NEW THERAPEUTIC STRATEGIES IN THE TREATMENT OF OPTIC NERVE DISEASES: PROSPECTS AND LIMITATIONS

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The aim of the study was to evaluate the clinical efficacy of the irrigation-infusion method of local glucocorticosteroid (GCS) therapy in patients with optic neuritis (ON).

Material and methods: The study involved 40 patients (49 eyes) with ON aged 17 to 36 years (mean age 26.4±5.7 years). Depending on the method of administration of GCS dexamethasone, patients were divided into 2 groups: the main group (23 patients - 28 eyes) and the control group (17 patients - 21 eyes). In patients in the main group, dexamethasone was administered to the optic nerve (ON) in the first half of the day at a dose of 2 mg through an irrigation system implanted in the retrobulbar space. In the first 4 days, dexamethasone was administered 4 times - a daily dose of 8 mg; on days 5, 6 and 7 - 3 times (6 mg); on days 8 and 9 - 2 times (4 mg); on day 10 - 1 time (2 mg). The total dose of dexamethasone was 60 mg. In the control group, dexamethasone was administered intravenously at a dose of 8 mg for the first 4 days, then 6 mg for 3 days, 4 mg for 2 days, and 2 mg on day 10. In addition, patients were given retrobulbar injections of dexamethasone at a dose of 2 mg daily for the same 10 days. The total dose of dexamethasone for the course of treatment was 80 mg.

Results and discussion: In both groups of patients with ON, after the end of GCS therapy, improvements in all studied parameters were noted. However, significant positive changes and a reduction in the time to onset were observed in the main group of patients during topical GCS therapy using the irrigation-infusion method compared to the control group using the traditional GCS treatment regimen.

Conclusion: The clinical and functional advantages of the infusion-irrigation method of retrobulbar administration of GCS compared to the traditional administration scheme are a 1.3-fold increase in visual acuity and a 2.7-fold decrease in the incidence of postneuritic atrophy of ON during the 12-month follow-up period.

Compared with the traditional GCS therapy regimen, the irrigation-infusion method of introducing GCS into the retrobulbar space reduces the duration of the period of restoration of lost visual functions by 3 times and reduces the total course dose of GCS by 1.2 times.

Keywords: optic neuritis, corticosteroid therapy, targeted delivery, dexamethasone.

Introduction: The article is devoted to new possibilities for increasing the effectiveness of pathogenetic treatment of optic neuritis.

New opportunities for increasing the effectiveness of pathogenetic treatment of optic neuritis. Optic neuritis (ON) accounts for 30-40% of optic nerve diseases (ON) [1]. In 30-60% of cases of ON, bilateral lesions of ON are observed. ON is characterized by a particularly severe clinical course, a high risk of visual impairment and disability. Practical blindness in ON occurs in 21% of cases, 15% of patients have impaired vision, which determines the high medical and social importance of this problem [2-4].

The success of rehabilitation of patients with ON largely depends on timely therapeutic interventions on the pathogenetic mechanisms of the disease.

It has been established that in the pathogenesis of ON (regardless of the cause of its occurrence) there is an activation of neuroglia, excessive formation of pro-inflammatory cytokines and other inflammatory mediators by neuroglia and immune system (IS) cells, impaired microcirculation and intravasation, increased vascular permeability, increased expression of IS factors (T- and B-lymphocytes) to ON axons and their sensitization. As a result of the disruption of immune resistance mechanisms, cell-mediated immunopathological reactions of axonal damage of MNs are initiated [6-8].

As a rule, the causative agents of the changes described above are acute and chronic viral and bacterial infections.

The specifics of the treatment of ON (until the etiology of the disease is determined) include the immediate implementation of therapeutic measures aimed at suppressing the immunopathological mechanisms of the inflammatory reaction in ON and restoring visual functions.

The main and most effective method of emergency pathogenetic therapy in the early stages of the clinical manifestation of ON is the systemic (IV, oral) and/or local (retrobulbar) administration of glucocorticosteroids (GCS), which block the immunopathological, biochemical and pathophysiological mechanisms of the development of the inflammatory process [9-12].

However, with systemic use of GCS, due to the autonomy of the organ of vision in the ON, therapeutic concentrations of the drug are not achieved, which is sufficient for rapid and complete

elimination of the inflammatory process and restoration of vision. Daily retrobulbar injections of GCS can lead to the formation of intraorbital hematoma, traumatic damage to the ON, and perforation of the sclera of the eyeball, with a high risk of irreversible loss of vision [13, 14].

To achieve optimal anti-inflammatory effects in patients with ON, we used the irrigation-infusion method of local GCS therapy, in which the infusion of this drug into the retrobulbar space is carried out through an irrigation system [15]. The proposed method provides a constant therapeutic concentration of GCS, which is necessary for rapid and sustained elimination of the inflammatory process in ON [16-18].

Objective: The aim of this study was to evaluate the clinical efficacy of the irrigation-infusion method of local corticosteroid therapy in patients with ON.

Material and methods: The clinical study included 40 subjects (49 eyes) with ON aged 17 to 36 years (mean 26.4±5.7 years). Patients with ON in multiple sclerosis and other neurological diseases requiring concomitant treatment with a neurologist were excluded from the study.

According to clinical, anamnestic, laboratory and instrumental monitoring, among the entire population of patients examined in the spectrum of causes leading to the development of ON, herpesvirus infection prevailed (26 people, 65%), significantly less common causative agents of the inflammatory process in ON were acute respiratory viral infections, focal infections (28%, influenza) (sinusitis, tonsillitis, otitis (6 people, 15%).

As an urgent pathogenetic therapy, all patients with ON are given 100.0 ml of reamberin solution, which has strong detoxifying, antioxidant and antihypoxic properties; 5.0 ml of 2% intramuscular solution intravenously; 2.0 ml of 12.5% Dicinon solution to reduce exudative edema of ON

At the same time, all patients with exacerbations of chronic bacterial infection are prescribed systemic antibacterial therapy - 100.0 ml of 0.2% ciprofloxacin solution intravenously.

Depending on the route of administration of GCS dexamethasone, patients with ON were divided into 2 groups: main (23 people - 28 eyes) and control (17 people - 21 eyes). The study groups were compared by gender, age, severity of the inflammatory process in ON and initial visual functions ($p<0.05$).

In the main group of patients, dexamethasone was administered to the ON through an irrigation system installed in the retrobulbar space. Taking into account the daily rhythm of endogenous GCS secretion, dexamethasone infusions were carried out in a single dose of 2 mg in the first half of the day. In this case, in the first 4 days, dexamethasone was administered 4 times (daily dose - 8 mg), on days 5, 6 and 7 - 3 times (6 mg), on days 8 and 9 - 2 times (daily dose - 4

mg), on day 10 - 1 time (2 mg per day). The total dose of dexamethasone was 60 mg. In the afternoon, 0.5 ml of 1% emoxipine and 5 mg of retinalamine were administered through the infusion system twice every 2 hours. These drugs have a direct antioxidant and immunomodulatory effect, are able to optimize capillary perfusion of nervous tissue, and also activate the myelination of visual acuity axons. The course of treatment lasted 10 days.

In the control group of patients, dexamethasone was administered intravenously at a dose of 8 mg for the first 4 days, then 6 mg for 3 days, 4 mg for 2 days, and 2 mg on day 10. In addition, during these 10 days, patients received retrobulbar injections of dexamethasone at a dose of 2 mg per day. The total dose of dexamethasone for the course of treatment was 80 mg. For 10 days, patients in the control group were given additional retrobulbar injections of 0.5 ml of 1% emoxipine solution every afternoon. After the end of the course of treatment, patients in group 2 were prescribed for 1 month to consolidate the result obtained and restore impaired capillarization in the ON. oral picamilon 20 mg 3 times a day. This drug has antiplatelet and antihypoxic effects and is able to improve blood supply to the vessels of the optic nerve. In addition, a 0.1% solution of Semax, which has a pronounced antioxidant, antihypoxic, angioprotective and neurotrophic effect, was administered intranasally. Monitoring of ophthalmological parameters included: visometry using a Carl Zeiss Jena sign projector (Germany), indirect non-contact ophthalmoscopy with a 90-diopter lens and static computer perimetry using the Humphrey apparatus (Germany). In addition, electrical sensitivity (ES) and electrical lability (EL) of visual acuity were studied using the Diagnostician apparatus (Russia), and visual evoked potentials (VEP) were studied using the Neuro-MEP apparatus (multifunctional computer complex, Russia). The diameter of the retrobulbar part of the ON (DBP) was determined using the ultrasound scanning method on the Logiq multifunctional ultrasound system (universal linear sensor from 4 to 12 MHz, USA). All studies were conducted before the start of treatment, 10 days, 1, 3 and 12 months later. After the end of the course of GCS therapy. In patients with unilateral ON, clinical and functional parameters of the intact eyes were considered normal. Statistical analysis of the results obtained was carried out using the Microsoft Excel computer program, determining the reliability of differences using the Student's t-test. **Results and discussion:** Etiotropic antiviral chemotherapy was prescribed 5-7 days after receiving laboratory results of ELISA tests.

The results of the ophthalmological examination on the day of admission showed that in most cases, in patients with the main (16 people, 69.5 ± 2.3%) and control groups (12 people, 70.6 ± 2.5%) ON occurred in the form of papillitis and was accompanied by a typical ophthalmoscopic picture: hyperemia and increased dilation of the optic disc; dilation of venules and small linear and

petechial hemorrhages into the disc tissue and peripapillary retina; the presence of inflammatory exudate in the posterior parts of the vitreous body and in the vascular infundibulum of the ON disc.

The remaining patients in the main group (7 people, 30.5 ± 1.9%) and the control group (5 people, 29.4 ± 2.5%) had retrobulbar neuritis without obvious ophthalmoscopic changes in the ON disc, confirmed by the results of VEP indices and ultrasound B-scan of its retrobulbar part.

Initial visual acuity at the time of admission to the clinic decreased sharply: on average 0.14±0.02 relative. unity in patients in the main group and up to 0.18±0.03 in patients in the control group. During static perimetry, absolute and relative scotomas were detected in the central visual field (0-20 degrees) of patients in both groups, the total number of which did not have reliable intergroup differences ($p>0.05$) and averaged 18.6±1.5 and 14.1±0.5 in patients in the main group, and 17.0±0.4 ± 17.0 in the control group.

In both the main and control groups, at baseline, patients with ON had equivalent abnormalities in electrophysiological parameters compared with those without visual impairment: a significant increase in latent periods and a decrease in the amplitude characteristics of the positive component of the visual electric potential (VEP) P100; a statistically significant increase in PEC and a decrease in the EL of the ZN ($p<0.05$). According to the data of ultrasound B-scanning, a proportional increase in the diameter of the retrobulbar part of the ON was recorded in both groups of patients with ON, up to 5.2±0.5 mm in the main group and 5.05±0.57 mm in the control group, compared with the norm of 3.5±0.09 mm.

The dynamics of clinical, functional, and ultrasound indicators in patients with ON using different methods of GCS administration are presented in Table 1.

Analysis of the presented data showed that in both groups of patients with ON, after the end of GCS therapy, an improvement in all studied parameters was noted. However, in the patients of the main group during topical GCS therapy using the irrigation-infusion method, compared with the control group using the traditional GCS treatment regimen, significant positive changes and a reduction in the time of their onset were observed. The data of electrophysiological studies after the end of GCS therapy in patients of the main group, compared with the initial data, were characterized by an average decrease in latency by 17.4 ± 1.5% and an increase in the amplitude of the P100 VEP by 15.9 ± 0.9%; an almost 2-fold increase in EL and a 3.4-fold decrease in PEC ZN and did not differ statistically significantly from the norm ($p\geq0.05$). At the same time, the control group of patients receiving GCS therapy using the traditional method showed a less pronounced clinical and functional effect compared to the initial values: a decrease in latency by 8.1% ± 0.5, an increase in the amplitude of the P100 VEP by 6.8 ± 0.4%, an increase in the

amplitude of the P100 by 6.8 ± 0.4%, an increase in the EL by 1.6 times, an increase in the EL by 1.6 times. And only after 1 month. After treatment, the average values of clinical and functional indicators in patients in the control group reached values corresponding to the norm ($p>0.05$).

Thus, immediately after the end of the course of GCS therapy, visual acuity in the main group of patients increased by an average of 5.3 times compared to the initial level, while in the control group of patients it increased by an average of 3.3 times ($p<0.05$).

According to computer perimetry, after the end of the course of infusion-irrigation GCS therapy in all patients in the main group, a 3.5-fold decrease in the total number of scotomas was noted, which by 1 month. observations completely disappeared. In the control group, after the end of conventional GCS therapy, a less significant decrease in the total number of scotomas was noted (on average 1.3 times compared to the initial level), and their presence was diagnosed in 72% of patients even up to 3 months. observations.

During ultrasound examination, a close relationship was found between the rate of restoration of the normal diameter of the retrobulbar part of the ON and the lost visual functions. In patients in the main group, immediately after the end of infusion-irrigation GCS therapy, the diameter of the retrobulbar part of the ON reached normal values, which corresponded to the maximum improvement of clinical and functional indicators. In the control group, after the conventional GCS therapy regimen, an extension of the period of restoration of the normal diameter of the retrobulbar part of the ON was observed (up to 1 month), which was accompanied by an extension of the time to improve visual functions.

Conclusion: within 12 months. After the end of the course of treatment with ON GCS, the previously achieved treatment result in most patients in the main group remained stable (21 people - 26 eyes (92.9%) and only in 2 eyes (7.1%) there was a tendency to a decrease in visual acuity to 0.7-0.8 in 2 people, which is 0.1-0.2 lower than before). Discoloration of the temporal half of the optic disc and we considered this as evidence of the development of postneuritic partial atrophy of the optic nerve, during this observation period, postneuritic partial atrophy of the optic nerve was diagnosed 2.7 times more often than in the main group, and in all these patients the level of vision decreased (40%). 0.7 (0.2-0.3 lower than the previously achieved level) and electrophysiological indicators and optic disc discoloration were also recorded ophthalmoscopically

Topical retrobulbar infusion-irrigation GCS therapy optimizes the effectiveness of medical rehabilitation of patients with ON by rapidly stopping the inflammatory reaction, fully restoring and maintaining the ability of ON nerve fibers to function normally.

The clinical and functional advantage of the infusion-irrigation method of retrobulbar administration of GCS over the traditional administration scheme is a 1.3-fold increase in visual acuity and a 2.7-fold decrease in the incidence of postneuritic atrophy of ON during the 12-month follow-up period.

Compared with the traditional GCS therapy regimen, the irrigation-infusion method of introducing GCS into the retrobulbar space reduces the duration of the period of restoration of lost visual functions by 3 times, which reduces the total course dose of GCS by 1.2 times, which is especially important given their known side effects in clinical pharmacotherapy.

The proposed method of targeted delivery of GCS to the optic nerve tissue is low-traumatic, easy to use, does not cause side effects, and can be recommended for widespread use in clinical practice due to its high efficiency.

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