doi: 10.13241/j.cnki.pmb.2017.10.023

康柏西普与雷珠单抗治疗年龄相关性黄斑变性的临床研究

赵晨皓 刘庆淮△ 曹二兵 顾刘伟 黄军龙

（南京医科大学第一附属医院眼科 江苏 南京 210029）

摘要 目的：探讨康柏西普联合雷珠单抗治疗年龄相关性黄斑变性（AMD）的临床疗效。**方法**：选择 2015 年 6 月到 2016 年 10 月我院收治的 60 例 AMD 患者，按随机数字表法分为对照组和治疗组。对照组患者给予康柏西普治疗，治疗组患者给予康柏西普联合雷珠单抗治疗，两组患者均治疗 3 个月。评价并比较两组患者临床疗效。统计并比较两组患者治疗后的视网膜渗漏总改善率。观察并比较两组患者治疗前后最佳矫正视力和黄斑视网膜厚度。**结果**：治疗后，治疗组患者的视力提高率为 80.00%，明显高于对照组的 55.00%，差异具有统计学意义（X^2=4.104，P=0.043）。治疗后，治疗组患者的视网膜渗漏总改善率为 92.50%，明显高于对照组的 70.00%，差异具有统计学意义（X^2=5.294，P=0.021）。治疗前，两组患者最佳矫正视力、黄斑视网膜厚度比较差异无统计学意义（P>0.05）；治疗后，两组患者最佳矫正视力均明显大于治疗前，黄斑视网膜厚度均明显小于治疗前，并且治疗组均明显优于对照组，差异均具有统计学意义（P<0.05）。**结论**：康柏西普联合雷珠单抗治疗 AMD 的临床疗效显著，能够明显提高视力，减轻视网膜渗漏，值得在临床上推广应用。

关键词：康柏西普；雷珠单抗；年龄相关性黄斑变性；疗效

中图分类号：R774.5 **文献标识码**：A **文章编号**：1673-6273(2017)10-1889-03

Clinical Study on Ranibizumab and Conbercept in the Treatment of Patients With Age-Related Macular Degeneration

ZHAO Chen-hao, LIU Qing-huai△, CAO Er-bing, GU Liu-wei, HUANG Jun-long

(Department of Ophthalmology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, 210029, China)

ABSTRACT Objective: To study the clinical efficacy of Ranibizumab and Conbercept in the treatment of patients with age-related macular degeneration (AMD). **Methods:** A total of 60 patients (60 eyes) with AMD in our hospital from June 2015 to October 2016 were enrolled, the subjects were divided into control group and treatment group according to the random number table method. The control group was treated with Ranibizumab, and the treatment group were treated with Ranibizumab combined with Conbercept. The two groups were treated for 3 months. The clinical efficacy of the two groups were compared. The total improvement rate of the retinal leakage of the two groups after treatment were compared.And the best corrected visual acuity and macular thickness of the two groups before and after treatment were compared. **Results:** The increase rate of the vision of the treatment group was 80.00%, which was significantly higher than 55.00% of the control group, the difference was statistically significant (X^2=4.104, P=0.043). The total improvement rate of the retinal leakage of the treatment group was 92.50%, which was significantly higher than 70.00% of the control group, the difference was statistically significant (X^2=5.294, P=0.021). There were no significantly differences of the best corrected visual acuity and macular thickness of the two groups before treatment (P>0.05). The best corrected visual acuity of the two groups after treatment were significantly higher than before treatment, the macular thickness of the two groups after treatment were significantly lower than before treatment, and the treatment group were better than the control group, the difference was statistically significant (P<0.05). **Conclusion:** Ranibizumab combined with Conbercept have good clinical efficacy in the treatment of patients with AMD,which can significantly improve eyesight and reduce the leakage of the retina, it is worthy of clinical application.

Key words: Conbercept; Ranibizumab; Age-related macular degeneration; Efficacy

Chinese Library Classification(CLC): R774.5 Document code: A

Article ID: 1673-6273(2017)10-1889-03

前言

年龄相关性黄斑变性（age-related macular degeneration，AMD）是眼科常见的一种视网膜黄斑部退行性病变，可双眼先后发病或同时发病，以致损伤患者视力[1,2]。AMD 多发生于 50 岁以上的老年人群中，调查表明我国 52-64 岁人群中的发病率为 1.6%，75-85 岁老年人群中的发病率为 27.9%，并且近年来随着老龄化进程的加剧，AMD 的发病率有逐年增高的趋势，已成为我国老年人群的第 3 大致盲眼病，严重威胁着人们的日常生活和身体健康[3-5]。依照临床表现症状，AMD 主要分为渗出型（湿性）和萎缩型（非渗出性或干性）两种，其中渗出型 AMD 病

作者简介：赵晨皓（1982-），男，硕士，主治医师，从事眼科学方面的研究，E-mail: zhaochenhao82@sina.com

△ 通讯作者：刘庆淮（1963-），男，博士，教授、主任医师，从事眼科学方面的研究

(收稿日期：2016-12-02 接受日期：2016-12-24)

例占 10%左右，但其对患者的视力损伤相对更为严重，占视力丧失病例的 90%左右[6,7]。目前临床治疗 AMD 主要采用激光光凝、抗血管内皮生长因子（VEGF）玻璃体腔注射、玻璃体切割术、口服药物支持治疗、经瞳孔温热疗法等多种措施，在众多治疗方法中玻璃体腔 VEGF 注射是近年来出现的一种新型治疗方法，具有明确的治疗效果[8,9]。康柏西普和雷珠单抗是两种主要的抗 VEGF 药物，本研究探讨康柏西普联合雷珠单抗治疗 AMD 的临床疗效，研究结果如下。

1 资料与方法

1.1 一般资料

选择我院于 2015 年 6 月到 2016 年 10 月收治的 60 例 AMD 患者作为研究对象，患者均为单眼，有 60 只眼。病例纳入标准：⑴ 经眼底荧光造影或光学断层扫描确诊为 AMD 患者；⑵ 年龄 >50 岁；⑶ 近半年内未使用过眼部治疗药物患者。病例排除标准：⑴ 伴有其他类型视网膜病变患者；⑵ 青光眼患者；⑶ 合并有传染性疾病患者；⑷ 肝肾功能不全患者；⑸ 不接受本研究治疗方案患者。所有纳入病例均按照随机数字表法进行分组，分为对照组 20 例和治疗组 40 例。对照组患者男 11 例，女 9 例；年龄 50-80 岁，平均年龄（61.25± 8.92）岁；病程 6-117 个月，平均病程（40.30± 11.48）个月；其中左眼 13 例，右眼 7 例。治疗组患者男 29 例，女 11 例；年龄 51-79 岁，平均年龄（62.84± 10.50）岁；病程 6-129 个月，平均病程（42.84± 14.33）个月；其中左眼 26 例，右眼 14 例。对比两组患者的临床一般资料，包括性别、年龄、病程，均无统计学差异（P>0.05），故有可比性。所有病例均于研究开展前进行沟通，患者同意接受本研究且签署知情同意书，另外本研究经过医院伦理委员会批准实施。

1.2 治疗方法

所有病例均于术前连续使用 3 d 的妥布霉素（购自 s.a. Alcon-Couvreur n.v.，规格：15 mg/ 瓶）滴眼，4 次 /d，术前 1 d 应用碘伏冲洗结膜囊，应用 5%的托吡卡胺（购自武汉五景药业有限公司，规格 15 mg/ 瓶）散瞳，两组患者均于手术室中给予玻璃体腔注射给药。对照组患者给予康柏西普（商品名：郎沐，购自成都康弘生物科技有限公司，规格 10 mg/mL，0.2 mL/ 支）治疗，0.5 mg/ 次，1 次 / 月；治疗组患者给予雷珠单抗联合康柏西普联合治疗，具体为：雷珠单抗（商品名：诺适得，购自 Novartis Pharma Schweiz AG，规格 10 mg/mL，0.2 mL/ 瓶），0.5 mg/ 次，1 次 / 月，康柏西普，0.5 mg/ 次，1 次 / 月。所有病例均接受以上相应的治疗措施，连续治疗 3 个月。

1.3 检测指标

1.3.1 视力疗效评价 视力疗效的评价标准为[10]：⑴ 下降：通过国际标准视力表检查，视力下降 2 行及以上；⑵ 不变：通过国际标准视力表检查，视力变化为 1 行以内；⑶ 提高：通过国际标准视力表检查，视力提高 2 行及以上。

1.3.2 检测指标 观察两组患者治疗前和治疗后的最佳矫正视力和黄斑视网膜厚度，并进行比较。观察视网膜渗透面积，统计两组治疗后视网膜渗漏消失患者例数、视网膜渗漏面积明显缩小患者例数以及视网膜渗漏面积无明显变化患者例数，计算并比较两组治疗后视网膜渗漏总改善率，视网膜渗漏总改善率 =（视网膜渗漏消失例数 + 视网膜渗漏面积明显缩小例数）/ 总例数 × 100%[11]。

1.4 数据处理

本研究所有数据均采用 SPSS19.0 软件包处理，其中计数资料以率（%）表示，采用 X^2 检验，计量资料以均数± 标准差（$\bar{x}$± s）表示，采用 t 检验，P<0.05 表示比较具有统计学差异。

2 结果

2.1 两组患者治疗后视力提高率比较

治疗后，治疗组患者的视力提高率为 80.00%，明显高于对照组的 55.00%，差异具有统计学意义（P<0.05）。见表 1。

表 1 两组患者治疗后视力提高率比较[n(%)]

Table 1 Comparison of the increase rate of the vision of the two groups after treatment [n(%)]

Groups	n	Decreased	Unchanged	Improved
Control group	20	2(10.00)	7(35.00)	11(55.00)
Treatment group	40	2(5.00)	6(15.00)	32(80.00)
X^2 value		2.446	3.142	4.104
P value		0.118	0.076	0.043

2.2 两组患者治疗后视网膜渗漏总改善率比较

治疗后，治疗组患者的视网膜渗漏总改善率为 92.50%，明显高于对照组的 70.00%，差异具有统计学意义（P<0.05）。见表 2。

2.3 两组患者治疗前后最佳矫正视力、黄斑视网膜厚度比较

治疗前，两组患者最佳矫正视力、黄斑视网膜厚度比较差异无统计学意义（P>0.05）；治疗后，两组患者最佳矫正视力均明显大于治疗前，黄斑视网膜厚度均明显小于治疗前，并且治疗组患者最佳矫正视力、黄斑视网膜厚度变化均明显优于对照组（P<0.05）。见表 3。

3 讨论

目前，AMD 的发病机制仍旧尚不明确，大多认为脉络膜新生血管形成是发病的主要因素，从而导致患者黄斑部水肿、出血、瘢痕、渗出、视功能受损，严重者甚至导致视力丧失[12,13]。雷珠单抗是一种第二代的重组鼠抗 VEGF 单克隆抗体片段，于 2006 年 6 月被 FDA 批准用于治疗 AMD，其结构类同于第一代产品 - 贝伐单抗，通过同时作用于多个 VEGF 亚型及其降解

表 2 两组患者治疗后视网膜渗漏总改善率比较 [n(%)]

Table 2 Comparison of the total improvement rate of the retinal leakage of the two groups after treatment [n(%)]

Groups	n	Retinal leakage disappeared	Retinal leakage area significantly narrowed	Retinal leakage area no changed	Total improvement
Control group	20	12(60.00)	2(10.00)	6(30.00)	14(70.00)
Treatment group	40	29(72.50)	8(20.00)	3(7.50)	37(92.50)
χ 2 value	—	—	—	—	5.294
P value	—	—	—	—	0.021

表 3 两组患者治疗前后最佳矫正视力、黄斑视网膜厚度比较

Table 3 Comparison of the best corrected visual acuity and macular thickness of the two groups before and after treatment

Groups	n	Time	Best corrected visual acuity	Macular thickness(um)
Control group	20	Before treatment	0.08± 0.05	320.45± 16.54
		After treatment	0.24± 0.10*	257.30± 14.82*
Treatment group	40	Before treatment	0.07± 0.06	318.74± 17.68
		After treatment	0.43± 0.12*#	203.43± 12.71*#

Note: Compared with before treatment, *P<0.05; Compared with the control group, #P<0.05.

产物来发挥抑制新生血管生成、减轻黄斑水肿、视网膜渗出的作用,从而稳定甚至提高患者的视力[14]。康柏西普是一种分子量仅为 142KD 的基因工程重组人融合蛋白，是由人 VEGF 受体 2 的免疫球蛋白样区域 3、4 和 VEGF 受体 1 的免疫球蛋白样区域 2 共同融合到人 IgG1 的 Fc 片段制备成融合蛋白,能够直接抑制影响新生血管生成的因子 VEGF，发挥治疗 AMD 的作用,另外其还具有半衰期长、亲和力更高的优点[15-17]。本研究探讨康柏西普联合雷珠单抗治疗 AMD 的临床疗效,以期为临床治疗 AMD 选用安全有效的治疗方案提供一定的依据。

本研究结果显示,治疗后治疗组患者的视力提高率明显高于对照组(P>0.05)。提示康柏西普联合雷珠单抗能够明显提升 AMD 患者的视力,临床疗效显著。这可能是由于康柏西普和雷珠单抗具有协同作用,两者共同作用于多种 VEGF 亚型,抑制 VEGF 与受体的结合，从而抑制新生血管的形成，发挥治疗 AMD 的作用[18]。另外本研究结果显示,治疗后,治疗组患者的视网膜渗漏总改善率为 92.50%,明显高于对照组的 70.00%,差异具有统计学意义(X^2=5.294,P=0.021)。治疗前,两组患者最佳矫正视力、黄斑视网膜厚度比较差异无统计学意义(P>0.05);治疗后,两组患者最佳矫正视力均明显大于治疗前,黄斑视网膜厚度均明显小于治疗前，并且治疗组患者最佳矫正视力、黄斑视网膜厚度变化均明显优于对照组(P<0.05)。提示康柏西普联合雷珠单抗能够明显提高 AMD 患者视力、减轻视网膜渗漏、改善黄斑视网膜中心凹厚度。这可能是两种药物均能够使黄斑水肿、出血及渗出的吸收明显增加,从而极大的改善视网膜组织的微循环,具有明显的治疗效果[19,20]。

综上所述,康柏西普联合雷珠单抗治疗 AMD 的临床疗效显著,能够明显提高视力,减轻视网膜渗漏,值得在临床上推广应用。

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