Efficacy and Safety of Micropulse Transscleral Cyclophotocoagulation

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SUMMARY

Purpose: To evaluate the efficacy and safety of micropulse transscleral cyclophotocoagulation (MP-CPC) in glaucoma patients and to assess differences among glaucoma subtypes.

Material and Methods: A retrospective study was conducted on 40 eyes of 35 patients with various types of glaucoma. Micropulse cyclophotocoagulation was indicated for glaucoma which was uncontrolled on maximum medical therapy. The procedures were performed using micropulse mode (2000 mW, 0.5 ms on, 1 ms off, mean energy 129.4 J). Follow-up examinations were conducted at 1 and 3 months and at 6–12 and 12–24 months. Success of treatment was defined as a reduction of intraocular pressure (IOP) by ≥20%. A subgroup without modification of therapy was analyzed separately.

Results: Success rates were 33.3% at 1 month, 25.0% at 3 months, 35.3% at 6–12 months, and 30.0% at 12–24 months. Higher efficacy was observed in patients without modification of therapy (up to 41.7%). The most stable and sustained outcomes were seen in primary open-angle glaucoma, whereas secondary glaucomas and primary angle-closure glaucoma efficacy was short-term. Additional glaucoma surgery was required in 30% of eyes. No statistically significant change in best-corrected visual acuity compared to baseline was observed at any follow-up interval, although a trend toward worsening was observed in the early time intervals.

Conclusion: MP-CPC demonstrates limited and variable efficacy. The outcomes depend on glaucoma type, baseline IOP, and modifications of treatment. The procedure appears relatively safe, although it may have a temporary impact on visual acuity.

Key words: cyclophotocoagulation, micropulse laser, glaucoma, intraocular pressure

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INTRODUCTION

Glaucoma represents a group of chronic diseases characterized by progressive optic neuropathy and ranks among the main causes of irreversible blindness [1]. The basic aim of treatment is to slow the progression of the disease, mainly by reducing intraocular pressure (IOP). Besides pharmacological and surgical treatment, an important position is also occupied by laser methods, including CPC (cyclophotocoagulation), which is used in classic and micropulse versions. Classic (continuous) CPC, which targets energy into the tissue in points, but in a continuous mode, is traditionally used for refractory forms of glaucoma. However, it is associated with a higher risk of complications [2]. A more recent variant of this method is micropulse transscleral CPC, which uses intermittent impulses of laser energy with the aim of reducing damage to the surrounding tissues [3]. A higher safety profile is expected, while retaining the therapeutic effect [4,5]. However, the results of the published studies are variable, and are probably dependent upon the parameters of the procedure and the characteristics of the cohort.

The aim of this study is to evaluate the efficacy and safety of micropulse transscleral CPC within the conditions of a single ophthalmological center, and to analyze the factors influencing its efficacy.

MATERIAL AND METHODS

Cohort of patients

The observed cohort incorporated a total of 40 eyes of 35 patients, with various subtypes of glaucoma. The cohort comprised 23 women and 12 men with a mean age of 77.3 years, median age 79 years. The procedure was per-

formed on 21 right and 19 left eyes. The indication for performing micropulse CPC was decompensated glaucoma despite maximally tolerated topical antiglaucoma therapy. Decompensation was defined as IOP exceeding the individually determined target IOP as stipulated according to the recommendations of the European Glaucoma Society [6], or progression of the pathology documented by changes on the optic nerve or in the visual field.

The cohort comprised patients with IOP of ≤ 30 mmHg at maximum local therapy. Patients with advanced to pre-terminal stage of glaucoma were preferentially indicated for the procedure, and constituted a significant part of the cohort. The cohort encompassed a broad spectrum of subtypes of glaucoma, most frequently primary open-angle glaucoma (POAG), followed by primary angle-closure glaucoma (PACG), normal-tension glaucoma (NTG) and secondary types of glaucoma of various etiology, an overview of which is presented in Table 1.

As regards previous procedures, the cohort included both naïve eyes and eyes that had undergone a variety of ophthalmological procedures, including cataract surgery, selective laser trabeculoplasty or filtration procedures. An overview of these procedures is presented in Table 2.

Method and performance of procedure

The procedures were performed at the Clinic of Eye Treatments at the University Hospital Brno with the aid of the diode laser A.R.C. FOX 810 (A.R.C. Laser, Germany) in micropulse mode. The basic setting was based on the recommendations of the manufacturer and on published studies [7,8]: laser output 2000 mW, "on" phase 0.5 ms, "off" phase 1 ms, duty cycle 33.3%. The procedures were performed under sub-tenon anesthesia. The mean total applied energy in the cohort was 129.4 J (range 110–140 J).

The primary observed parameter was the change in IOP over time. Follow-up examinations were conducted at the following intervals: 1 month, 3 months, 6–12 months, 12–24 months; if the patients were examined repeatedly within the stated intervals, the IOP value from the first visit was used for the analysis. Success of the treatment was considered to be a decrease of IOP by ≥ 20% as against the baseline value. Secondary outcomes included best corrected visual acuity (BCVA), incidence of complications, necessity and timing of further glaucoma procedures. Changes in BCVA were evaluated using the limit ±0.1 according to Snellen. A Wilcoxon signed-rank test was used for the statistical evaluation of the data, in which the level of statistical significance was set at $\alpha = 0.05$.

Analysis of impact of changing therapy

With reference to the frequent modification of antiglaucoma therapy in clinical practice, a separate analysis was conducted on a subgroup of patients who did not change their medication during the observation period. The aim was to assess the effect of the procedure itself more precisely, without the confounding effect of changes in pharmacotherapy.

Table 1. Overview of glaucoma types in the dataset

Type of glaucoma	Number of eyes
Primary open-angle glaucoma	20
Primary angle-closure glaucoma	5
Normal-tension glaucoma	3
Uveal glaucoma	2
Pseudoexfoliative glaucoma	5
Pigmentary glaucoma	1
Neovascular glaucoma	1
Post-traumatic glaucoma	1
Mixed etiology	2

Table 2. Spectrum of procedures performed on eyes in the dataset

Performed procedure	Number of eyes
Naïve eyes	11
Cataract surgery	12
Selective laser trabeculoplasty	3
Cataract surgery and selective laser trabeculoplasty	4
Cataract surgery and filtration surgery	5
Cataract surgery and selective laser trabeculoplasty and filtration surgery	2
Cataract surgery and cyclophotocoagulation	1
Cataract surgery and pars plana vitrectomy	1
Cataract surgery and filtration procedure and cyclocryocoagulation	1

RESULTS

Success of treatment

Success of the treatment, defined as a reduction in IOP of ≥ 20 % from the baseline value, was achieved in 33.3% of eyes after 1 month, in 25.0% of eyes after 3 months, in 35.3% of eyes within the interval of 6–12 months, and in 30.0% of eyes within the interval of 12–24 months. The results show a rather weak effect of the procedure, with fluctuations of effectiveness over time; they are summarized in Table 3.

In the subgroup of patients without modification of antiglaucoma medication, higher efficacy of the procedure was recorded: after 1 month 37.0%, after 3 months 29.4%, within the interval of 6–12 months 41.7%, and within the interval of 12–24 months 33.3%; the detailed results are presented in Table 4.

Influence of subtype of glaucoma

The most stable effect was recorded in the case of POAG. By contrast, in the case of secondary forms of glaucoma and PACG the effect was frequently only short-term. The development of IOP throughout the entire cohort in the

Table 3. Treatment success in individual observation periods

Time	Number of successes	Number of eyes	Success percentage
1 month	12	36	33.3%
3 months	6	24	25.0%
6 to 12 months	6	17	35.3%
12 to 24 months	3	10	30.0%

Table 4. Treatment success in individual observation periods in subgroup without change of therapy

Time	Number of successes	Number of eyes	Success percentage
1 month	10	27	37.0%
3 months	5	17	29.4%
6 to 12 months	5	12	41.7%
12 to 24 months	3	9	33.3%

first months is illustrated in Graph 1. The development of IOP throughout the course of the entire observation period for patients with POAG, divided according to modification of treatment, is illustrated in Graph 2, in which a more rapid increase in IOP values is evident in patients who underwent a modification of treatment (usually involving a reduction in treatment).

Other glaucoma procedures

During the course of the observation period, it was necessary to perform another glaucoma procedure in 12 out of 40 eyes (30%); the types and frequency of the procedures are summarized in Table 5. These eyes were subsequently excluded from the further follow-up. The relative frequency of reoperations differed depending on the subtype of glaucoma (Table 6). Differences were observed in the time to treatment failure; in secondary forms of glaucoma the need for a further procedure arose earlier, in POAG later (Table 7). In the case of PACG, cataract surgery was also considered to constitute a glaucoma procedure.

Development of visual acuity

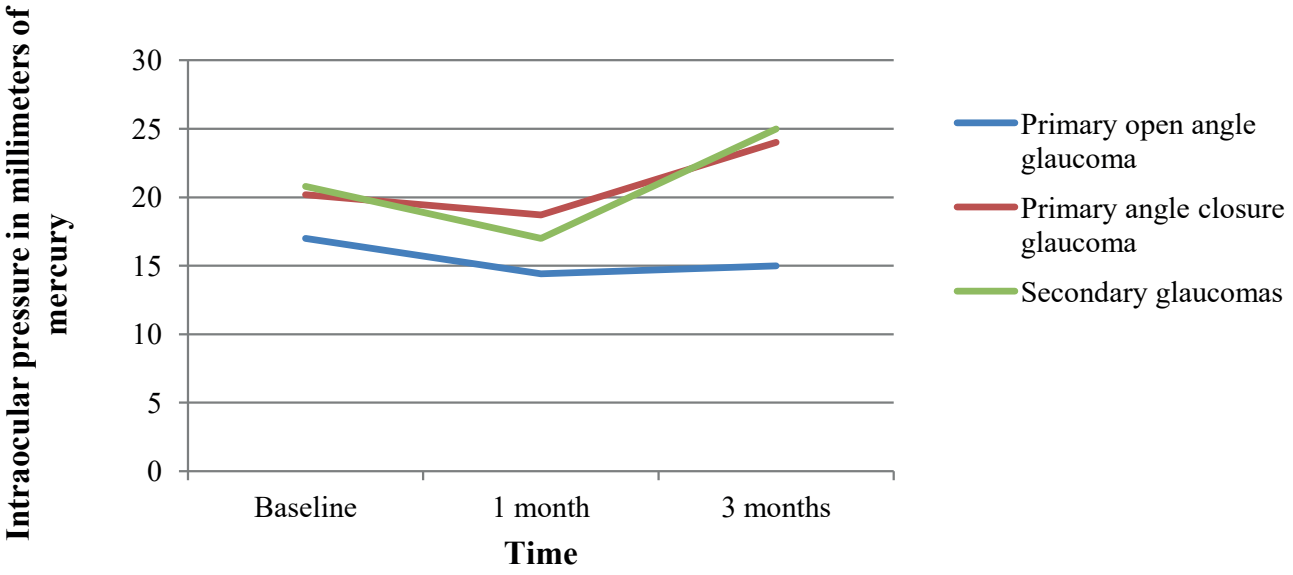
In the early postoperative period a trend towards deterioration of visual acuity was observed, although this did not reach the level of statistical significance throughout the entire observation period. From a clinical perspective, a high proportion of eyes showed stable BCVA without deterioration at all the observed intervals. The above information is summarized in Table 8, with all values expressed relative to preoperative visual acuity.

Complications

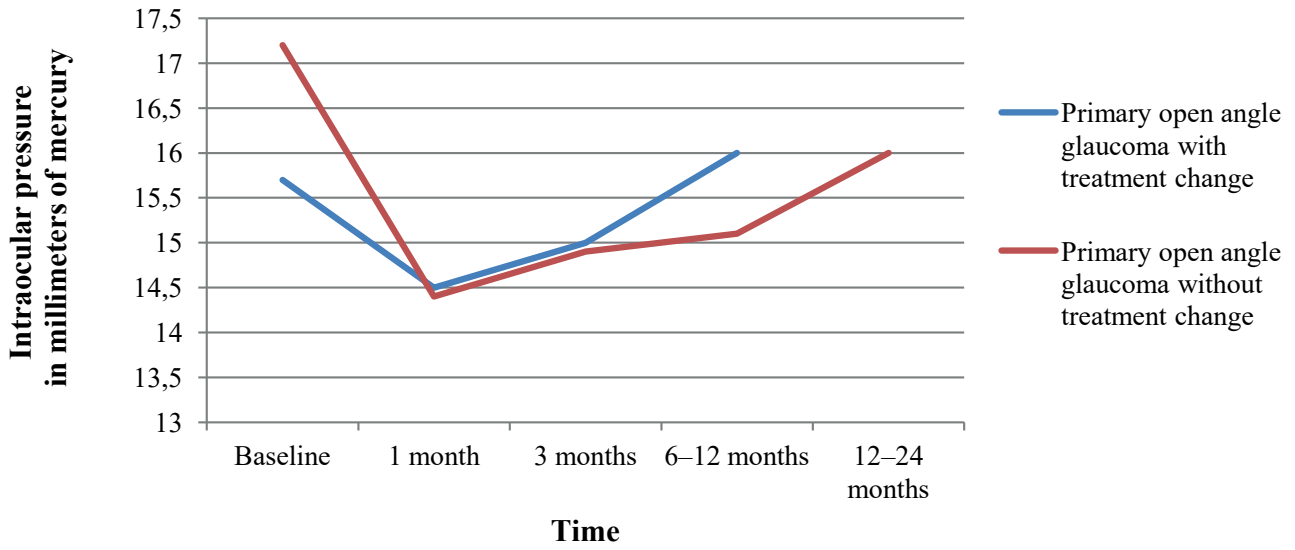
Various complications were recorded after the procedure, most often transitory deterioration of BCVA, disorders of pupil function (Figure 1), uveal irritation, and onset of cystoid macular edema. One patient suffered a dramatic deterioration of visual acuity immediately after the procedure, with no subsequent improvement during follow-up.

DISCUSSION

The aim of this study was to evaluate the efficacy of micropulse transscleral CPC in patients with different subtypes of glaucoma at a single ophthalmological center. The results indicate that with the chosen laser setting, this method has a rather limited effect on reducing intraocular pressure (IOP), in which its efficacy differs depending on the subtype of glaucoma and other baseline parameters.



Graph 1. Development of intraocular pressure in individual types of glaucoma during the first three months



Graph 2. Development of intraocular pressure over the entire follow-up period in patients with primary open-angle glaucoma in the group without and with change of therapy

Table 5. Spectrum of subsequent antiglaucoma procedures according to type of glaucoma

Type of procedure	Primary angle-closure glaucoma	Primary open-angle glaucoma	Secondary glaucoma	Total
Cyclophotocoagulation	0	3	2	5
Cataract surgery	3	0	0	3
PreserFlo	0	1	2	3
Ex-Press 50	0	1	0	1
Total	3	5	4	12

Table 6. Relative frequency of reoperations by type of glaucoma

Type of glaucoma	Operated	Total in dataset	Percentage
Primary angle-closure glaucoma	3	5	60.0%
Secondary glaucoma	4	12	33.3%
Primary open-angle glaucoma	5	23	21.7%

Table 7. Timing of reoperations according to type of glaucoma

Type of glaucoma	Number	Mean (months)	Median	Range
Primary angle-closure glaucoma	3	3.0	3	3 to 3 months
Secondary glaucoma	4	2.5	2.5	2 to 3 months
Primary open-angle glaucoma	5	11	10	1 to 24 months

Table 8. Development of postoperative visual acuity in individual postoperative periods

Interval	Deterioration n (%)	No deterioration n (%)	Number	p-value (Wilcoxon)
1 month	17 (45.9%)	20 (54.1%)	37	p = 0.072
3 months	12 (44.4%)	15 (55.6%)	27	p = 0.088
6 to 12 months	4 (23.5%)	13 (76.5%)	17	p = 0.314
12 to 24 months	4 (36.4%)	7 (63.6%)	11	p = 0.172



Figure 1. Postoperative pupil plegia and mydriasis

Success of treatment, defined as a decrease of IOP by ≥ 20 % as against the baseline value, was achieved in approximately one third of eyes at the individual observed intervals. The success rate is lower than in the majority of the published studies, which present a success rate often ranging from 50% to 75% [2,4,7–12]. However, it is difficult to compare these results directly due to the differences in the methodology of the individual studies, in particular in the definition of success, the baseline values of IOP, the composition of the cohort and the laser setting.

One of the main factors that probably had an influence on the lower efficacy of treatment in our cohort is the relatively low baseline value of IOP. Whereas a large number of the published studies incorporate patients with a mean IOP of above 30 mm Hg [4,8,9,12,13], the patients in our cohort had IOP of less than 30 mmHg. It is probable that the effect of micropulse transscleral CPC is limited in the case of lower IOP values, which also corresponds with the conclusions of a number of authors [14,12].

With regard to the individual subtypes of glaucoma, the most stable effect was recorded in the case of POAG, whereas in the case of secondary forms of glaucoma and PACG the effect tended to be only short-term. This finding is in accordance with the literature, which states only small differences in efficacy between individual subtypes of glaucoma [17], but highlights the low stability of the effect and greater need for early reoperations, especially in the case of secondary forms of glaucoma [17]. The need for a further glaucoma procedure was recorded in 30% of eyes. The pronounced differences between the individual subtypes of glaucoma, especially the high frequency of reoperations for PACG and secondary forms of glaucoma, suggest that micropulse transscleral CPC may not represent an optimal method of first choice for these patients. By contrast, for patients with POAG the course of the disease after the procedure appears to be more stable, with a longer interval until any applicable reoperation.

From the perspective of safety, a trend towards deterioration of BCVA was observed in the early postoperative period, though this did not reach the level of statistical significance; deterioration did not occur in the subsequent observation period. This finding is in accordance with the literature, which describes long-term stability of visual functions after the procedure [16,18].

Although micropulse transscleral CPC is considered a safer alternative to classic CPC, in our cohort complications were nevertheless registered, including disorders of pupil function, uveal irritation and cystoid macular edema, which corresponds with the conclusions of other authors [19,20]. These results confirm that even less invasive laser methods are not entirely without risk, and that it is therefore necessary to consider indication for the procedure very carefully, especially for patients with good visual potential.

Another factor that may influence the efficacy and safety of the procedure is the laser setting and the total applied energy. In our cohort, higher energy than the recommended values was used on a number of the patients, which reflects the endeavor to increase the efficacy of treatment. However, with regard to the limited number of patients, for the time being it is not possible to unequivocally assess the relationship between higher energy and the therapeutic effect or incidence of complications on the basis of our cohort. This remains an open question and represents a potential avenue for further research.

We consider the main limitation of our study to be the relatively small cohort of patients, the heterogeneity of the cohort and modifications of glaucoma therapy in a number of the patients during the observation, though this nevertheless reflects the reality of clinical practice. A strength of the study is the analysis of reoperations, including the time frame and the separate evaluation of the subgroup without modification of therapy.

The results indicate that micropulse transscleral CPC may serve as a supplementary method in the treatment of glaucoma; nevertheless, its effect is limited and dependent upon the subtype of glaucoma and baseline parameters. Optimizing the results will probably require individualization of the procedure configuration and careful consideration of the indication in individual patients.

CONCLUSION

In our cohort, micropulse transscleral CPC was demonstrated to be a method with limited efficacy in reducing IOP, in which its effect tended to be short-term. The best results were achieved in the case of POAG, whereas in the case of PACG and secondary forms of glaucoma the treatment frequently resulted in failure, with the need for a further procedure. With regard to safety, a trend towards deterioration of visual acuity was observed in the early postoperative period, although within the framework of the entire observation period this did not reach the level of statistical significance. The results suggest that the effect of micropulse transscleral CPC is influenced in particular by the subtype of glaucoma, the baseline value of IOP, and the parameters of the procedure. Optimization of the results requires an individualized approach.

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