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# Complete recovery of visual acuity as the main goal of treatment in patients with dysthyroid optic neuropathy

## Powrót pełnej ostrości wzroku jako główny cel leczenia pacjentów z neuropatią nerwu wzrokowego w przebiegu orbitopatii Gravesa

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## Abstract

**Introduction:** To evaluate the effectiveness of methylprednisolone (MP) and surgical treatment in achieving complete reversal of dysthyroid optic neuropathy (DON) and predictive factors of this therapy.

**Material and methods:** The group consisted of 10 patients (18 eyes) with DON. The diagnosis of DON was based on at least two criteria from the following: (i) deterioration of visual acuity (VA < 1.0), (ii) loss of colour vision, (iii) optic disc swelling, and/or (iv) signs of DON in magnetic resonance imaging (presence of apical crowding and/or optic nerve stretching). A complete recovery of DON was defined as the normalisation of VA (VA = 1.0), normal colour vision, and reversal of optic disc swelling. A significant improvement was defined as improvement of VA of at least 0.2. The consecutive steps of treatment of DON consisted of: (i) first-line treatment — intravenous MP pulse therapy (3 × 1 g); (ii) second-line treatment — endoscopic intranasal orbital decompression of medial wall; (iii) additional treatment — additional MP therapy and/or surgical decompression.

**Results:** A significant improvement in VA could be achieved in the majority of patients; a complete recovery was noted in 22.2%, 33.3%, and 66.7% of eyes after first-line, second-line, and additional treatment, respectively. Positive predictive factors were: younger age (p = 0.049), shorter duration of DON (p = 0.035), and a higher Graves' orbitopathy clinical activity score (p = 0.035).

**Conclusions:** By using combination therapy (intravenous MP pulse therapy and surgical decompression), a complete recovery can be achieved in the majority of patients with DON. **(Endokrynol Pol 2016; 67 (2): 166–173)**

***Key words:*** *dysthyroid optic neuropathy; Graves' orbitopathy; Graves' disease; orbital decompression; methylprednisolone; endoscopic intranasal orbital decompression*

## Streszczenie

**Wstęp:** Celem badania była ocena skuteczności leczenia metyloprednizolonem (MP) i leczenia chirurgicznego w uzyskaniu ustąpienia klinicznych cech neuropatii nerwu wzrokowego w przebiegu orbitopatii Gravesa (DON) oraz wskazanie czynników prognostycznych skuteczności terapii DON.

**Materiał i metody:** Grupę badaną stanowiło 10 pacjentów (18 gałek ocznych) z DON. Rozpoznanie DON było stawiane na podstawie spełnienia co najmniej dwóch kryteriów z powyższych: a) pogorszenie ostrości wzroku (VA < 1,0), b) pogorszenie widzenia kolorów, c) obrzęk tarczy nerwu wzrokowego i/lub d) obraz typowy dla DON w badaniu rezonansu magnetycznego (stłoczenie w szczycie oczodołu i/lub naprężenie nerwu wzrokowego). Jako pełną poprawę uznano normalizację VA (VA = 1,0), prawidłowe widzenie barw i brak obrzęku tarczy nerwu wzrokowego. Kolejnymi etapami leczenia DON były: a) leczenie pierwszoplanowe — pulsy MP (3 × 1 g); b) leczenie drugoplanowe — endoskopowa wewnątrznosowa dekompresja ściany przyśrodkowej oczodołu; c) leczenie dodatkowe — podanie dodatkowych pulsów MP i/lub chirurgiczna dekompresja.

**Wyniki:** Znaczącą poprawę VA uzyskano u większości pacjentów. Pełną poprawę stwierdzono w 22,2%, 33,3% i 66,7% gałek ocznych odpowiednio po leczeniu: pierwszoplanowym, drugoplanowym i dodatkowym. Czynnikami pozytywnie korelującymi z osiągnięciem pełnej poprawy były: młodszy wiek (p = 0,049), krótszy czas trwania DON (p = 0,035), wyższa aktywność kliniczna orbitopatii Gravesa (p = 0,035).

**Wnioski:** Zastosowanie złożonej terapii (pulsy MP i chirurgiczna dekompresja) umożliwia osiągnięcie pełnej poprawy u większości pacjentów z DON. **(Endokrynol Pol 2016; 67 (2): 166–173)**

***Słowa kluczowe:*** *neuropatia nerwu wzrokowego; orbitopatia Graves'a; choroba Gravesa i Basedowa; dekompresja; metyloprednizolon; endoskopowa wewnątrznosowa dekompresja oczodołu*

## Abbreviations

CAS — clinical activity score
DON — dysthyroid optic neuropathy
EUGOGO — European Group on Graves' Orbitopathy
EIODM — endoscopic intranasal orbital decompression of medial wall
GO — Graves' orbitopathy

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ivMP — intravenous methylprednisolone pulse therapy
ivGCS — intravenous glycocorticosteroid pulse therapy
MP — methylprednisolone
MR — magnetic resonance
TBII — TSH binding inhibitory immunoglobulin
VA — visual acuity

## Introduction

Dysthyroid optic neuropathy (DON) is a sight-threatening complication that occurs in approximately 5% of patients with Graves' orbitopathy (GO) [1]. The pathomechanisms of GO are inflammation, adipogenesis, and the production of glycosaminoglycans, which lead to an enlargement of eye muscles and expansion of the orbital connective tissue [2]. DON can be a result of optic nerve compression by swollen muscles and fat in the orbital apex [3, 4]; however, an ischaemic mechanism or optic neuritis is also considered [5]. There is no defined "gold standard" for diagnosis and management of DON. The European Group on Graves' Orbitopathy (EUGOGO) recommends intravenous glycocorticosteroid pulse therapy (ivGCS) and urgent decompression if there is no response for two weeks [6, 7]. Decompression of the medial orbital wall is the optimal surgical strategy [8]. However, there are no recommendations on how aggressive further therapy should be in cases where a complete recovery is not achieved. We believe that any worsening of visual acuity (VA) may be life-disturbing. Therefore, we decided to continue additional therapy to try to achieve a complete recovery (normalisation of VA, normal colour vision, and a normal-appearing optic disc) if ivGCS treatment and orbital decompression of the medial wall were insufficient.

The first aim of our study was to assess the effectiveness of combined ivGCS and orbital decompression in achieving a complete recovery of DON. The second aim was to define the predictive factors of this therapy.

## Material and methods

### *Patients*

The study was conducted at an academic referral centre. Patients with DON were consecutively recruited from the Department of Endocrinology, Medical University of Warsaw from 2009 to 2014. The inclusion criterion was a diagnosis of DON based on at least two signs, including (i) deterioration of VA (< 1.0), (ii) loss of colour vision (more than three errors in Ishihara plates), (iii) optic disc swelling, and/or (iv) signs of DON in a magnetic resonance (MR) scan (presence of apical crowding and/or optic nerve stretching). Exclusion criteria were: (i) other diseases that affect visual function, such as glaucoma, cataract, high myopia, or corneal exposition, and (ii) orbital decompression in the past. Ten patients (a total number of 18 eyes) were eligible for the study. The clinical characteristics of the analysed group are shown in Table I.

**Table I.** ***Characteristic of patients with DON (n = 10)***
**Tabela I.** ***Charakterystyka pacjentów z DON (n = 10)***

| | Number of patients/mean |
|---|---|
| Graves' Disease | 8 |
| Hashimoto Disease | 2 |
| Female | 9 |
| Age | 56 (range: 31 to 76) |
| Active Smokers | 5 |
| Duration of thyroid disease in weeks | 170 (range: 17 to 806) |
| Duration of GO in weeks | 29 (range: 20 to 806) |
| Duration of symptoms of DON in weeks | 10 (range: 3 to 127) |
| Previous treatment with GCS | 6 |
| TSH (reference range: 0.270–4.200 $\mu$IU/mL) | 0.45 (range: 0.005 to 2.96) |
| fT3 (reference range: 3.1–6.8 pmol/L) | 4.93 (range: 3.88 to 12.95) |
| fT4 (reference range: 12–22 pmol/L) | 17.43 (range: 12.3 to 23.21) |
| TBII (reference range: < 1.75 IU/L) | 21.6 (range: 0.1 to 40) |

DON — dysthyroid optic neuropathy; GO — Graves' Orbitopathy; GCS – glicocorticosteroids; TSH — thyroid-stimulating hormone; fT3 — free triiodothyronine, fT4 — free thyroxine; TBII — TSH binding inhibitory immunoglobulins

### *Ophthalmological and radiological examination*

All the patients were assessed according to EUGOGO criteria. A clinical activity score (CAS) including two symptoms (orbital ache and gaze-evoked pain) and five signs (conjunctival redness, eyelid erythema or oedema, chemosis, and swelling of the plica or caruncle) for each eye was evaluated. GO was assessed as active if CAS was ≥ 3/7. Proptosis was measured with a Hertel exophthalmometer. Colour vision was tested using Ishihara plates. VA was examined using Snellen charts and expressed as a decimal fraction. The ophthalmologic examination also included assessing the fundus and intraocular pressure. The Gorman score (no diplopia, intermittent diplopia, inconstant diplopia, and constant diplopia) was used to assess the severity of diplopia. All the ophthalmologist examinations for the all patients were carried out by the same ophthalmologist. The baseline ophthalmological and radiological characteristics of the analysed group are shown in Table II.

### *Laboratory evaluations*

Thyroid-stimulating hormone (TSH), free triiodothyronine, free thyroxine as well as TSH binding inhibitory immunoglobulin (TBII), thyroid peroxidase antibodies, and thyroglobulin antibodies concentrations were

**Table II.** *Baseline ophthalmological and radiological characteristic of eyes affected with DON (n = 18)*

**Tabela II.** *Wyjściowa ocena gałek ocznych z cechami DON w badaniu okulistycznym i radiologicznym (n = 18)*

| | Numbers of eyes/mean | % of all eyes |
|---|---|---|
| Apical crowding | 9 | 50% |
| Optic nerve stretching | 15 | 83% |
| Reduction of VA | 18 | 100% |
| VA = 0.8 | 4 | |
| VA = 0.7 | 2 | |
| VA = 0.6 | 3 | |
| VA = 0.5 | 5 | |
| VA = 0.4 | 2 | |
| VA = 0.3 | 1 | |
| VA = 0.2 | 1 | |
| Impaired colour sensitivity | 3 | 17% |
| Optic disc swelling | 3 | 17% |
| CAS | 4 (range 2–6) | |
| Proptosis [mm] | 21 (range 16–26) | |
| Diplopia in Gorman score: none/intermittent/inconstant/constant | 2/0/2/4 | |

DON — dysthyroid optic neuropathy; VA — visual acuity; CAS — clinical activity score

measured using an electro-chemiluminescence immunoassay performed on a Cobas 6000 analyser from Roche Diagnostics (Mannheim, Germany).

### *Treatment schedule*

The treatment schedule is shown in Figure 1. The consecutive steps of treatment of DON consisted of:

— first-line treatment - intravenous methylprednisolone (ivMP) pulse therapy (3 × 1.0 g given on three consecutive days);
— second-line treatment - endoscopic intranasal orbital decompression of medial wall (EIODM). EIODM was performed endonasally, employing an operative endoscopic technique described by Kennedy in 1990 [9]. After endonasal sphenoethmoidectomy, the orbital wall was resected to reveal the periorbit. Then a longitudinal cut of the periorbit was carried out, which allowed the adipose tissue of the orbit to fill the space of the former ethmoidal cells;
— additional treatment, which consisted of additional ivMP pulse therapy, additional orbital decompression (lateral, inferior or medial wall), or combined ivMP therapy and decompression. The decision about additional therapy was made individually for each patient by an endocrinologist, ophthalmologist, and laryngologist on the basis of the following factors: the degree of proptosis, MR findings after EIODM, and the effect of the first ivMP pulse therapy.

Patients with a complete recovery after the first- and second-line treatment were further treated with 12 pulses of ivMP in every week schedule (a cumulative dose of 4.5 g) tapered off with prednisone (a cumulative dose of 1.8 g). Patients with active GO (CAS ≥ 3) and impairment of ocular movement after the 12 pulses of ivMP were referred for retrobulbar radiotherapy. A cumulative dose of 20 Gy per orbit fractioned in 10 doses over a two-week period according to EUGOGO recommendations was adopted [6]. This therapy was conducted with concomitant prednisone administration.

Subjects with hyperthyroidism were treated with a combined therapy (an antithyroid drug and thyroxine) and those with hypothyroidism received L-thyroxine. All but one were euthyroid when DON treatment was initiated.

Before each ivMP pulse, a careful clinical examination (including symptoms/ signs of coronary artery disease, infections, psychiatric disorders, and high blood pressure) and lab tests were performed (including serum potassium, glucose concentration, AST and ALT activity, and urine analysis). All possible side effects of GCS therapy and orbital decompression were recorded.

### *Outcome analysis*

Complete recovery of DON was defined as normalisation of VA, normal colour vision, and a normal-appearing optic disc. Significant improvement was defined as final VA: + 0.2 in comparison to the baseline; stabilisation as final VA: ± 0.1 in comparison to the baseline, and deterioration as a worsening of VA of at least 0.2.

An ophthalmological examination with an assessment of VA, colour vision, and optic fundus was performed: before therapy (a baseline assessment), after first-line treatment with 3 g of ivMP, after second-line treatment - EIODM, after additional therapy, and after completing the whole therapy (Fig. 1).

Additionally, we analysed whether specific factors, such as baseline clinical and radiological signs of DON, CAS, age, smoking, TBII concentration, duration of GO, and symptoms of DON, are associated with a complete recovery after therapy.

### *Statistical analysis*

Median values (range: minimum value–maximum value) were used to present continuous variables, while categorical variables were expressed as numbers or percentage values. Comparisons of the continuous data were performed with the nonparametric unpaired Mann-Whitney U test. A Chi-squared test was used to analyse the differences in the categorical data. Statistical

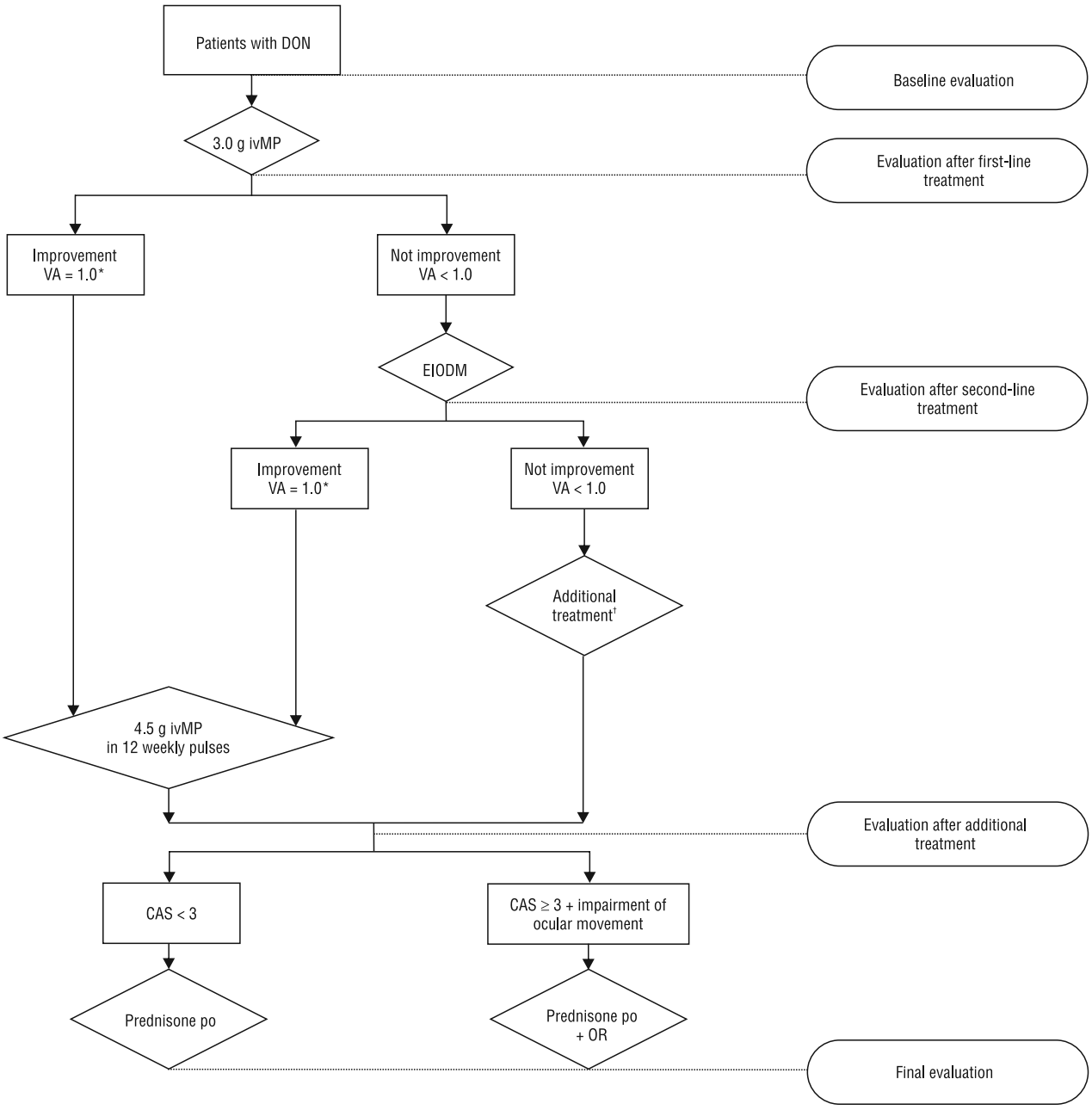


**Figure 1.** *Schedule of treatment of dysthyroid optic neuropathy*

**Rycina 1.** *Schemat zastosowanego leczenia neuropatii nerwów wzrokowych*

**without any clinical sings of DON, † additional treatment consisted of: a second decompression (one eye — decompression of lateral and inferior wall; 2 eyes — decompression of medial wall) and/or additional MP pulse therapy. ivMP — intravenous methylprednisolone; EIODM — endoscopic intranasal orbital decompression of medial wall*

significance was established for results using a p value of $< 0.05$. All analyses were made with the statistical software STATISTICA ver.10.0.

## Results

### *Effectiveness of therapy*

A complete recovery was noted in 22.2%, 33.3%, and 66.7% of eyes after first-line, second-line, and additional treatment, respectively (Fig. 2). VA, colour vision, and optic fundus findings remained stable during further therapy.

At the end of the therapy, all patients had normal colour vision and normal-appearing optic discs. The median of VA increased from 0.55 (range from 0.2 to 0.8) to 1.0 (range from 0.7 to 1.0); in 12 out of the 18 eyes VA was normalised (VA = 1.0); in four significant improvement was achieved; and in two VA remained

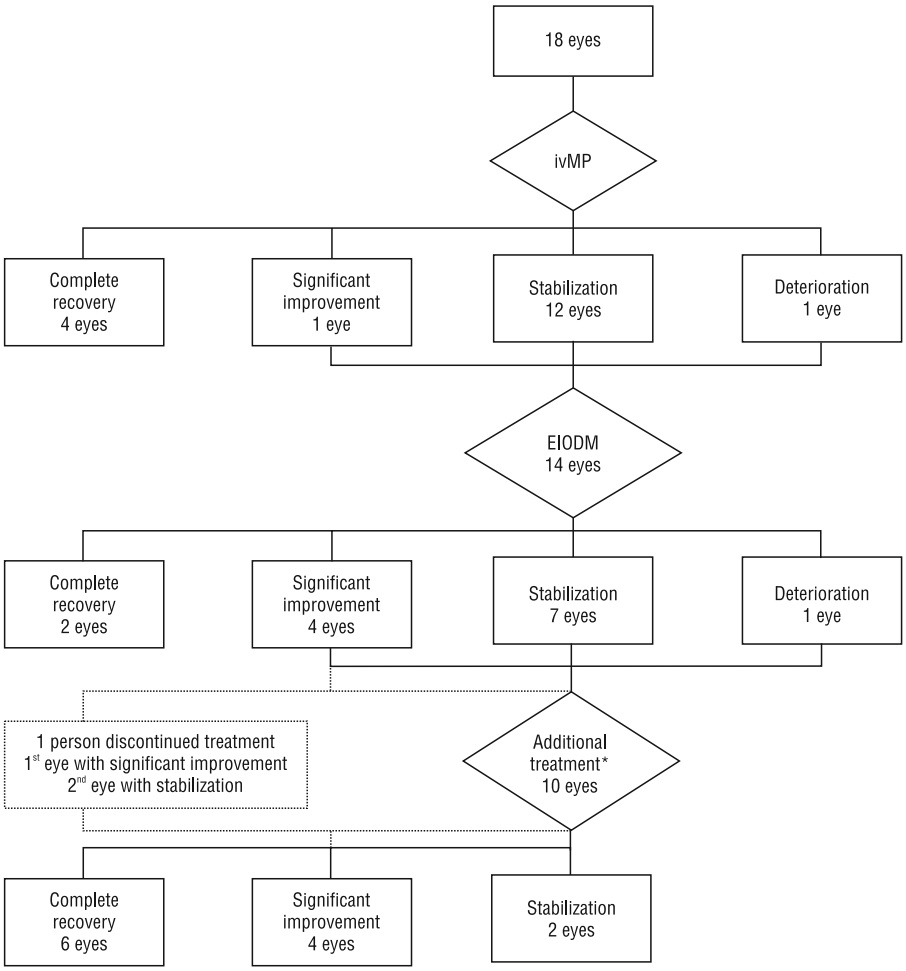


**Figure 2.** *Schedule of treatment with the number of eyes with: complete recovery, significant improvement, stabilization and deterioration after ivMP, after EIODM and after additional treatment*

**Rycina 2.** *Schemat leczenia oraz liczba gałek ocznych z całkowitą poprawą, znaczącą poprawą, stabilizacją oraz pogorszeniem u chorych po leczeniu ivMP, po wykonaniu EIODM oraz po zastosowaniu dodatkowego leczenia*

**additional treatment consisted of: a second decompression (one eye — decompression of lateral and inferior wall; 2 eyes — decompression of medial wall) and/or additional MP pulse therapy. ivMP — intravenous methylprednisolone; EIODM — endoscopic intranasal orbital decompression of medial wall*

stable. Of these patients, one discontinued therapy after second-line treatment, having achieved significant improvement in one eye and stabilisation in the second. At the end of therapy, the median CAS decreased from 4 (range from 3 to 6) to 2 (range from 0 to 3). Proptosis decreased from 21 (range from 16 to 26) to 20 (range from 15 to 25). Diplopia in primary gaze was noticed in seven patients (two new cases after EIODM).

Four patients (eight eyes) with active GO and eye muscle dysfunction at the end of therapy were referred for retrobulbar radiotherapy, which effected a decrease in CAS. Patients with constant diplopia were referred for anti-squint surgery when their GO was inactive and stable for at least six months.

### *Analysis in subgroups*

The analysis in subgroups with and without complete recovery after the end of the therapy (evaluation after additional treatment — Fig. 1) is shown in Table III. Patients with a complete recovery were significantly younger than those in the subgroup without complete recovery (53 *vs.* 68 years, respectively, $p = 0.049$), had a shorter duration of DON (8.4 *vs.* 29.7 weeks, respectively, $p = 0.035$), and had a higher GO activity (CAS 4 *vs.* 3, respectively, $p = 0.035$).

### *Side effects*

The mean cumulative dose of ivMP was 7.5 g (range 3.0 to 16.5 g); two patients received doses exceeding

**Table III.** *Comparison of selected data of patients with DON with and without complete recovery at the end of the therapy*
**Tabela III.** *Porównanie wybranych danych chorych oraz cech gałek ocznych z DON u chorych z całkowitą poprawą i bez poprawy po całkowitym leczeniu*

| | Complete recovery | Without complete recovery | P value |
|---|---|---|---|
| Apical crowding (n) | 6 | 3 | 1.00* |
| Optic nerve stretching (n) | 11 | 4 | 0.18* |
| Baseline VA (decimal fraction) | 0.6 | 0.5 | 0.96** |
| Impaired colour sensitivity (n) | 2 | 1 | 0.87* |
| Optic disc swelling (n) | 3 | 0 | 0.18* |
| CAS | 4 | 3 | **0.035**** |
| Proptosis [mm] | 21 | 21 | 0.74** |
| Age (years) | 53 | 68.5 | **0.049**** |
| Smokers (n) | 6 | 3 | 1.00* |
| TSH (reference range 0.270–4.200 $\mu$IU/mL) | 0.45 | 1.04 | 0.45** |
| TBII (reference range < 1.75 IU/L) | 24.69 | 17.95 | 0.22** |
| Duration of GO (weeks) | 25 | 416 | 0.20** |
| Duration of symptoms of DON (weeks) | 8.4 | 29.7 | **0.035**** |

DON — dysthyroid optic neuropathy; VA — visual acuity; CAS — clinical activity score; TSH — thyroid-stimulating hormone; TBII — TSH binding inhibitory immunoglobulins; GO — Graves' Orbitopathy. Values are presented as median or otherwise as indicated; *chi-squared test; **nonparametric unpaired Mann-Whitney U test

8.0 g (one — 9.3 g, the other — 16.5 g). After ivMP, we observed only mild and temporary side effects, such as insomnia (n = 1), dyspepsia (n = 1), facial flushing (n = 2), or harmless cardiac arrhythmias in the form of a single supraventricular extrasystole (n = 1). In one patient an increase of intraocular pressure was diagnosed and normalised successfully with antiglaucoma drops. We did not observe a significant (i.e. a fourfold) increase in transaminase activity after ivMP.

After EIODM recurrent sinusitis occurred in one patient. Additionally, a new onset of diplopia in the primary gaze was noticed in two patients: one without diplopia before treatment and the second with inconstant diplopia before treatment.

## Discussion

DON is a fairly rare medical problem, the diagnosis and treatment of which still remain a dilemma. Lower social class, higher social deprivation, smoking, and older age are factors associated with more severe types of GO, including DON [10–12]. It is worth emphasising that there is no pathognomonic feature of DON. Distinguishing DON from other causes of ophthalmological deterioration (*e.g.* cataract, corneal damage) can be difficult and is often delayed. Lack of appropriate treatment of DON may cause further worsening of ophthalmological complications and blindness. There have been no studies addressing the problem of how aggressive therapy should be in order to achieve a complete recovery. Clinical factors that predict a better outcome of DON treatment, and in particular a complete recovery, are largely unknown.

The diagnostic criteria of DON are not clearly defined. McKeag indicates impairment of colour vision and optic disc swelling together with radiological evidence of apical optic nerve compression, as frequently used for DON diagnosis [13]. Most authors suggest diagnosing DON on the basis of a combination of clinical and radiological features. However, at least one feature is obligatory (Curro et al. — at least one feature of DON in MR and at least two in ophthalmological examination, Mourits et al. — obligatory apical crowding in CT; Wakelkamp et al. — obligatory deterioration of VA < 0.67) [7, 14, 15]. We diagnosed DON if a patient fulfilled at least two of the following criteria: deterioration of VA and/or loss of colour vision and/or optic disc swelling and/or signs of DON in MR. The most common symptoms in our patients were optic nerve stretching (83%) and reduction of VA (100%).

The schedule of glucocorticoid treatment of DON is also vague. Wakelkamp et al. confirmed ivMP as an effective first-line treatment [7]. EUGOGO recommends initial therapy with ivGCs and urgent surgical decompression if the response is poor after one to two weeks [6, 7]. Curro et al. administered either 0.5 or 1.0 g of ivMP daily for three consecutive days, repeated after one week and followed with a tapering dose of steroids either orally or intravenously [14]. Hart et al. administered ivMP in three consecutive daily doses of

0.5 g and followed with oral prednisone [16]. Mourits et al. administered four single pulses of 0.5 g of ivMP every second day, tapered off with oral prednisone [15]. Guy et al. administered 1.0 g of ivMP divided into four daily doses of 0.250 g administered every six hours for three consecutive days [17]. There is still a lack of recommendations concerning patients without improvement after initial therapy. In such cases further therapy should be individualised.

We used pulses with 1.0 g of ivMP, given for three consecutive days. Then patients with a complete recovery were treated with 12 pulses of ivMP given once a week and prednisone in tapering doses. EIODM was performed in patients without complete improvement after therapy with 3.0 g of ivMP. This schedule of first- and second-line treatment enables a reduction of the cumulative doses of ivMP to less than 8.0 g with an opportunity for prolonged immunosuppressive therapy and stabilisation of VA during the follow-up. Exceeding the cumulative dose of over 8.0 g is associated with an increased risk of fatal side effects [6, 18]. However, two patients without a complete recovery after first- and second-line treatment received cumulative doses of over 8.0 g. No severe side effects were observed during a careful follow-up.

Different approaches to orbital decompression for DON are also described. Many authors recommend decompression of the medial wall as the best approach for patients with DON [8, 9, 19]. However, other surgical approaches are also presented: two-wall medial-lateral and three-wall medial-lateral-inferior orbital decompression combined with fat removal [20]. Due to such advantages as good visualisation of the orbital apex, the short time of hospitalisation, and lack of external scars, we performed EIODM. A new onset of diplopia in the primary gaze after EIODM was observed in two of the four patients without constant diplopia. Apart from a new onset of diplopia and recurrent sinusitis in one patient, we did not observe any other side effects resulting from this procedure. In patients with DON, ineffective ivMP pulse therapy, rituximab may be used. Unfortunately, this drug is not registered for GO treatment and we were unable to use it.

The criteria of improvement of DON are differently defined (Curro et al. — VA > 0.8 with normal visual fields and colour vision, Wakelkamp et al. — VA > 0.63 and no signs of DON, Mourits et al. — VA > 0.5 and improved or normal visual fields and colour vision, Hart et al. — the improvement in VA by two lines in the Snellen chart in the worst-affected eye) [7, 14–16]. However, even mild VA impairment could potentially deteriorate the health-related quality of life [21]. It was also confirmed in patients with GO that vision-related quality of life tended to be more severely impaired in patients with DON than in patients without DON [22]. We believe that any worsening of VA may be life-disturbing. Therefore, if a patient had any impairment of VA with no other concomitant eye disease, we tried to achieve normalisation of VA. If baseline therapy was ineffective, additional procedures were introduced according to individual considerations.

As mentioned above, in literature various criteria of improvement after treatment of DON are used, so comparison of treatment schedules are difficult. First-line treatment with ivMP was efficient in about 50% of eyes in the mentioned studies (Wakelkamp et al. — 55%, Mourits et.al — 39%, Curro et al. — 42%) [7, 14, 15]. Mourits et al. have shown that improvement (described as VA > 0.5) was achieved in 83% of eyes (ivMP plus orbital decompression if necessary) [15]. In cases of insufficient improvement additional therapy should be introduced without delay. In a retrospective study performed by Soares-Welch, who evaluated the efficiency of transantral orbital decompression (about half of the patients with preceding corticosteroid therapy), an improvement by ≥ 3 Snellen lines was observed in 54% of eyes with VA ≤ 20/40 before decompression [23]. In a recent study evaluating an augmented endoscopic transethmoid medial orbital wall decompression with fat decompression 95.8% had a statistically significant improvement in VA (mean improvement of 0.55 ± 0.17) [19]. Our main therapeutic goal was the complete recovery of VA including a reversal of other clinical symptoms of DON such as achieving normal colour vision and a normal-appearing optic disc.

The results of our study support the strategy of combination therapy (ivMP and surgical decompression), which can lead to a significant improvement in almost all the patients in the study and a complete recovery in the majority of eyes (about 70%). The lowest VA after completion of therapy was 0.7.

Based on further analysis, we found that the younger age of patients was a positive predictor of a complete recovery after full treatment. Patients with DON are older compared to patients with GO but without DON [12]. The average age of patients with DON is about 55 years [15, 23, 24], which is similar to our results. An older age may be associated with adverse factors related to reconstruction in the muscles, which may affect the therapeutic efficacy. The treatment schedule in this group should probably be combined and divided into many steps to avoid serious side effects. Additionally, we found that a shorter duration of DON and higher activity score of GO are predictive factors of a complete recovery. The early phase of DON could be associated with a higher CAS and better outcome of treatment. Recognition during the later phase diminishes the effectiveness of therapy and often requires additional

treatment. It should focus our attention on the early recognition and treatment of DON.

The main limitations of the study were the small number of patients and the retrospective analysis. However, the results of our study allow the following conclusions to be drawn.

## Conclusions

1. By using combination therapy (ivMP and surgical decompression), improvement can be achieved in almost all eyes with DON, with a complete recovery in the majority of cases. In many instances after first- and second-line treatments, an individual approach to patients with DON is needed.
2. Younger age, shorter duration of DON, and higher CAS are predictive factors of a complete recovery after combination therapy.

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