ORIGINAL RESEARCH PAPER
VOLUME-6 | ISSUE-7 | JULY-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

DEXAMETHASONE, THE POOR MAN'S DRUG: AN ALTERNATIVE TO METHYLPREDNISOLONE IN OPTIC NEURITIS

Ophthalmology

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ABSTRACT

Aim: To assess the visual function outcome and response of intravenous dexamethasone in the treatment of optic neuritis in a tertiary health care centre.

Materials and Methods: Study included 30 patients of acute optic neuritis presenting within eight days of onset and with visual acuity less than 20/60 in the affected eye. Patients received intravenous dexamethasone 100 mg in 250 ml of 5% dextrose over 1-2 hours daily, for three consecutive days[7] . Parameters tested were pupillary reactions, visual acuity, fundus findings, color vision, contrast sensitivity and visual fields for all patients at presentation and follow-up over a period of 1 year and results compared with standard pattern of outcome already laid down by randomised controlled trials such as ONTT(Optic Neuritis Treatment Trial) which used intravenous methylprednisolone 250 mg/six-hourly for three days followed by oral prednisolone for 11 days for treatment of optic neuritis and proved its efficacy.

Results: Improvement in visual acuity was statistically significant for distance on day 3 (P =0.000434) and for near vision on day 3 (P = 0.000045); improvement in color vision was statistically significant on day 3 (P =0.000143) . Significant improvement in RAPD,contrast sensitivity and visual fields were seen by 1 month ($p<0.05$). No serious side effects were observed. At one year, 78.12% (25 out of 32) eyes had visual acuity $\geq$ 20/40.

Conclusion: Intravenous dexamethasone is a cost effective alternative to methylprednisolone treatment for optic neuritis.

KEYWORDS:

intravenous dexamethasone, methylprednisolone, optic neuritis

Introduction:

Optic neuritis is a demyelinating inflammation of the optic nerve. It is also known as optic papillitis (when the head of the optic nerve is involved) and retrobulbar neuritis (when the posterior part of the nerve is involved). It is most often associated with multiple sclerosis, and it may lead to complete or partial loss of vision in one or both eyes[1].

Optic neuritis is clinically characterized by a sudden diminution of vision to varying extent, with associated pain on ocular movements. In acute optic neuritis, the fundus appears normal because two thirds of cases of optic neuritis are retrobulbar. With time, the optic nerve may become pale.

One third of patients with optic neuritis have a swollen disc (papillitis). The disc edema of optic neuritis often is diffuse. The presence of segmental changes, altitudinal swelling, pallor, arterial attenuation, and splinter hemorrhages suggest other diagnoses (eg, AION)[11].

Although more than three-quarters of patients make an excellent spontaneous recovery to a visual acuity of 20/30 or better, some have a lasting visual deficit[2]. The treatment had been controversial until the optic neuritis treatment trial (ONTT) provided convincing evidence, that intravenous methylprednisolone leads to quicker recovery of vision. However the long term visual outcome was comparable with placebo and oral steroids.[3],[4],[5],[6]

As methylprednisolone is expensive and the 6 hourly regimen of methylprednisolone as recommended by ONTT is cumbersome, dexamethasone as a daily single injection has been used in many centres with good outcome. Dexamethasone is a highly selective glucocorticoid with flourination at C9 and methyl group at C16(fig1). It is a cheaper treatment option, with fewer side-effects and is easier to administer as compared to methylprednisolone. A prospective clinical trial to ascertain the effectiveness of dexamethasone compared to methylprednisolone in acute optic neuritis was designed and we hereby present the results of this analysis and share our experience of using dexamethasone, which has not so far been extensively reported in the literature.

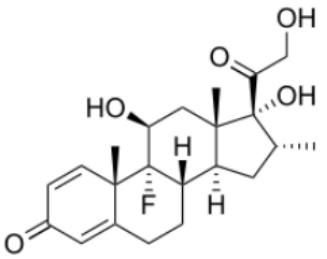


Fig 1

Materials and methods: This was a prospective, observational institution-based study including 30 patients of acute optic neuritis presenting within eight days of onset and with visual acuity less then 20/60 in the affected eye . Written informed consent regarding the nature of study and the treatment to be given was taken from all patients.

Intravenous dexamethasone 100 mg (in 250 ml 5% dextrose solution) was given over one and a half to two hours once a day for three days.[7]

All cases with known systemic disease other than multiple sclerosis that might be the cause of the optic neuritis were excluded. Cases with history of previous attacks of optic neuritis or diagnosis of multiple sclerosis for which the patient had already received corticosteroids or evidence of optic atrophy in the currently affected eye were also excluded. Cases with preexisting ocular abnormalities that might affect assessment of visual functions or cases with any systemic condition which contradicts the use of corticosteroids were also excluded.

A thorough systemic and neurological examination was performed. A complete ophthalmic examination was performed with slit-lamp evaluation of the anterior segment and evaluation of the posterior segment with slit-lamp biomicroscopy and indirect opthalmoscopy. The pupillary reactions, visual acuity and fundus findings were assessed before and during institution of treatment. Color vision, contrast sensitivity and Humphrey fields were recorded for all patients

after giving full refractive correction whenever the visual acuity permitted. Magnetic resonance imaging was done where deemed a necessity .

Visual acuity was assessed using Snellen (at a distance of 6m) visual acuity charts. Color vision was recorded using Ishihara pseudoisochromatic color vision plates. The color vision was quantified as the number of plates read on Ishihara pseudoisochromatic plates. Contrast sensitivity was recorded using Pelli-Robson charts (Clement Clarke, UK) at a distance of 1 m. Humphrey visual fields using Humphrey field analyser for both the eyes were done. The intravenous steroids were infused by slow intravenous drip over a period of one and a half to two hours. The pulse and blood pressure were recorded prior to the institution of therapy and monitored throughout at 30-min intervals till the completion of the infusion and for one hour thereafter. The doses were repeated on day 2 and day 3.

The patients were examined every day during the institution of treatment and later at one week, one month, three months and 6months.

Statistical analysis: Statistical analysis was done using corrected chi-square test for the clinical parameters.

Results :

Table 1: clinical profile of cases

Male:female	8:7
Mean age	31±6years
Range	10-45
Mean age of presentation	5days

Table2: colour vision,contrast sensitivity,RAPD grading in group receiving dexamethasone

Colour vision	Pre-treatment	Day3	1week	1month	3months	6months
TCB	28	12	6	5	4	4
PCB	4	20	18	10	4	4
Normal	0	0	8	17	22	22
Total no of eyes	32	32	32	32	30	30
P value		<0.01	<0.01	<0.01	<0.01	<0.01

Contrast sensitivity	Pre-treatment	Day3	1week	1month	3months	6months
≤70(severe loss)	30	28	20	12	4	2
71-169(mod loss)	2	2	4	10	8	5
170-below normal(mild loss)	0	2	4	5	10	5
Normal	0	0	4	5	8	18
Total no of eyes	32	32	32	32	30	30
P value		0.95	0.13	<0.01	<0.01	<0.01

RAPD	Pre-treatment	Day3	1week	1month	3months	6months
Grade3-4	18	12	8	4	2	2
Grade2	12	14	12	11	8	8
Grade1	2	6	8	10	10	10
No RAPD	0	0	4	7	10	10

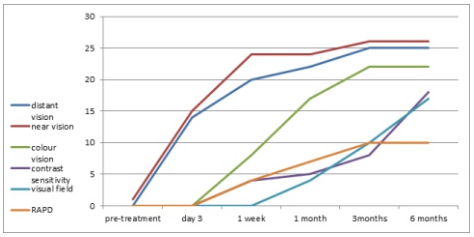
Table3: visual acuity in eyes treated with intravenous dexamethasone

Visual acuity(distance)	Pre-treatment	Day3	1week	1month	3months	6months
≥20/40	0	14	20	22	25	25
20/120-20/60	9	9	6	6	2	2
10/200-20/200	3	3	1	0	0	0
<10/200	20	6	5	4	3	3
Total no of eyes	32	32	32	32	30	30
P value		<0.01	<0.01	<0.01	<0.01	<0.01
Visual acuity(near)						
≤N36	14	6	4	3	2	2
N36-N18	16	6	4	2	1	1
N12-N10	2	7	0	3	1	1
N8-N6	1	15	24	24	26	26
Total no of eyes	32	32	32	32	30	30
P value		<0.01	<0.01	<0.01	<0.01	<0.01

Table 4: visual field analysis trend in group receiving intravenous dexamethasone

Humphrey visual field					
Type of defect	**Pre-treatment**	**1week**	**1month**	**3months**	**6months**
Diffuse(severe)	18	10	4	4	4
Diffuse(moderate)	8	18	4	4	4
Diffuse(minimal)	2	1	8	12	5
Centrocaecal	2	2	2	0	0
Paracentral	2	1	0	0	0
Inferior altitudinal	0	0	0	0	0
Peripheral vision	0	0	0	0	0
Double arcuate	0	0	0	0	0
Normal	0	0	4	10	17
Total no of eyes	32	32	32	30	30
P value			<0.01	<0.01	<0.01

Fig1: outcome trend in various parameters with iv dexamethasone therapy in optic neuritis



The mean age of the group of patients was 31years. 28 cases were unilateral and 2 cases were bilateral with 16 males and 14 females. Out of 30, 22 cases were of papillitis,6 cases of retrobulbar neuritis and 2 cases of neuroretinitis.

Visual function showed rapid recovery following treatment with intravenous dexamethasone . Out of 30 patients,28patients completed all tests for assessment of visual function till 1 year,2 cases were lost to follow up after 3months.

Statistical analysis was done for 30 patients(32eyes) and followed up for a period of 1year. Significant improvement began within 24hrs and statistically significant improvement on day 3 could be seen(p= 0.000143 for colour vision, and p= 0.000434 for distant vision).Visual fields,contrast sensitivity and RAPD were slow to recover. No significant alteration in vitals or biochemical parameters were noted.

Three months after treatment, VA of 20/20 was achieved in 18 (60%) eyes, 20/30 in 5 (16.66%) and 20/40 in 2 (6.66%). Two eyes (6.66%) had a VA of 20/120-20/60 and 3 eyes (10%) had VA < 10/200. At 6 months, 25 (83.33%) eyes had VA ≥ 20/40. Visual acuity remained stable thereafter, up to 1 year follow-up. 1 year of follow-up was completed in 30 eyes (of 28 patients).

After 3 months, color vision returned to normal in 22 eyes (73.33%). Of the remaining eyes with persistent residual color vision defects, 4 eyes (13.33%) had partial color deficiency, while 4 eyes (13.33%) were total colour blind. These patients had near vision, adequate to be able to read the numbers. Normal contrast sensitivity values were regained in only 8 eyes (26.66%) in 3 months follow up,which increased to 18(60%) in 6months follow up. The remaining patients had subnormal contrast sensitivity scores.

In 3rd month,Humphrey visual fields returned to normal in 10 eyes (33.33%) out of 30 eyes, while the remaining 12 eyes (40.00%) eyes had persistent diffuse defects . In 6th month,the visual fields returned to normal in 17 patients(56.66%).

Discussion :

In a poor developing country as in India,due to financial considerations, dexamethasone is often routinely used instead of methylprednisolone to treat optic neuritis and other disorders with a mega dose of intravenous steroids in many hospitals.[8],[9]. In the

natural course of optic neuritis, spontaneous recovery generally starts within one week of onset, but may take longer in some cases. In the absence of improvement in visual function before starting any treatment and the dramatic onset of improvement (within 24 hours) in recovery of visual acuity after dexamethasone therapy, the rapid recovery of vision can be attributed to the intervention with dexamethasone therapy. This was confirmed by the results of the statistical analysis.

Statistically significant improvement was observed in all visual function parameters. Improvement in VA for distance and near vision was the fastest, followed by color vision, contrast sensitivity, RAPD and visual fields. In all,at 6months follow up,83.33 % eyes regained VA ≥ 20/40 and 6.66% eyes VA of 20/120-20/60. Only 10% eyes failed to improve beyond 10/200 at 6 months. In our study, 60% of eyes regained the normal VA of 20/20 at 6 months. This is as compared with 57.33% (61.59% in the methylprednisolone group, 56.66% in the placebo group and 53.85% in the oral prednisolone) in the ONTT.[10]. Our results for improvement to near normal in various visual function parameters at 6months for contrast sensitivity(60%),visual fields(56.6%) and colour vision(73.3%) was comparable to the outcome of ONTT trial at 6months(62.3% for contrast sensitivity,80.1% for visual fields and 66.9% for colour vision)[12]. A similar study by Tandon R et al conducted in RP Centre for Ophthalmic sciences AIIMS,New Delhi in 2006 which at 3months follow up reported near normal contrast sensitivity in 21.4%,colour vision in 75%,visual acuity in 82.14% and visual fields in 32.14% which were comparable to our results in 3months follow up(26.6%,73.3%,83.3% and 33.3% respectively). A study by Mehrotra A et al(2007),which compared the efficacy of dexamethasone with methylprednisolone also found similar results. In our study,out of 30 patients (32 eyes) who were able to complete all tests for assessment of visual functions initially, 2 patients (2 eyes) were lost to follow-up at 3months. 28 patients (30 eyes) completed 1 year follow-up. Statistical analysis of visual outcome has been done for these 32 eyes (of 30 patients). This is an inherent problem in situations where the patients come from far off places. Since we do not know the exact clinical status, they have not been included in analysis after 3months. Overall, 2 eyes (of 2 patients) were not included in the final analysis.

In our study,all patients treated with intravenous dexamethasone therapy fared well, with no pulse or blood pressure variation and serum electrolyte disturbance during the period. No serious complications or side effects were observed in any of the treated patients and no oral steroids were given after intravenous dexamethasone therapy. Good results with intravenous dexamethasone therapy alone, suggests that tapered treatment with oral steroids may not be required. Although intravenous methylprednisolone is considered the standard treatment to enhance the recovery of visual function in optic neuritis, our results suggest that dexamethasone can also be used for this purpose, in case there are financial constraints in a developing nation such as India.

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