎。术后持续给予抗生素抗感染 1 周,并于术后 72 h 拔出引流管。

1.3 观察指标

①比较两组患者的治疗效果优良率;②术后随访 1 年,比较两组患者治疗前后的膝关节评分(AKS)评分、疼痛视觉模拟评分法(VAS)评分;③比较两组患者治疗前后的血清超氧化物歧化酶(SOD)、一氧化氮(NO)、肿瘤坏死因子- α (TNF- α)水平。

1.4 疗效评价标准

参考相关文献根据 HSS 评分关于 KOA 疗效标准^[14],分为①优:经治疗后 HSS 评分总分 ≥ 90 分;②良:经治疗后 HSS 评分总分在 75~89 分;③差:经治疗后 HSS 评分总分在 60~74 分;④经治疗后 HSS 评分总分 <60 分。抽取患者外周静脉血 5.0 mL,常温静置 10 min 后,置于 3000 r/min 离心机分离 10 min,保存于 -60℃冰箱待测,采用比色法检测血清 SOD 和 NO、TNF- α 水平,所有步骤均严格参考操作说明书进行。

1.5 统计学方法

所有数据采用 SPSS21.0 统计学软件进行分析,计量资料以均数 $\pm$ 标准差表示,组间比较采用 t 检验,计数资料以率(n%)表示,组间比较采用 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者的治疗效果比较

治疗后,两组患者优良率分别为 93.61%、65.96%,观察组显著高于对照组($P<0.05$),见表 1。

表 1 两组患者的治疗效果优良率比较[例(%)]

Table 1 Comparison of the excellent therapeutic effect between the two groups[n(%)]

Groups	Excellent	Good	Bad	Poor	Excellent and good rate(%)
Control group(n=47)	19(40.43)	12(25.53)	11(23.40)	5(10.64)	65.96
Observation group(n=47)	34(72.34)	10(21.27)	2(4.26)	1(2.13)	93.61
<i>P</i>		-			0.00
χ^2		-			11.15

2.2 两组患者治疗前后的 AKS 和 VAS 评分比较

治疗后,观察组患者的 VAS 评分明显低于对照组($P<0.01$),

AKS 中膝评分和功能评分均明显高于对照组($P<0.01$),详见表 2。

表 2 两组患者治疗前后的 AKS 和 VAS 评分比较($\bar{x} \pm s$)

Table 2 Comparison of the AKS and VAS score between the two groups before and after treatment($\bar{x} \pm s$)

Groups	VAS scores		AKS scores			
	Before treatment	After treatment	Knee score		Functional score	
			Before treatment	After treatment	Before treatment	After treatment
Control group(n=47)	7.59± 1.42	4.70± 0.97 [°]	25.92± 8.35	31.88± 7.97 [°]	22.31± 6.52	28.61± 7.74 [°]
Observation group(n=47)	7.54± 1.38	2.26± 0.63 [°]	26.03± 8.42	39.14± 8.58 [°]	22.56± 6.70	35.89± 8.23 [°]
P	0.86	0.00	0.79	0.00	0.77	0.00
t	0.15	14.46	0.22	4.25	0.24	4.42

Note: [°] compared with before treatment, $P < 0.05$.

2.3 两组患者治疗前后的血清 SOD、NO、TNF- α 水平比较

治疗后,两组患者血清 SOD、NO、TNF- α 水平较治疗前

显著改善, 观察组 SOD 水平明显高于对照组, 血清 NO 和

TNF- α 水平显著低于对照组($P < 0.01$), 详见表 3。

表 3 两组患者治疗前后的血清 SOD、NO、TNF- α 水平的比较($\bar{x} \pm s$)

Table 3 Comparison of the serum SOD, NO and TNF- levels before and after treatment between the two groups($\bar{x} \pm s$)

Groups	SOD(nU/mL)		NO(μ mol/L)		TNF- α (pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group(n=47)	5.56± 0.73	11.79± 1.12 [°]	35.81± 5.73	20.15± 3.13 [°]	55.81± 7.92	47.26± 6.68 [°]
Observation group(n=47)	5.49± 0.78	17.25± 1.30 [°]	36.04± 5.82	13.67± 2.40 [°]	55.67± 8.02	40.13± 6.35 [°]
P	0.85	0.00	0.80	0.00	0.83	0.00
t	0.16	21.81	0.21	11.26	0.18	5.30

Note: [°] compared with before treatment, $P < 0.05$.

3 讨论

KOA 是骨关节科的常见、多发性疾病,具有慢性起病、病情较长等特点,好发于老年人群中。据统计,我国 60 岁以上人群 KOA 患病率高达 50.0%, 且近年来随着人口老龄化加重, KOA 患病率及人群正逐年提高^[15,16]。膝关节软骨变薄、断裂、磨损甚至消失以及周围骨性关节炎面磨损、骨质增生及骨赘生物形成是 KOA 的主要病理改变,患者主表现为膝关节局部疼痛、稳定性降低等症^[17,18],病情重者常伴有膝关节内外翻畸形,且以内翻畸形最为常见,导致膝关节内翻负荷增加,使内侧关节面磨损变薄甚至消失,加重膝关节疼痛和不稳定等症状,出现病情的恶性循环,严重影响患者正常生活及工作^[19,20]。既往临床治疗 KOA 多以药物、理疗、早期功能训练等保守治疗方案,其对于早期病情较轻患者具有一定疗效,但对晚期或病情较重者疗效欠佳^[21],因此,如何提高晚期病情较重 KOA 患者治疗疗效,改善膝关节功能以及减轻疼痛等症状已成为临床研究热点。

目前,对于晚期或病情较重 KOA 患者,临床多主张采用外科手术,常用的术式包括关节清理术、截骨术、骨关节炎手术疗法等,但很难达到令人满意的手术效果。近年来,随着外科手术技术及医疗器械发展,TKA 在临床得到广泛应用,常被用于治疗创伤性关节炎、KOA、膝关节内外翻畸形、类风湿性关节炎、膝关节不稳定以及严重疼痛等疾病治疗,其手术效果已得到一致认可^[22,23]。多项研究证实^[24,25]TKA 能有效改善患者膝关节功能、矫正关节内外翻畸形,增强关节稳定性,且能够显著降低疼痛感,手术综合效果优良率普遍在 90.0%以上,给晚期病情严

重膝关节疾病患者提供治愈可能。本研究将 TKA 用于 KOA 治疗中,首先通过术前抗凝和抗生素处理有效降低手术感染风险,同时术中应用合适的生物型人工膝关节假体有效恢复患者膝关节功能,提高其稳定性,同时对髌上囊、滑膜、磨损半月板、脂肪垫、交叉韧带清除,有效改善关节炎症反应,减轻炎症坏死所致的自由基损伤,进而改善患者疼痛等症状^[26,27]。本研究结果显示观察组的膝评分、功能评分均明显高于对照组,而 VAS 评分明显低于对照组,证实 TKA 能够有效改善中重度 KOA 患者膝关节功能和减轻疼痛感,与既往研究报道基本一致^[28]。

SOD 是机体重要的自由基清除剂,其含量不仅可反映机体自由基含量,同时可反映抗自由基损伤能力。此外,NO 含量增高可刺激基质金属蛋白酶(MMP)活性,从而加快胶原及蛋白聚糖裂解,导致机体前列腺素 E(PGE)分泌增多,加重软骨基质破坏^[18]。TNF- α 是机体重要的炎症因子,在 KOA 发生软骨基质降解和软骨破坏中起着重要作用^[29]。研究显示^[30]血清 SOD、NO、TNF- α 水平改变与 KOA 患者疼痛等病情程度密切相关。本结果显示观察组血清 NO 和 TNF- α 水平明显低于对照组, SOD 水平则高于对照组,提示 TKA 能够有效减轻 KOA 患者的炎症按压。

综上所述,KA 治疗 KOA 患者的手术效果显著优于传统保守药物治疗,其能明显降低膝关节疼痛感,促进膝关节功能恢复,其机制可能与升高血清 SOD 水平,降低血清 NO 和 TNF- α 水平有关。

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