Clinical Application Analysis of Calcium Dobesilate Combined with Ranibizumab in Patients with Macular Edema Secondary to Branch Retinal Vein Occlusion

LEILEI YU, KAI TANG, YUNJIU RONG, ZHI LI, XUELING SONG, XUEPEI CHEN AND LINA SONG*

Department of Ophthalmology, The 80th Group Army Hospital of the Chinese People's Liberation Army, Weifang, Shandong 261021, China

We attempts to discuss the clinical efficacy and application of calcium dobesilate combined with ranibizumab in patients with macular edema secondary to branch retinal vein occlusion. We randomly selected 100 patients with macular edema secondary to branch retinal vein occlusion who had accepted therapy in our hospital from September 2019 to September 2021 as general data. Then divided them into two groups, one was observation group and the other was control group (n=50). Among them, control group was treated with ranibizumab and observation group was treated with calcium dobesilate combined with ranibizumab. Observation group had better changes of best corrected visual acuity and macular foveal thickness after 1 mo, 3 mo and 6 mo treatment than control group. Observation group had better clinical efficacy than control group. Control group had more serious complications than observation group. Calcium dobesilate combined with ranibizumab has a significant clinical effect on patients with macular edema secondary to branch retinal vein occlusion and can reduce complications in patients.

Key words: Calcium dobesilate, ranibizumab, macular edema, clinical efficacy

Retinal vein occlusion is a common retinal vascular disease. We can divide it into central Retinal Vein Occlusion (RVO) and Branch Retinal Vein Occlusion (BRVO) according to occlusion. Among them, BRVO embolism is the most common[1]. Ranibizumab is a clinically common Vascular Endothelial Growth Factor (VEGF) inhibitor in recent years. The study found that after 6 mo of continuous injection, the patient's vision correction and macular edema were remarkably improved. Now, the treatment of calcium dobesilate combined with ranibizumab has become a new hot point in BRVO treatment[2]. In this study, we randomly selected 100 patients with macular edema secondary to BRVO who had accepted therapy in our hospital from September 2019 to September 2021 as general data. We attempts to discuss the clinical efficacy and application of calcium dobesilate combined with ranibizumab on patients with macular edema secondary to BRVO through observation and comparison. This study randomly selected 100 patients with macular edema secondary to BRVO who had accepted therapy in our hospital from September 2019 to September 2021 as general data. Then divided them into two groups, one was observation group and the other was control group (n=50). Among them, treated control group with ranibizumab; treated observation group with calcium dobesilate combined with ranibizumab. Gender and age distribution of patients in control group: 25 males and 25 females included, ages were from 17 to 69 y old, average were about (43.6±9.45) y old. Gender and age distribution of patients in observation group: 18 males and 32 females included, ages were from 18 to 70 y old and average was about (46.1±8.99) y old. Comparison of both groups on data possessed no significant difference, so it had no statistical significance ($p>0.05$) and can be compared. Inclusion criteria includes mydriatic fundus examination caused temporal branch or temporal branch block. Optical Coherence Tomography (OCT) examination showed macular thickening, edema and cystic effusion under the retina. Fundus fluorescein angiography showed slow and circuitous venous filling with or without perfusion area[3]. It meets the diagnostic criteria of macular edema secondary to BRVO; had complete clinical data and signed a voluntary informed letter. Exclusion criteria includes that there is no absolute contraindication of

***Address for correspondence**
E-mail: sln32298@163.com

surgery, such as patients with severe cardiovascular and cerebrovascular diseases and mental disorders[4]; the presence of another eye merger may cause macular edema, such as diabetic retinopathy, hypertensive retinopathy and other symptoms[5]; previous history of glaucoma and high intraocular pressure; there are active eye diseases, such as keratitis, conjunctivitis, uveitis and other symptoms and there is severe refractive interstitial opacity, which affects the observation[6]. Control group adopted ranibizumab treatment. Used tobramycin eye drops routinely for anti-infection. The patient took the supine position and was anesthetized with hydrochloric acid C-main eye drops. Rinsed conjunctival sac with 0.9 % sodium chloride solution and applied aseptic carving fixation. Then used a syringe to enter the sclera slowly at 3.5 mm (without intraocular lens implantation) or 3.5~4.0 mm (intraocular lens implantation) perpendicular to the corner of the eye and injected ranibizumab into fundus. After putting down the needle, press with a sterile cotton swab[7]. Adopted bandage to place dexamethasone in conjunctival sac. Observation group-Adopted calcium dobesilate combined with ranibizumab treatment. After receiving the same treatment as control group, after the injection of ranibizumab, treated them with calcium dobesilate, one tablet at a time three times a day. Calcium dobesilate capsules (Haochang), specification: 250 mg/tablet, batch number: 1131118, manufactured by Ningxia Keya Pharmaceutical Co., Ltd. Specification: 10 mg/tablet, batch number: X1990, produced by Beijing Novartis Pharmaceutical Co., Ltd[8]. Finally, observed and recorded the related conditions of both groups after 1 mo, 3 mo, 6 mo and 1 y of treatment respectively. Compared and analyzed the changes of best corrected visual acuity of both groups; compared and analyzed the changes of macular foveal thickness of both groups; compared and analyzed the clinical effects of both groups and compared and analyzed the complications of both groups. Adopted Statistical Package for the Social Sciences (SPSS) 20.0 software to process the data collected in this research. Used ($\bar{x}\pm s$) to indicate measurement data, comparison between groups tested by t and comparison of enumeration data tested by χ^2. $p<0.05$, indicating that the data obtained in the study possessed statistical significance. Comparison of the best corrected visual acuity changes of both groups was remarkably different, so it possessed statistical significance ($p<0.05$). Please check the specifications in Table 1 below. After 1 mo, 3 mo and 6 mo of treatment, observation group had better changes of best corrected visual acuity than control group. Comparison of the changes in macular foveal thickness of both groups was remarkably different, so it possessed statistical significance ($p<0.05$). Please check the specifications in Table 2 below. After 1 mo, 3 mo and 6 mo of treatment observation group had better changes of macular foveal thickness than control group. Comparison of clinical efficacy of both groups was remarkably different, so it possessed statistical significance ($p<0.05$). Please check the specifications in Table 3 below. The total effective rate=significant effective rate+effective rate. Observation group had effective rate (2 %) and significant effective rate (94 %), so the total effective rate is 96 %. Control group had effective rate (2 %) and significant effective rate (80 %), so the total effective rate is 82 %. It can be seen that observation group had better clinical efficacy than control group. Comparison of complications of both groups was remarkably different, so it possessed statistical significance ($p<0.05$). Please check the specifications in Table 4 below. There were 1 patient with elevated intraocular pressure and 1 patient with bulbar conjunctival hemorrhage in observation group, so 2 patients with complications, accounting for 4 %. There were 5 patients with elevated intraocular pressure and 4 patients with bulbar conjunctival hemorrhage in control group, so 9 patients with complications, accounting for 18 %. It can be seen that control group had more serious complications than observation group. Macular edema caused by BRVO can cause macular cell dysfunction, as the disease develops, retinal receptor cells will suffer irreversibly damage, resulting in a serious decline in patients' vision, so restoring vision is the key to improve visual status[9]. Regression of retinal ischemia, ischemia and macular edema, the reason for macular edema caused by BRVO is that the blood flow is affected after BRVO, the venous pressure increases, resulting in retinal ischemia and hypoxia[10]. VEGF expression in retina increases retinal vascular permeability and contributes to the formation of retinal and macular edema. At present, the main treatment method of BRVO is ranibizumab in clinic. The basic principle is that after injection, the oxygen consumption of diseased retinal tissue is reduced, the capillary perfusion of ischemia and hypoxia is significantly improved and the retinal barrier is damaged. Stabilize vascular closure and retinal vascular leakage symptoms to treat macular edema[11]. However, clinical studies have indicated that ranibizumab alone has a low effect on the treatment of BRVO macular edema, slow speckle

edema and poor reactivity in the early lesion area, but it is close to the center of the lesion's macular fovea. If enhance force, the damage will increase, resulting in a thicker central depression of the macula, which hinders the early recovery of vision and delays the optimal recovery period[12]. Many clinical studies have proved that the occurrence and development of macular edema caused by BRVO have close relationship with body inflammatory factors and VEGF levels. Therefore, macular edema caused by calcium dobesilate treatment has important effect on BRVO. Its mechanism of action reduces vascular permeability and resists new blood vessel formation. The rapid absorption and drainage of the retina can reduce the degree of macular edema. This study finds that the clinical efficacy of calcium dobesilate combined with ranibizumab is remarkably improved and the more significant the best corrected visual acuity and central macular thickness values, the significantly lower the incidence of complications. The combined use of approved anti-angiogenesis inhibitors and VEGF can promote vascular endothelial proliferation, inhibit angiogenesis, reduce neovascular permeability, retina release, reduce drainage and absorption, and reduce macular edema. Therefore, it is believed that the licensed calcium dobesilate combined with ranibizumab in the treatment of macular edema caused by BRVO has a significant effect on reducing central depression thickness and improving patients' vision. Calcium dobesilate combined with ranibizumab treatment can not only reduce the damage to the retina, but also reduce the recurrence rate and reduce the number of vitreous injections. Therefore, calcium dobesilate combined with ranibizumab has a significant effect on the treatment of macular edema caused by BRVO, reducing macular central depression thickness and improving patients' vision, which is worth generalizing extensively.

TABLE 1: COMPARISON AND ANALYSIS OF THE BEST CORRECTED VISUAL ACUITY CHANGES OF BOTH GROUPS (n, %)

Group	Cases	After 1 mo treatment	After 3 mo treatment	After 6 mo treatment
Control group	50	0.43±0.12	0.21±0.09	0.32±0.21
Observation group	50	0.49±0.23	0.23±0.27	0.18±0.16
χ^2		1.231	1.671	1.089
p		0.002	0.001	0.004

TABLE 2: COMPARISON AND ANALYSIS OF THE CHANGES IN MACULAR FOVEAL THICKNESS OF BOTH GROUPS (n, %)

Group	Cases	After 1 mo therapy	After 3 mo therapy	After 6 mo therapy
Control group	50	418.5±101.2	264.5±89.6	309.2±78.9
Observation group	50	419.9±111.4	276.8±87.9	247.2±76.4
χ^2		1.221	1.323	1.433
p		0.004	0.003	0.004

TABLE 3: COMPARISON AND ANALYSIS OF THE CLINICAL EFFICACY OF BOTH GROUPS (n, %)

Group	Cases	Significant effective	Effective	Invalid	Total effective rate
Observation group	50	47 (94 %)	1 (2 %)	2 (4 %)	48 (96 %)
Control group	50	40 (80 %)	1 (2 %)	9 (18 %)	41 (82 %)
χ^2					1.436
p					0.004

TABLE 4: COMPARISON AND ANALYSIS OF COMPLICATIONS OF BOTH GROUPS (n, %)

Group	Cases	Elevated intraocular pressure	Bulbar conjunctival hemorrhage	Other	Total
Observation group	50	1 (2 %)	1 (2 %)	0 (2 %)	2 (4 %)
Control group	50	5 (10 %)	4 (8 %)	0 (0 %)	9 (18 %)
χ^2					1.332
p					0.003

Conflict of interests:

The authors declared no conflicts of interest.

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