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鹿瓜多肽注射液与补肾壮骨胶囊对膝关节骨性关节炎患者血清 BALP、BGP、TRACP-5b 及 CTX-I 水平的影响 *

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摘要 目的:研究鹿瓜多肽注射液联合补肾壮骨胶囊对膝关节骨性关节炎的临床疗效及对血清骨特异性碱性磷酸酶(BALP)、骨钙素(BGP)、抗酒石酸盐酸性磷酸酶异构体 5b(TRACP-5b)、I 型胶原 C 端肽(CTX-I)水平的影响。**方法:**选取 2015 年 4 月至 2016 年 3 月我院收治的 84 例膝关节骨性关节炎患者,根据患者入院顺序分为观察组和对照组,42 例每组。对照组使用鹿瓜多肽注射液,观察组在此基础上加以补肾壮骨胶囊。比较两组患者临床疗效,治疗前后血清 BALP、BGP、TRACP-5b、CTX-I 水平、视觉模拟评分法(VAS)的变化。**结果:**治疗后,观察组临床总有效率显著高于对照组[90.48%(38/42)比 64.29%(27/42)] ($P<0.05$);两组患者血清 BALP、BGP 水平均较治疗前显著升高($P<0.05$),血清 TRACP-5b、CTX-I 水平、VAS 评分均较治疗前显著降低($P<0.05$),且观察组的血清 BALP、BGP 水平显著高于对照组($P<0.05$),血清 TRACP-5b、CTX-I 水平、VAS 评分明显低于对照组($P<0.05$)。**结论:**鹿瓜多肽注射液联合补肾壮骨胶囊治疗膝关节骨性关节炎的临床疗效明显优于鹿瓜多肽注射液单药治疗,其能显著升高患者的血清 BALP、BGP 水平,降低血清 TRACP-5b、CTX-I 水平,改善患者骨代谢。

关键词:鹿瓜多肽注射液;补肾壮骨胶囊;膝关节骨性关节炎

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Clinical Efficacy of Lugu Peptide Injection Combined with Bushenzhuanggu Capsule on Knee Joint Osteoarthritis and Effect on the Serum BALP, BGP, TRACP-5b and CTX-I Levels*

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ABSTRACT Objective: To study the efficacy of Lugu Peptide Injection combined with Bushenzhuanggu Capsule on the knee osteoarthritis and effect on the serum bone specific alkaline phosphatase (BALP), osteocalcin (BGP), tartrate Phosphatase isoform 5b (TRACP-5b), type I collagen C-terminal peptide (CTX-I) levels. **Methods:** From April 2015 to March 2016, 84 cases of patients with knee osteoarthritis were divided into the observation group and the control group. The control group was treated with lugu peptide injection, and the observation group was supplemented with Kidney Zhuanggu Capsule. The clinical efficacy, changes of serum BALP, BGP, TRACP-5b, CTX-I levels and visual analogue scale (VAS) before and after treatment were compared between the two groups. **Results:** After treatment, the total effective rate of observation group was significantly higher in the observation group than that of the control group [90.48% (38/42) vs 64.29% (27/42)] ($P<0.05$). Compared with before treatment, the serum levels of BALP and BGP were significantly higher in both groups after treatment ($P<0.05$). The serum TRACP-5b, CTX-I levels and VAS scores were significantly lower than those before treatment ($P<0.05$). The levels of serum BALP and BGP in the observation group were significantly higher than those in the control group ($P<0.05$), the serum TRACP-5b, CTX-I levels and VAS scores were significantly lower in the observation group than those in the control group ($P<0.05$). **Conclusion:** The clinical efficacy of Lugu Peptide Injection combined with Bushenzhuanggu Capsule in the treatment of knee osteoarthritis is superior to that of Lugu polypeptide injection, which can significantly increase the serum BALP and BGP levels, decrease the serum TRACP-5b, CTX-I levels and improve the bone metabolism.

Key words: Lugu Peptide Injection; Bushen Zhuanggu Capsule; Knee Joint Osteoarthritis

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前言

膝关节骨性关节炎也被称之为老年性关节炎、增生性关节

炎、退行性关节炎、骨关节病等,主要是因为关节软骨退行性病变而导致的关节功能障碍及关节疼痛,在老年人群中属于较为常见的一种疾病^[1]。此病的发病部位以膝关节为主,临床表现主

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要为关节功能障碍、活动受限、肿胀、膝关节疼痛等,给中老年生活质量造成严重影响^[2]。当前治疗此病主要以缓解病情进展、改善关节功能及尽量修复受损关节软骨为主,主要包括外科治疗、药物治疗及物理治疗等^[3]。

鹿瓜多肽注射液经提取后而制作而成的药剂,对骨吸收和形成的骨源性生长因子的合成具有明显促进作用,同时能促使滑膜细胞和骨细胞的分化及有丝分裂^[4]。在治疗膝关节骨性关节炎中经补肾壮骨胶囊能促使软骨基质细胞合成,可降低骨基质的代谢能力,延缓软骨的破坏^[5]。为给临床在治疗膝关节骨性关节炎提供可借鉴之处,本研究主要探讨了鹿瓜多肽注射液联合补肾壮骨胶囊治疗膝关节骨性关节炎的临床疗效及对血清骨特异性碱性磷酸酶(BALP)、骨钙素(BGP)、抗酒石酸盐酸性磷酸酶异构体 5b(TRACP-5b)、I 型胶原 C 端肽(CTX-I)的影响。

1 资料与方法

1.1 临床资料

选取 2015 年 4 月至 2016 年 3 月我院收治的 84 例膝关节骨性关节炎患者。纳入标准:① 所有患者大部分时间均存在膝关节疼痛;② 骨性膨大;③ 伴有骨擦音;④ 晨僵时间不足 30 min。排除标准:① 类风湿、风湿关节炎合并者,难以完成单一指标观察者;② 多种内科疾病合并者,如肝肾功能受损、糖尿病、冠心病难以按照要求进行试验者;③ 对本次研究中的药物过敏者;④ 伴有局部皮肤破损、精神疾病、继发或原发肌肉病者。本研究已取得我院伦理委员会批准,及得到患者及家属同意。根据患者入院顺序分为观察组和对照组,42 例每组。观察组中,女性 27 例,男性 15 例;年龄为 43~72 岁,平均(62.12±2.76)岁;病程为 2.31~16.24 年,平均(9.25±1.52)年;X 线片分级:I 级 12 例,II 级 15 例,III 级 13 例,IV 级 2 例。对照组中,女性 29 例,男性 13 例;年龄为 44~73 岁,平均(62.16±2.79)岁;病程为 2.33~16.31 年,平均(9.28±1.57)年;X 线片分级:I 级 11 例,II 级 14 例,III 级 14 例,IV 级 3 例。两组患者性别、年龄、病程比较差异无明显统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

对照组使用鹿瓜多肽注射液(生产厂家:哈尔滨誉衡药业

股份有限公司,规格:2 mL:4 mg×10 支/盒,生产批号:20150213)完成治疗,将 16mg 的鹿瓜多肽注射液和 250 mL 5% 的葡萄糖注射液混合后,采取静脉滴注的方式给药,1 次/天。观察组在对照组治疗基础上加以补肾壮骨胶囊(生产厂家:武汉健民药业集团股份有限公司,规格:0.58 g×12s×3 板,生产批号:20150211)完成治疗,5 粒/次,2 次/天。所有患者共需连续治疗 21 天。

1.3 观察指标

根据《中医病证诊断疗效标准》^[6]对本次临床疗效进行评价,标准如下:经治疗后,活动功能恢复正常,关节肿胀、疼痛消失,实验室检查指标均为正常则为痊愈;经治疗后,活动功能明显好转,关节肿胀、疼痛明显缓解则为显效;经治疗后,活动功能有所好转,关节肿胀、疼痛有所减轻则为有效;经治疗后,关节肿胀及疼痛无变化则为无效。总有效=痊愈+显效+有效。

分别在治疗前后抽取两组患者 5 mL 的空腹静脉血,转速 3000 r/min,离心 15 min,分离血清后放置在 -50℃ 低温箱中待测,使用 ALISEI 全自动酶免分析仪检测骨特异性碱性磷酸酶(BALP),使用放射免疫法检测骨钙素(BGP),使用血清 TRACP-5b 酶免试剂盒检测抗酒石酸盐酸性磷酸酶异构体 5b (TRACP-5b),使用双抗体夹心酶联免疫法检测 I 型胶原 C 端肽(CTX-I)。通过视觉模拟评分法(VAS)评价两组患者治疗前后膝关节疼痛情况,在标度尺为 0~10 上进行标识,共包括 11 个疼痛等级,其中距离疼痛则为 10,无痛则为 0,总分为 10 分。

1.4 统计学处理

选取 SPSS11.5 软件包对本次实验数据予以处理,计量资料以($\bar{x} \pm s$)表示,组间比较进行 t 检验,计数资料以[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 两组患者临床疗效的比较

治疗后,观察组临床总有效率显著高于对照组[90.48% (38/42)比 64.29%(27/42)],差异具有统计学意义($P<0.05$),见表 1。

表 1 两组患者临床疗效的比较[例(%)]

Table 1 Comparison of the clinical efficacy between two groups[n(%)]

Group	Case	Cure	Effective	Valid	Invalid	Total effective
Observation	42	18(42.86)	13(30.95)	7(16.67)	4(9.52)	38(90.48)*
Control	42	8(19.05)	3(7.14)	16(38.09)	15(35.71)	27(64.29)

Note: Compared with control group, * $P<0.05$.

2.2 两组患者治疗前后骨代谢指标的比较

治疗前,两组患者血清 BALP、BGP、TRACP-5b、CTX-I 骨代谢水平比较差异无统计学意义($P>0.05$);治疗后,两组患者血清 BALP、BGP 水平较治疗前显著升高($P<0.05$),血清 TRACP-5b、CTX-I 水平较治疗前显著降低($P<0.05$),和对照组相比,观察组的血清 BALP、BGP 水平较高($P<0.05$),血清 TRACP-5b、CTX-I 水平较低($P<0.05$),见表 2。

2.3 两组患者治疗前后疼痛情况的比较

治疗前,两组患者 VAS 评分比较差异无统计学意义($P>$

0.05);治疗后,两组患者 VAS 评分较治疗前显著降低($P<0.05$),和对照组相比,观察组的 VAS 评分较低($P<0.05$),见表 3。

3 讨论

膝关节骨性关节炎主要是因为关节畸形、关节先天性异常及创伤或年老等因素而导致的关节软骨非炎症性退行性变化,进而形成关节边缘骨赘,在临床中伴有关节畸形、活动受限、关节疼痛等症状^[7,8]。在现代医学看来,软骨细胞供养较差、局部循环障碍和骨性关节炎的发生存在着密切关联性^[9]。中医将骨性

表 2 两组治疗前后血清骨代谢指标的比较($\bar{x} \pm s$)Table 2 Comparison of the serum bone metabolism indexes between two groups before and after treatment($\bar{x} \pm s$)

Groups	Case	Time	BALP(U/L)	BGP(μ g/L)	TRACP-5b(U/L)	CTX-I(μ g/L)
Observation	42	Before treatment	36.34 $\pm$ 3.12	5.13 $\pm$ 0.52	7.86 $\pm$ 0.71	452.32 $\pm$ 42.98
		After treatment	59.24 $\pm$ 5.13* [#]	7.15 $\pm$ 0.74* [#]	3.12 $\pm$ 0.33* [#]	201.37 $\pm$ 21.87* [#]
Control	42	Before treatment	36.38 $\pm$ 3.17	5.14 $\pm$ 0.53	7.87 $\pm$ 0.72	453.01 $\pm$ 43.03
		After treatment	43.98 $\pm$ 4.76*	6.27 $\pm$ 0.62*	4.87 $\pm$ 0.49*	372.45 $\pm$ 32.87*

Note: Compared with before treatment, * $P < 0.05$; Compared with control group after treatment, [#] $P < 0.05$.

表 3 两组患者治疗前后疼痛情况的比较($\bar{x} \pm s$)Table 3 Comparison of the pain situation between two groups before and after treatment($\bar{x} \pm s$)

Groups	Case	Time	VAS(points)
Observation	42	Before treatment	4.87 $\pm$ 0.49
		After treatment	1.24 $\pm$ 0.16* [#]
Control	42	Before treatment	4.91 $\pm$ 0.51
		After treatment	2.65 $\pm$ 0.27* [#]

Note: Compared with before treatment, * $P < 0.05$; Compared with control group after treatment, [#] $P < 0.05$.

关节炎划分为血瘀痹证、瘀血凝滞、脉络闭阻、气血运行不畅及骨痹范畴,因而关节出现刺痛不移,内因主要以气血不足、肝肾亏虚为主,外因主要是风寒湿热之邪外袭^[10-11]。中医学提出肾主骨、藏精,肝主筋、藏血,膝作为筋之府^[12]。因此,当外部受到热、湿、寒、风之邪,经络痹阻,气血不通,不通则痛,因此出现骨痹。此病的发生还和肾、脾、肝存在着密切关联性。可见,在治疗中应以活血化瘀、舒筋通络、滋补肝肾为主,并辅助化瘀止痛、强壮筋骨药物^[13,14]。

补肾壮骨胶囊主要由甘草、穿山甲、红花、制川乌、土鳖虫、当归、威灵仙、牛膝、杜仲、山茱萸、川续断、熟地黄、淫羊藿等中草药组合而成^[15]。其中,山茱萸、熟地黄、淫羊藿三者联合使用为君药,在治疗筋脉瘀滞所导致的活动不利、关节疼痛中能发挥显著疗效,同时能治疗肝肾亏虚^[16,17]。制川乌、威灵仙、牛膝、川续断、杜仲联合使用为臣药,具备痛经止痛、去风寒湿邪、滋补肝肾的作用。穿山甲具有通经活络的作用。土鳖虫、红花、当归三者联合使用为佐药,具有通经活络、活血化瘀的作用^[18,19]。甘草能滋补、调和中气,能增强药物的有效性。在膝关节骨性关节炎通过补肾壮骨胶囊治疗,可促进骨质内血液循环的改善,有利于骨内压力的降低,能促使关节功能的恢复^[20,21]。

鹿瓜多肽注射液主要从中草药甜瓜籽和梅花鹿四肢骨骼中提纯、分离的复方制剂,常常运用在创伤恢复、腰腿疼痛、骨关节炎、骨质的早期愈合、类风湿性关节炎、风湿等疾病中^[22,23]。甜瓜籽的提取物主要来自于葫芦科植物甜瓜成熟干燥的种子,通过特殊工艺提取而成,可促使局部血运障碍的恢复,降低炎性渗出,减少骨折局部毛细血管通透性,还能改善骨痂局部的血液循环,减少红细胞聚集程度及全血黏度,给骨细胞营造良好的供血环境^[24]。现代药理学表明鹿瓜多肽注射液可缓解骨和软骨的受损程度,阻碍炎症介质的释放,缓解滑膜组织炎症细胞浸润^[25,26]。

骨形成和骨吸收作为人体正常的骨代谢过程,一旦骨形成少于骨吸收时,会减少骨量^[27]。BALP 来自于成骨细胞,能增加局部磷酸含量,同时为骨基质矿化所需,可有效反映成骨细胞

活性,属于骨形成的特异性指标^[28]。BGP 由肥大软骨细胞、成骨细胞、成骨细胞合成分泌,骨吸收和骨形成耦联时,此指标可有效反映骨形成。TRACP-5b 由破骨细胞分泌的,能有效评估骨吸收和破骨细胞功能。CTX 能反映骨吸收和骨转化。

本次研究结果显示鹿瓜多肽注射液联合补肾壮骨胶囊治疗的膝关节骨性关节炎患者血清 BALP、BGP 水平显著上升,血清 TRACP-5b、CTX-I 水平明显降低,且上述指标的降低效果显著优于单纯鹿瓜多肽注射液治疗者,提示鹿瓜多肽注射液联合补肾壮骨胶囊可调节患者体内骨代谢,且效果明显优于鹿瓜多肽注射液单药治疗。究其原因主要是因为两种药物联合治疗能促进骨的形成和抑制骨的吸收,进而实现骨折愈合和改善骨结构的目的^[30]。同时,鹿瓜多肽注射液联合补肾壮骨胶囊治疗膝关节骨性关节炎的疗效显著高于单纯鹿瓜多肽注射液治疗者,患者的疼痛状况也有所缓解,主要是因为联合治疗更能促使软骨和骨的再生,阻碍炎性渗出,可有效改善骨的新陈代谢,进而改善患者临床症状和疼痛感。

总之,鹿瓜多肽注射液联合补肾壮骨胶囊治疗膝关节骨性关节炎的临床疗效明显优于鹿瓜多肽注射液单药治疗,其能显著升高患者的血清 BALP、BGP 水平,降低血清 TRACP-5b、CTX-I 水平,改善患者骨代谢。

参考文献(References)

- [1] Junbo W, Sijia L, Hongying C, et al. Effect of low-magnitude different-frequency whole-body vibration on subchondral trabecular bone microarchitecture, cartilage degradation, bone/cartilage turnover, and joint pain in rabbits with knee osteoarthritis [J]. BMC Musculoskelet Disord, 2017, 18(1): 260
- [2] Cherian JJ, Parvizi J, Bramlet D, et al. Preliminary results of a phase II randomized study to determine the efficacy and safety of genetically engineered allogeneic human chondrocytes expressing TGF- β 1 in patients with grade 3 chronic degenerative joint disease of the knee[J]. Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society, 2015, 23(12): 2109-2118
- [3] Bansal H, Comella K, Leon J, et al. Intra-articular injection in the knee

- of adipose derived stromal cells (stromal vascular fraction) and platelet rich plasma for osteoarthritis [J]. *J Transl Med*, 2017, 15(1): 141
- [4] Moyer R, Wirth W, Eckstein F. Sensitivity of different measures of frontal plane alignment to medial and lateral joint space narrowing: From the osteoarthritis initiative [J]. *Seminars in arthritis and rheumatism*, 2015, 45(3): 268-274
- [5] State Administration of Traditional Chinese Medicine. TCM diagnosis and treatment of disease standard [M]. Nanjing: Nanjing University Press, 1994: 30
- [6] Park JS, Kim DK, Shin HD, et al. Apigenin Regulates Interleukin-1 β -Induced Production of Matrix Metalloproteinase Both in the Knee Joint of Rat and in Primary Cultured Articular Chondrocytes[J]. *Biomolecules & therapeutics*, 2016, 24(2): 163-170
- [7] Culvenor AG, Engen CN, Øiestad BE, et al. Defining the presence of radiographic knee osteoarthritis: a comparison between the Kellgren and Lawrence system and OARS atlas criteria [J]. *Knee surgery, sports traumatology, arthroscopy: official journal of the ESSKA*, 2015, 23 (12): 3532-3539
- [8] Tagesson S, Öberg B, Kvist J. Static and dynamic tibial translation before, 5 weeks after, and 5 years after anterior cruciate ligament reconstruction [J]. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA*, 2015, 23(12): 3691-3697
- [9] Roller BL, Monibi F, Stoker AM, et al. Characterization of Meniscal Pathology Using Molecular and Proteomic Analyses [J]. *The journal of knee surgery*, 2015, 28(6): 496-505
- [10] Beckwée D, Vaes P, Shahabpour M, et al. The Influence of Joint Loading on Bone Marrow Lesions in the Knee: A Systematic Review With Meta-analysis [J]. *The American journal of sports medicine*, 2015, 43(12): 3093-3107
- [11] Davidson R, Gardner S, Jupp O, et al. Isothiocyanates are detected in human synovial fluid following broccoli consumption and can affect the tissues of the knee joint[J]. *Sci Rep*, 2017, 7(1): 3398
- [12] Hakky M, Jarraya M, Ratzlaff C, et al. Validity and responsiveness of a new measure of knee osteophytes for osteoarthritis studies: data from the osteoarthritis initiative [J]. *Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society*, 2015, 23(12): 2199-2205
- [13] Cherian JJ, Parvizi J, Bramlet D, et al. Preliminary results of a phase II randomized study to determine the efficacy and safety of genetically engineered allogeneic human chondrocytes expressing TGF- β 1 in patients with grade 3 chronic degenerative joint disease of the knee [J]. *Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society*, 2015, 23(12): 2109-2118
- [14] Moyer R, Wirth W, Eckstein F. Sensitivity of different measures of frontal plane alignment to medial and lateral joint space narrowing: From the osteoarthritis initiative [J]. *Seminars in arthritis and rheumatism*, 2015, 45(3): 268-274
- [15] Schotanus MG, van Haaren EH, Hendrickx RP, et al. Accuracy of CT-based patient-specific guides for total knee arthroplasty in patients with post-traumatic osteoarthritis[J]. *European journal of orthopaedic surgery & traumatology: orthope die traumatologie*, 2015, 25 (8): 1313-1320
- [16] Trombini-Souza F, Matias AB, Yokota M, et al. Long-term use of minimal footwear on pain, self-reported function, analgesic intake, and joint loading in elderly women with knee osteoarthritis: A randomized controlled trial[J]. *Clinical biomechanics (Bristol, Avon)*, 2015, 30(10): 1194-1201
- [17] Eckstein F, Collins JE, Nevitt MC, et al. Brief Report: Cartilage Thickness Change as an Imaging Biomarker of Knee Osteoarthritis Progression: Data From the Foundation for the National Institutes of Health Osteoarthritis Biomarkers Consortium [J]. *Arthritis & rheumatology (Hoboken, N.J.)*, 2015, 67(12): 3184-3189
- [18] Murray AM, Thomas AC, Armstrong CW, et al. The associations between quadriceps muscle strength, power, and knee joint mechanics in knee osteoarthritis: A cross-sectional study [J]. *Clinical biomechanics (Bristol, Avon)*, 2015, 30(10): 1140-1145
- [19] Hatfield GL, Stanish WD, Hubley-Kozey CL. Relationship between knee adduction moment patterns extracted using principal component analysis and discrete measures with different amplitude normalizations: Implications for knee osteoarthritis progression studies [J]. *Clinical biomechanics (Bristol, Avon)*, 2015, 30 (10): 1146-1152
- [20] Parsons MA, Moghbel M, Saboury B, et al. Increased ¹⁸F-FDG uptake suggests synovial inflammatory reaction with osteoarthritis: preliminary in-vivo results in humans [J]. *Nuclear medicine communications*, 2015, 36(12): 1215-1219
- [21] Thawait GK, Demehri S, AlMuhit A, et al. Extremity cone-beam CT for evaluation of medial tibiofemoral osteoarthritis: Initial experience in imaging of the weight-bearing and non-weight-bearing knee [J]. *European journal of radiology*, 2015, 84(12): 2564-2570
- [22] Fransen M, McConnell S, Harmer AR, et al. Exercise for osteoarthritis of the knee: a Cochrane systematic review [J]. *British journal of sports medicine*, 2015, 49(24): 1554-1557
- [23] Niu J, Felson DT, Neogi T, et al. Patterns of Coexisting Lesions Detected on Magnetic Resonance Imaging and Relationship to Incident Knee Osteoarthritis: The Multicenter Osteoarthritis Study[J]. *Arthritis & rheumatology(Hoboken,N.J.)*, 2015, 67(12): 3158-3165
- [24] Ip D. Does addition of low-level laser therapy (LLLT) in conservative care of knee arthritis successfully postpone the need for joint replacement[J]. *Lasers in medical science*, 2015, 30(9): 2335-2339
- [25] Hall M, Wrigley TV, Metcalf BR, et al. Mechanisms underpinning the peak knee flexion moment increase over 2-years following arthroscopic partial meniscectomy[J]. *Clinical biomechanics (Bristol, Avon)*, 2015, 30(10): 1060-1065
- [26] Park JS, Kim DK, Shin HD, et al. Apigenin Regulates Interleukin-1 β -Induced Production of Matrix Metalloproteinase Both in the Knee Joint of Rat and in Primary Cultured Articular Chondrocytes [J]. *Biomolecules & therapeutics*, 2016, 24(2): 163-170
- [27] Roller BL, Monibi F, Stoker AM, et al.Characterization of Meniscal Pathology Using Molecular and Proteomic Analyses [J]. *The journal of knee surgery*, 2015, 28 (6): 496-505
- [28] Magni NE, McNair PJ, Rice DA. The effects of resistance training on muscle strength, joint pain, and hand function in individuals with hand osteoarthritis: a systematic review and meta-analysis[J]. *Arthritis Res Ther*, 2017, 19(1): 131