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重组人 γ -干扰素辅助治疗脊柱结核手术的临床研究*

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摘要 目的:观察重组人 γ -干扰素辅助治疗脊柱结核手术的临床疗效。**方法:**选择 2009 年 6 月至 2012 年 6 月在我院治疗脊柱结核患者 110 例,随机分成实验组和对照组,每组 55 例。对照组患者行手术治疗,手术前后予抗结核治疗,观察组在对照组治疗的基础上加用 γ -干扰素治疗。观察和比较两者患者症状改善情况、Frankel 分级、并发症及复发率。**结果:**治疗组优良率为(96.4%)高于对照组(83.6%),两组患者功能评价比较差异均有统计学意义($X^2=8.0, p=0.005$);治疗组并发症发生率为 5.5%,对照组为 18.2%,治疗组并发症发生率比对照组低($X^2=8.3, p=0.004$),两组相互比较差异均有统计学意义;治疗组患者神经功能 Frankel 分级 E 级比例(98.2%)较对照组为(81.8%)高,差异有统计学意义($X^2=5.1, p=0.02$)。**结论:**人重组 γ -干扰素有改善脊柱结核患者的临床症状,促进伤口愈合,减少并发症及复发率等特点,值得在临床推广。

关键词:重组;干扰素;脊柱结核;手术

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Clinical Research on Recombined Human Interferon-Gamma Adjuvant Therapy with Spinal Tuberculosis Operation*

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ABSTRACT Objective: To observe the clinical effect of recombined human interferon-gamma adjuvant therapy with spinal tuberculosis operation. **Methods:** 110 cases diagnosed with spinal tuberculosis accepting treatment from June 2009 to June 2012 in our hospital were divided into two groups randomly, the control group was treated with operation, Anti-tuberculosis treatment before and after operation, while the treating group was treated with interferon-gamma. **Results:** The excellent rate in the treating group (96.4%) was higher than that (83.6%) in the control group (83.6%), which is statistically significant ($X^2=8.0, p=0.005$); complication rate in the treating group (5.5%) is (18.2%) than control group (18.2%), which is of statistical significance ($X^2=8.3, P=0.004$), Nerve function Frankel E classification in treating group (98.2%) is higher than control group (81.8%), which is statistical ($X^2=5.1, p=0.02$). **Conclusion:** The clinical effect of recombined human interferon-gamma treating in the spinal tuberculosis operation is convincing and reliable. Being able to promote wound healing, reduce complications and recurrence rate, it is worth promoting.

Key words: Recombined; Interferon-gamma; Spinal tuberculosis; Operation

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前言

近年来随着结核菌耐药菌株的出现与扩散,致使全球结核病疫情恶化,结核感染患者逐年增多,据世界卫生组织统计,全球每年新发病例约 800 万例^[1,2]。我国是结核病高发国家,现有 400 多万活动性肺结核患者。脊柱结核是常见的肺外结核,占骨关节结核的 50%,脊柱结核可破坏骨质,累及椎管,压迫脊髓、神经,因脊柱结核引起截瘫率可高达 10%,对患者家庭和社会均造成沉重经济负担^[3-5]。临床上对脊柱结核患者选择化疗+手术的治疗方式已被广大临床医生认同^[6-8]。通过外科治疗能达到彻底清除病灶、有效减压和维持脊柱稳定性。本研究旨在观察对脊柱结核手术前后化疗+ γ -干扰素的治疗效果,现报道如下。

1 资料与方法

1.1 一般资料

收集我院 2008 年 6 月至 2012 年 6 月入院,依据 2001 年结核诊断与治疗指南标准确诊为脊柱结核患者 110 例随机分为治疗组和对照组各 55 例。治疗组男 38 例,女 17 例,年龄 16~45 岁,平均 30 ± 2 岁,病程 2 个月~8 年,平均 1.3 年;初发结核患者 42 例,复发结核患者 13 例;结核部位:颈椎 7 例,胸椎 34 例,腰椎 14 例;神经功能 Frankel 分级 C 级 5 例、D 级 23 例、E 级 27 例。对照组男 36 例,女 19 例,年龄 13~47 岁,平均 32 ± 2 岁,病程 5 个月~7 年;平均 1.2 年;初发结核患者 44 例,复发结核患者 11 例;脊柱结核部位:颈椎 4 例,胸椎 33 例,腰

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椎 18 例;神经功能 Frankel 分级 C 级 4 例、D 级 25 例、E 级 26 例。两组患者在性别、年龄、病程、脊柱结核部位和神经功能 Frankel 分级上无明显差异($P>0.05$),具有可比性。

1.2 治疗方法

对照组采用四联(异烟肼、利福平、链霉素、乙胺丁醇)SHRZ/5HRZ 抗痨疗法治疗 2-3 周,并予以护肝、维生素 B6 等治疗,每周复查 ESR,患者全身中毒症状明显改善,ESR 呈现下降趋势后即进行手术治疗。手术采用经前路方式对骨质破坏严重的椎体进行次全切除,根据情况进行骨植入和内固定,彻底清除脓肿、死骨和肉芽组织等病灶,双氧水浸泡病灶,生理盐水冲洗,彻底冲洗后局部应用链霉素 1 g、异烟肼 0.5 g,放置引流管,术后 24~36 h 拔除引流管,每 3 个月复查 x 线片、血、尿常规,确认植骨融合后开始下床活动,常规抗痨治疗 12 个月后复查。治疗组术前在对照组化疗的基础上肌注人重组 γ -干扰素 100U,每周 3 次,术后维持 2 个月。

1.3 观察指标

功能评价标准:体力劳动、生活不受限制评为优;体力劳动

后会出现腰背部疼痛,工作生活轻度受限评为良;腰背部疼痛不适反复发作,工作生活中度限制评为可;不能正常的工作评为差。比较两组的优良率(优良率 = 优 + 良 / 总例数)、并发症发生率、神经功能 Frankel 分级 E 级的比例。

1.4 统计学分析

采用 SPSS18.0 统计学软件,所有数据以均数 $\pm$ 标准差($\bar{X} \pm S$)表示,计量资料采用 t 检验,计数资料采用 χ^2 检验,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组患者功能评价的比较

治疗组患者手术 12 个月后随访,优 45 例,良 8 例,可 2 例,差 0 例,优良率为 96.4%(53/55)。对照组患者手术 12 个月后随访,优 36 例,良 10 例,可 7 例,差 2 例,优良率为 83.6%(46/55);两组患者功能评价比较差异均有统计学意义($X^2=8.0$, $P=0.005$)(见表 1)。

表 1 两组患者功能评价的比较[n/(%)]

Table 1 Comparison of the function evaluation between two groups[n/(%)]

Group	Case	Excellent	Fine	General	Bad	Excellent and fine total
Treatment group	55	45(81.8%)	8(14.6%)	2(3.6%)	0	53(96.4%)*
Control group	55	36(65.4%)	10(18.2%)	7(12.8%)	2(3.6%)	46(83.6%)

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

2.2 两组患者并发症发生率的比较

治疗组患者手术后均脓肿和无窦道形成,2 例手术伤口延期愈合,1 例 II 期愈合,并发症发生率为 5.5%(3/55),对照组患者手术后 1 例脓肿,1 例窦道形成,3 例手术伤口延期,5 例 II

期愈合,并发症发生率为 18.2%(10/55),治疗组并发症发生率比对照组低($\chi^2=8.3$, $P=0.004$),两组相互比较差异均有统计学意义(见表 2)。

表 2 两组患者并发症发生率的比较[n/(%)]

Table 2 Comparison of the incidence of complications between two groups[n/(%)]

Group	Case	Abscess	Sinus	Delayed healing	II healing	Total
Treatment group	55	0	0	2(3.6%)	1(1.8%)	3(5.5%)**
Control group	55	1(1.8%)	1(1.8%)	3(5.5%)	5(9.1%)	10(18.2%)

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

表 3 两组患者神经功能 Frankel 分级的比较[n/(%)]

Table 3 Comparison of the clinical effect between two groups[n/(%)]

Group	Case	Frankel C	Frankel D	Frankel E
Treatment group	55	0	1(1.8%)	54(98.2%)*
Control group	55	1(1.8%)	9(16.4%)	45(81.8%)

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

2.3 两组患者神经功能 Frankel 分级的比较

治疗组患者神经功能 Frankel 分级 C 级 0 例、D 级 1 例、E 级 54 例, Frankel 分级 E 级比例为 98.2%(54/55)。对照组患者神经功能 Frankel 分级 C 级 1 例、D 级 9 例、E 级 45 例, Frankel 分级 E 级比例为 81.8%(45/55)。两组患者 Frankel 分级 E 级比例相互比较,差异有统计学意义($X^2=5.1$, $P=0.02$)(见表 3)。

3 讨论

近年来,结核病发病率不断上升,而且耐药菌株越来越多,病流行抽样调查结果显示,我国结核杆菌耐多药率高达 6.8%,这给结核病的防治带来了很大困难^[9,10]。脊柱结核约占骨关节结核的一半,并且脊柱结核的耐药更高,有学者报道脊柱

结核总耐药率高达 66.7%,已成为目前脊柱结核外科治疗所面临的难题^[11-13]。以往的治疗方式多采用长期卧床、石膏固定,但长期卧床易引起褥疮、肺部感染等并发症,因而复发率高。近年来,随着医学科学发展脊柱结核的治疗方法增多,特别是手术方法的进步,脊柱结核外科治疗由传统的结核病灶清除植骨术发展到椎间植骨内固定重建脊柱稳定,其优点有:首先,通过清除结核病灶组织及硬化骨、切除直至正常骨质,可以有效破坏结核菌生存、繁殖的封闭环境,使化疗药物更有效的进入病变处,从而达到消灭结核菌的目的;其次,彻底清除病灶,能解除神经压迫,促进植骨融合;再次,重建脊柱的稳定性,恢复脊柱的生理曲度及功能,减轻了患者的痛苦,缩短了治愈时间^[14-16]。

γ -干扰素属于 II 型干扰素,主要由活化的 CD4⁺ 及 CD8⁺ T 细胞和 NK 细胞产生,可激活巨噬细胞^[17,18]。增强吞噬结核分枝杆菌的能力,增强巨噬细胞抗原提呈功能,促进巨噬细胞分泌 IL-12,促进 MHC 分子表达;促进 TH1 分泌,抑制 TH2 细胞增殖;激活中性粒细胞,促进 NK 细胞杀伤活性^[19,20]。

本研究显示,脊柱结核病人在接受手术及正规抗结核治疗的同时,肌注重组 γ -干扰素后患者的功能评价明显增高,患者术后伤口愈合好,术后并发症发生率、复发率、Frankel 分级明显降低,因此,人重组 γ -干扰素有改善脊柱结核患者的临床症状,促进伤口愈合,减少并发症及复发率等特点,值得在临床推广。

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