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Transpupillary thermotherapy (TTT) with injections of triamcinolone acetonide under posterior Tenon's capsule in the treatment of exudative age-related macular degeneration (AMD)

Przezrenniczna termoterapia z iniekcjami octanu triamcinolonu pod tylną pochewkę Tenona w leczeniu wysiękowej postaci zwyrodnienia plamki związanego z wiekiem

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Summary:

Purpose: To evaluate the efficacy of transpupillary thermotherapy (TTT) with injection of triamcinolone acetonide under posterior Tenon's capsule for exudative age-related macular degeneration (AMD).

Material and methods: The study included two groups of patients with subfoveal choroidal neovascularization (CNV) due to AMD: group I (n = 20) received TTT alone and group II (n = 20) received TTT combined with sub-Tenon's injection of 40 mg of triamcinolone acetonide (TA). The best corrected visual acuity (BCVA), Amsler grid test, contrast sensitivity and fluorescein angiography (FA) at 10-12 weeks after treatment were compared to the baseline values.

Results: The average age for group I was 72.3 years and for group II 74.6 years. Occult CNV was present in 54% and 43%; predominately classic in 22% and 25%; and minimally classic in 24% and 32% of group I and II respectively. The baseline BCVA in group I ranged from 0.02 to 0.2 and in group II – from 0.03 to 0.1. BCVA was maintained or improved in 7 patients (35%) in group I and in 12 eyes (60%) in group II. The deterioration of the BCVA was noted in 13 patients (65%) and in 8 patients (40%) in group I and II respectively. In 65% of eyes in group I and in 83% in group II the improvement in contrast sensitivity was observed. The rate of color vision improvement was 62% and 91%. Regression of metamorphopsia and/ or scotoma in central visual field was observed in 11 cases (55%) and in 14 cases (70%) in group I and II respectively. FA showed complete or partial closure of CNV in 9 and 14 eyes (p = 0.02) in group I and II, respectively.

Conclusions: The results of our preliminary study indicate that TTT combined with sub-Tenon's injections of triamcinolone acetonide may be a beneficial treatment modality with tendency to better functional results than TTT alone, in patients with exudative AMD. However for the precise evaluation of efficacy of this therapy a larger group of patients and longer follow-up are necessary.

Słowa kluczowe:

termoterapia przezrenniczna, iniekcje pod tylną pochewkę Tenona, octan triamcinolonu, zwyrodnienie plamki związane z wiekiem.

Key words:

transpupillary thermotherapy, sub-Tenon's injections, triamcinolone acetonide, age-related macular degeneration.

Introduction

It has been demonstrated that steroids injected periocularly penetrate the sclera and decrease the intraocular inflammation. Since 1950s under Tenon's capsule and retrobulbar injections of long-lasting corticosteroids, have been used for the treatment of uveitis and for pseudophakic and diabetic macular edema (1,2). There are also many publications indicating that intravitreal injections of triamcinolone have been found to improve vision in patients with diabetic macular edema (3). However, under Tenon's capsule injections are easier to per-

form than intravitreal injections and carry less risk of endophthalmitis (4).

There is evidence suggesting that steroids may have a beneficial effect in patients with choroidal neovascularization (CNV). Eyes with CNV have histopathologic signs of inflammation, and neovascularization is a frequent component of local inflammatory processes (5,6). Histopathological examination of CNV complexes has shown the presence of inflammatory cells (5,6). In addition the amount of vascular endothelial growth factor (VEGF), the major cytokine involved in angiogenesis, has

been shown to be proportional to the amount of inflammatory cells present in CNV (7). Corticosteroids have a direct antiangiogenic effects (8-10). Triamcinolone acetonide and other steroids have been shown to be effective in inhibiting neovascularization in animal models (8,9). It has been demonstrated that transpupillary thermotherapy (TTT) is effective method of treatment in some cases of choroidal neovascularization in a course of AMD. Transpupillary therapy (TTT) is a technique in which heat is delivered to the choroid and retinal pigment epithelium through the pupil using an 810 nm infrared diode laser. The wavelength of the diode laser is mainly absorbed by melanin at the level of the choroid and retinal pigment epithelium, enabling treatment of choroidal lesions (11). Investigations performed on patients treated with PDT have shown increased local production of vascular endothelial growth factor (VEGF) induced by PDT (12). This finding suggests that the frequent recurrence of CNV after PDT may be caused by persistence of the original factors that caused CNV; increased local production of VEGF and inflammation originated by the treatment (13). Combining PDT with an angiogenesis suppressor has been proposed on the basis of choroidal hypoperfusion inducing the recurrence of CNV by a reactive angiogenic mechanism. The use of triamcinolone acetonide with PDT was established to combine antiinflammatory and antiangiogenic action, as has been demonstrated on animal models (13,14).

Presently, it is considered necessary to find combined therapies to improve the cost-effective relationship between the high number of retreatments and the progressive loss of BCVA in spite of treatment.

We found only two papers concerning the combined treatment of transpupillary thermotherapy (TTT) with intravitreal injections of triamcinolone, but there is no report that evaluates the effect of under Tenon's capsule injections of steroids with TTT (4,15). The aim of our study was to evaluate the efficacy of TTT with under posterior Tenon's capsule injection of triamcinolone acetonide for exudative age-related macular degeneration (AMD).

Material and methods

The study included two groups of patients with subfoveal choroidal neovascularization (CNV) due to AMD: group I (n = 20; in age 67.5 – 88 years, mean age – 73.6 yrs), received TTT alone and group II (n = 20; in age 66-84 years, mean age – 72.3 yrs), received TTT combined with under posterior Tenon's capsule injection of 40mg of triamcinolone acetonide (TA). The best corrected visual acuity (BCVA), Amsler grid test, contrast sensitivity and fluorescein angiography (FA) at 10-12 weeks after treatment were compared to the baseline values.

All patients received a thorough explanation of the treatment and were provided with written informed consent. In all cases the basic ophthalmic examination was performed with additional fluorescein angiography (Topcon, Tokyo, Japan). Based on the results of angiographic results type, localization, and size of CNV were determined. In all cases TTT was delivered using a diode laser (IRIS Medical Instruments, Mountain View, California, USA), at 810 nm wavelength and for a duration of 60 seconds for each spot with power settings of 530- -800 mW. A three mirror Goldmann lens was used for the treatment. The

laser beam size spot varied from 1.2 to 4.5 mm. In cases with CNV diameter larger than 4.5 mm, first the central area of the lesion was treated and then the peripheral zone with smaller non-overlapping spots. If any retinal whitening was observed the power of the laser was decreased by 100 mW. Immediately after TTT and topical instillation of oxybuprocaine, 1 ml/40 mg of triamcinolone acetonide (Polcortolon, Jelfa, Poland) was injected via a 25-gauge needle in the upper –temporal quadrant into the sub-Tenon's space. The best corrected visual acuity (BCVA), Amsler grid test, contrast sensitivity, and fluorescein angiography (FA) at 10-12 weeks after treatment were compared to the baseline values. The criteria of the evaluation of BCVA changes were categorized as stabilization, improvement and deterioration. Stabilization was defined as no BCVA changes or improvement of BCVA by 1 line on Snellen charts. Improvement of BCVA was defined if patient's BCVA improved by at least by two lines and deterioration was noted when BCVA failed at least by 2 lines.

The results of FA were scored as complete or partial closure of CNV.

The values of follow-up were statistically analyzed using the Mann-Whitney test, Wilcoxon test and χ^2 test. A probability value of less than 0.05 was considered to be statistically significant for each statistical analysis.

Results

Baseline BCVA in both group of patients showed no statistical significant difference. The proportion of patients improved or maintained BCVA was 35% and 60% for group I and II respectively. The deterioration of BCVA was observed in 65% and in 40% of cases in group I and II, respectively. The changes of BCVA in both groups of patients in a follow-up period are demonstrated in figure 1 and 2.

Rate of CNV closure was 45% and 70% for group I and II at three months, respectively. In both groups the closure of CNV was present mainly in eyes with occult CNV. In 55% and 30% for group I and II FA showed persistent leakage.

All the above presented data were not statistically significant when compared to baseline and between both groups of

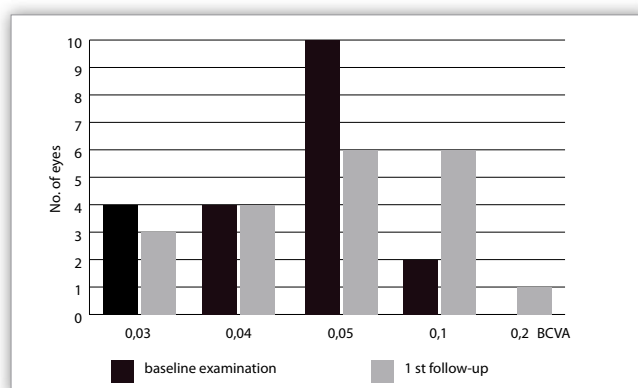


Fig. 1. Changes of BCVA (best corrected visual acuity) in a group of patients with exudative AMD treated with TTT alone in a follow-up period.

Ryc. 1. Zmiany najlepiej skorygowanej ostrości wzroku (BCVA) w grupie chorych z wysiękową postacią AMD leczonych TTT widoczne w okresie obserwacji.

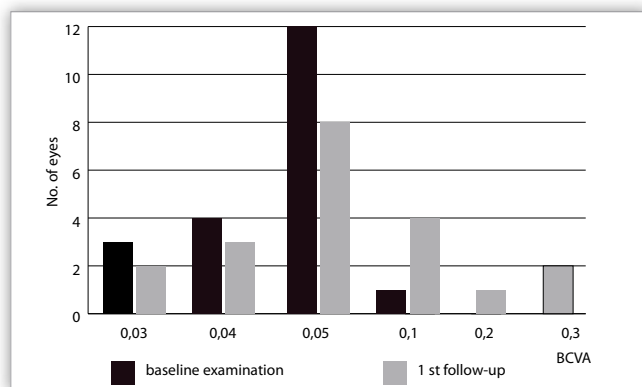


Fig. 2. Changes of BCVA (best corrected visual acuity) in a group of patients with exudative AMD treated with TTT and injections under posterior Tenon's capsule of triamcinolone acetonide in a follow-up period.

Ryc. 2. Zmiany najlepiej skorygowanej ostrości wzroku (BCVA) w grupie chorych z wysiękową postacią AMD leczonych TTT i iniekcjami octanu triamcinolonu pod tylną pochewkę Tenona widoczne w okresie obserwacji.

patients. However we noticed a tendency towards better functional and anatomical results in group of patients treated with TTT and TA injections. The results of this study showed also that eyes with occult CNV had a better response to combined therapy than classic type.

During follow-up in our group of patients an increase of intraocular pressure was noted in 2 cases, both of which were controlled by topical hypotensive agents (beta-blockers). One patient developed ptosis.

Discussion

There are many therapeutic options for exudative AMD. PDT with verteporfin can be used as a treatment in a minority of patients with AMD and in addition patients require multiple retreatments. Recently the anti-VEGF therapy become a new therapeutic strategy that becomes the one that can not only stabilized but also improve vision in about 40% of cases (16). However as PDT the anti-VEGF therapy also requires retreatments – multiple intravitreal injections.

In 1999 Reichel et al. presented a group of 16 patients with occult subfoveal CNV treated with TTT with 12 months of follow-ups (17). Visual acuity (VA) improved two or more lines in 19%, and stabilized in 56% of cases. The leakage on fluorescein angiography (FA) decrease in 94% of patients. Other authors presented results of TTT and they showed benefits in both classic and occult CNV. They described improvement in VA (two or more lines) between 12.4% to 30% and stabilization in 40% to 43% of cases (18-21). The reduction of CNV leakage on FA ranged from 61-100%. Also the results of our study showed that TTT can be an effective and safe method of treatment in some cases of occult and classic CNV in a course of wet AMD. We found improvement of VA in 30.1% of eyes, stabilization in 46.6% and 23.3% showed deterioration of visual function. FA showed no CNV leakage in 79.5% of eyes (22).

To improve the results of treatment of AMD and to decrease the number of retreatments new therapeutic options are being searched. The future strategies for AMD are focused on combined therapies. There are several reasons to continue TTT with

steroids (acetonide triamcinolone). The TTT elevates a local temperature inducing apoptosis with thermal inhibition of angiogenesis and vascular thrombosis (14,15). All these phenomena are associated with local production of inflammatory mediators that can be inhibited with steroids. Based on new theories regarding the pathogenesis of AMD it has been suggested that CNV formation is associated with activation of local inflammation and the increased VEGF activity – the major cytokine involved in angiogenesis. Experimental studies showed that VEGF concentration has been proportional to the amount of inflammatory cells accumulation. Corticosteroids inhibit inflammatory cytokines and growth factors and they inhibit prostaglandin and leukotriene synthesis, which results in local reduction of inflammatory mediators (23,24). Corticosteroids have a direct antiangiogenic effects and they have been shown to be effective in inhibiting neovascularization through modulation the production and reduction the vascular permeability by VEGF (25). These effects would not be expected to occur with TTT alone.

It has been demonstrated that the use of steroids in diabetic macula edema patients can improve vision (3,26). Several methods of steroids administration, including periocular injection, intraocular implants and intravitreal injections of triamcinolone acetonide have been studied. Injections under Tenon's capsule are easier to perform than intravitreal injections and carry less risk of endophthalmitis but the treatment effect is not as quick or as long-lasting (3). There are several clinical studies presented the results of TTT with intravitreal injection of TA in patients with CNV due to AMD. Agurto-Rivera et al. showed that the combination of TTT along with intravitreal injections of TA offers the possibility of better functional results than TTT alone (4).

Based on the observation that periocular steroids are beneficial in treatment of posterior uveitis, cystoid macular edema, we decided to combine TTT with injections under Tenon's capsule of TA. To our knowledge there is no publication on TTT combined with injections under Tenon's capsule of TA in AMD patients. The results of our study showed positive results of this method of treatment; we observed better functional and anatomical results in group treated with TTT and TA comparing to patients underwent TTT alone.

Conclusions

The results of our preliminary study indicate that TTT combined with injections under Tenon's capsule of triamcinolone acetonide may be a beneficial treatment modality with tendency to better functional results than TTT alone, in patients with both occult and classic CNV due to exudative AMD. However for the precise evaluation of efficacy of this therapy a larger group of patients and longer follow-up are necessary.

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