# A Prospective Randomized Trial of Megadose Methylprednisolone and High Dose Dexamethasone for Traumatic Optic Neuropathy

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**Abstract**

**Purpose :** To determine whether the improvement in visual acuity obtained when using high dose dexamethasone in the treatment of traumatic optic neuropathy was comparable to that of megadose methylprednisolone.

**Method :** A total of forty-four patients with traumatic optic neuropathy were prospectively randomized and selected to receive intravenous high dose dexamethasone or megadose methylprednisolone within 2 weeks of injury. Age, gender, cause of injury, interval from injury to treatment, initial, post-pulse, and final visual acuity were analysed statistically to compare the dexamethasone and methylprednisolone groups.

**Results :** The mean interval to treatment was not significantly different (p=0.28) for the dexamethasone group at 5.5 days compared to the methylprednisolone group at 4.1 days. Visual improvement of at least two lines of the Snellen chart or two levels of unmeasured visual acuity was shown in 9 patients (37.5%) of the dexamethasone group and 10 patients (50%) of the methylprednisolone group. There was no statistically significant difference between the initial and post-pulse visual acuity (p=1.0) and the initial and final visual outcome (p=0.60) in the dexamethasone group compared with the methylprednisolone group.

**Conclusion :** There was no significant difference in the visual acuity obtained after treatment with intravenous dexamethasone or methylprednisolone for traumatic optic neuropathy.

**Key word :** Traumatic Optic Neuropathy, High Dose Dexamethasone, Megadose Methylprednisolone

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Traumatic optic neuropathy is defined as an indirect injury to the optic nerve that causes loss of vision which occurs without external or initial ophthalmoscopic evidence of injury to the eye or its nerve. The incidence is estimated to be between 0.7 per cent and 1.5 per cent of all skull injuries[1]. Available studies have documented spontaneous improvement of vision in 20-40 per cent of untreated cases[2-4], while others have demonstrated that the dexamethasone at a dosage of 1-5 mg/kg/day improved the vision in a patient with traumatic optic neuropathy[5,6]. The proposed mechanisms of visual improvement after treatment by corticosteroids are stabilization of lipid membrane by inhibition of oxygen free radical-induced lipid peroxidation and reduction of neural tissue edema, microcirculatory spasm and neural necrosis[5].

Many reports have been published supporting the evidence that high dose corticosteroid is useful in the treatment of traumatic optic neuropathy[6-8].

After the National Acute Spinal Cord Injury Study[9,10], clinical studies of traumatic optic neuropathy indicated the benefit of methylprednisolone [11,12]. However, some authors have retrospectively studied accounts of groups of patients with traumatic optic neuropathy in whom treatment by methylprednisolone produced similar results compared with treatment by dexamethasone. This prospective randomized study was to determine whether the improvement in visual acuity using high dose dexamethasone was comparable to megadose methyl-prednisolone in the treatment of traumatic optic neuropathy.

## MATERIAL AND METHOD

Forty-four patients diagnosed with traumatic optic neuropathy without any associated penetrating ocular injuries were prospectively and randomly treated with high dose dexamethasone or megadose methylprednisolone after giving written, informed consent according to the tenets of the declaration of Helsinki, between June 1995 and May 2001. All participants were given treatment within two weeks of injury. An imaging study was performed immediately if an orbital fracture was suspected. Seventy-eight patients whose injury treatment interval was more than two weeks, who had evidence of optic nerve compression or undergone optic nerve fenestration were excluded from the study. Data collection included age, gender, laterality, interval from injury to the start of treatment, cause of injury and conscious level after the injury, initial, post-pulse and final best corrected visual acuity (BCVA).

The patients were randomized to two groups: the dexamethasone group and the methylprednisolone group. The dexamethasone group was treated with high dose dexamethasone at a dosage of 0.7 mg/kg body weight followed by a 0.35 mg/kg/dose every six hours for 72 hours and subsequently oral prednisolone 1 mg/kg was administered for two weeks. A megadose of methylprednisolone was given in the methylprednisolone group at a dosage of 30 mg/kg body weight initially, then maintained by 5.4 mg/kg/hour in a continuous infusion for 72 hours and followed by oral prednisolone at the same dosage and duration as the dexamethasone group. The mean follow-up period was 6.4 months in the dexamethasone group and 17.0 months in the methylprednisolone group. BCVA and a complete ocular and ophthalmoscopic fundal examination were monitored daily during the period of pulse therapy and follow-up was done at one week, one month and every six months after the start of treatment. BCVA was measured using a standard Snellen acuity chart in the office and was converted to logMAR (log of the minimum angle of resolution) values (logMAR= log[1/Snellen visual acuity]) for statistical analysis. The unmeasured visual acuity was at the following logMAR values: counting fingers corresponded to 2.6 logMAR, hand motion to 2.9 logMAR, light perception to 3.1 logMAR and no light perception to 3.4 logMAR.

An improvement in visual function was defined as an improvement in BCVA of at least two lines of the Snellen chart or two levels of unmeasured visual acuity from the initial BCVA to the final vision outcome.

### Statistical analysis

Between group comparisons of categorical variables such as gender, cause of trauma, associated injury, level of consciousness after injury and vision improvement after treatment were performed using a chi-square test. Whereas group comparisons of age, interval from injury to treatment and initial, post-pulse and final visual acuity were statistically analyzed by *t*-test.

## RESULTS

The demographic characteristics and results of the dexamethasone group and the methylprednisolone group are shown in Table 1 and 2 respectively. Table 3 presents the statistical analysis of the study. There was no significant difference (p=0.97) in the mean age of 23.0 ± 8.6 years of the dexamethasone group compared with the mean age of 23.1 ± 9.4 years of the methylprednisolone group. There was also no significant difference (p=0.45) in gender between the dexamethasone group (23 men and 1 woman) and the methylprednisolone group (15 men and 5 women). The cause of injury in the 14 dexamethasone-treated patients (58.3%) and 15 methylprednisolone-treated patients (75%) was motor vehicle accidents, in 6 dexamethasone-treated patients (25%) and 2 methylprednisolone-treated patients (10%) it was assault, in 3 dexamethasone-treated patients (12.5%) and 2 methylprednisolone-treated patients (10%) it was falling down and in one patient each it was an explosion and tripping respectively. The severity of injury was determined by level of consciousness and the presence of craniofacial fractures which were found in the patients after trauma. Thirteen patients (54.2%) in the dexamethasone group and 10 patients (50%) in the methylprednisolone group experienced immediate loss of consciousness, the duration of which extended from half an hour to 5 hours except for one methylprednisolone-treated patient in whom initial visual acuity dropped to no light perception and who was unconscious for 48 hours following the accident. Orbital or skull fractures were found in 7 patients (29.2%) in the dexamethasone group and 5 patients (25%) in the methylprednisolone group.

The mean interval from injury to treatment showed no difference (p=0.28) between the dexamethasone group at 5.48 ± 5.1 days and the methylprednisolone group at 4.08 ± 3.2 days. The mean initial log MAR for the dexamethasone group was 2.47 ± 1.15 (approximate Snellen visual acuity of counting fingers). The mean initial log MAR for the

**Table 1. Characteristic of patients with traumatic optic neuropathy treated with highdose dexamethasone.**

| No | Age (years) sex laterality | Interval from injury to treatment (days) | Cause of trauma | Fracture | Loss of concious ness | Visual acuity | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Initial | Post-pulse | Final |
| 1 | 17, M, R | 14 | MCA | - | - | NLP | NLP | NLP |
| 2 | 13, M, R | 6 | MCA | Orbital roof | + | CF | 6/60 | 6/60 |
| 3 | 28, M, L | 14 | Assaulted | Orbital wall | - | 6/36 | 6/6 | 6/6 |
| 4 | 38, M, L | 6 | Assaulted | - | - | NLP | NLP | NLP |
| 5 | 30, M, R | 8 | Assaulted | - | + | 6/12 | 6/9 | 6/9 |
| 6 | 21, M, L | 1 | MCA | - | + | NLP | 6/24 | 6/36 |
| 7 | 17, M, R | 10 | MCA | - | - | HM | HM | HM |
| 8 | 28, M, L | 7 | MCA | - | + | 2/60 | 6/60 | 2/60 |
| 9 | 22, M, L | 4 | Fell down | - | + | CF | 6/60 | 6/60 |
| 10 | 20, M, R | 0.5 hour | MCA | - | - | 6/18 | 6/5 | 6/5 |
| 11 | 14, M, L | 3 | MCA | Trimalar | + | NLP | NLP | NLP |
| 12 | 48, F, R | 20 hours | Fell down | - | - | HM | 6/36 | 6/36 |
| 13 | 23, M, R | 5 | MCA | Skull base | - | 6/9 | 6/6 | 6/6 |
| 14 | 18, M, L | 12 hours | Explosion | - | - | NLP | NLP | NLP |
| 15 | 15, M, L | 14 | MCA | - | + | HM | CF | CF |
| 16 | 27, M, L | 1 | MCA | - | - | NLP | NLP | NLP |
| 17 | 20, M, R | 14 | Assaulted | - | + | NLP | NLP | NLP |
| 18 | 21, M, R | 7 | MCA | - | - | NLP | NLP | NLP |
| 19 | 13, M, R | 12 | Fell down | Orbital roof | + | LP | LP | LP |
| 20 | 18, M, R | 3 | MCA | - | + | NLP | NLP | NLP |
| 21 | 37, M, L | 2 hours | Assaulted | - | - | 6/60 | 6/60 | 6/12 |
| 22 | 26, M, L | 2 hours | MCA | Frontal bone | + | NLP | NLP | NLP |
| 23 | 22, M, L | 1 hour | Assaulted | - | + | 2/60 | 6/36 | 6/24 |
| 24 | 17, M, L | 1 | MCA | Orbital floor | + | CF | 1/60 | 6/18 |

MCA = motorcycle accident; NLP = no light perception; LP = light perception; CF = counting fingers; HM = hand motion.

**Table 2. Characteristic of patients with traumatic optic neuropathy treated with methylprednisolone.**

| No | Age (years) sex laterality | Interval from injury to treatment (days) | Cause of trauma | Fracture | Loss of concious ness | Visual acuity | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Initial | Post-pulse | Final |
| 1 | 13, M, R | 2 hours | Fell down | - | - | NLP | NLP | NLP |
| 2 | 33, M, R | 4 | Tripped | Orbital floor | - | NLP | NLP | NLP |
| 3 | 21, M, L | 10 hours | MCA | - | + | CF | 6/60 | 2/60 |
| 4 | 16, M, L | 7 | MCA | - | + | NLP | NLP | NLP |
| 5 | 37, M, L | 1 | Fell down | Orbital floor | - | NLP | NLP | NLP |
| 6 | 16, M, R | 1 hour | MCA | - | + | NLP | NLP | CF |
| 7 | 22, M, R | 5 | MCA | Trimalar | + | 6/36 | 6/9 | 6/9 |
| 8 | 23, M, R | 6 | MCA | Ant$^{r}$ cranial | + | NLP | NLP | NLP |
| 9 | 27, M, R | 6 | MCA | Fossa | + | NLP | NLP | NLP |
| 10 | 30, F, R | 7 | Assaulted | - | - | 6/36 | 6/6 | 6/6 |
| 11 | 28, M, L | 4 | MCA | - | - | LP | 3/60 | 3/60 |
| 12 | 23, M, R | 4 | MCA | - | - | 6/60 | 6/12 | 6/12 |
| 13 | 13, F, R | 8 | MCA | Zygoma | + | NLP | HM | CF |
| 14 | 18, F, R | 4 | MCA | - | - | NLP | 4/60 | 6/18 |
| 15 | 11, F, R | 7 | MCA | - | - | NLP | NLP | NLP |
| 16 | 15, F, R | 3 hour | MCA | Orbital floor | + | NLP | NLP | 6/6 |
| 17 | 18, M, L | 2 | MCA | - | + | NLP | NLP | NLP |
| 18 | 16, M, L | 12 | MCA | - | - | NLP | NLP | NLP |
| 19 | 42, M, L | 2 | MCA | - | + | 2/60 | 2/60 | 6/12 |
| 20 | 40, M, L | 2 | Assaulted | - | - | HM | HM | CF |

MCA = motorcycle accident; NLP = no light perception; LP = light perception; CF = counting fingers; HM = hand motion.

**Table 3. Comparison between dexamethasone group and methylprednisolone group.**

| | Dexamethasone group | Methylprednisolone group | P value |
|---|---|---|---|
| Mean age | 23.0 ± 8.6 | 23.1 ± 9.4 | 0.97 |
| Male : Female | 23 : 1 | 15 : 5 | 0.45 |
| Right eye : Left eye | 11 : 13 | 12 : 8 | 0.17 |
| Interval to treatment | 5.5 ± 5.1 | 4.1 ± 3.2 | 0.28 |
| Cause of trauma | | | 0.42 |
| Motor vehicle accident | 14 | 16 | |
| Assaulted | 6 | 1 | |
| Fell down | 3 | 2 | |
| Explosion | 1 | 0 | |
| Tripping | 0 | 1 | |
| Mean initial visual acuity ± SD | 2.47 ± 1.15 | 2.84 ± 0.97 | 0.14 |
| Mean post-pulse visual acuity ± SD | 1.97 ± 1.39 | 2.43 ± 1.30 | 0.19 |
| Mean final visual acuity ± SD | 1.95 ± 1.39 | 2.12 ± 1.43 | 0.68 |

methylprednisolone group was 2.84 ± 0.97 (approximate Snellen visual acuity of hand motion). The mean post-pulse log MAR for the dexamethasone group was 1.97 ± 1.39 (approximate Snellen visual acuity of 1/60). The mean post-pulse log MAR for the methylprednisolone group was 2.43 ± 1.30 (approximate Snellen visual acuity of counting fingers). The mean final log MAR for the dexamethasone group was 1.95 ± 1.39 (approximate Snellen visual acuity of 1/60). The mean final log MAR for the methylprednisolone group was 2.12 ± 1.43 (approximate Snellen visual acuity between 1/60 and counting fingers).

The post-pulse visual acuity which was measured immediately after the termination of intravenous pulse therapy showed an improvement in visual acuity of at least two lines of the Snellen chart in 8 patients (33.3%) in the dexamethasone group

an in 7 patients (35%) in the methylprednisolone group. There was no statistically significant difference between the two groups (p=1.0). The mean final visual acuity determined at least one-month from treatment had improved in 9 patients (37.5%) who were treated with dexamethasone and in 10 patients (50%) who were treated with methylprednisolone. There was also no significant difference (p= 0.60) in the final visual acuity between the dexamethasone group and the methylprednisolone group. Of 10 patients whose initial visual acuity was no light perception in the dexamethasone group, one patient (10%) showed improvement in his visual acuity and of 13 patients with an initial visual acuity of no light perception in the methylprednisolone group, 4 patients (30.8%) also showed an improvement but only 2 patients (15.4%) recovered useful vision. Although the improvement in patients with an initial visual acuity of no light perception appeared to be slightly better in the methylprednisolone group than the dexamethasone group, the difference was not statistically significant (p=0.23).

Some patients complained of minimal symptoms of gastritis but this was relieved by medication which was taken routinely during the administration of pulse corticosteroid. In the present study, no patients developed serious side effects as a result of treatment with dexamethasone and methylprednisolone.

## DISCUSSION

The management of indirect traumatic optic neuropathy remains uncertain with regard to whether surgical decompression of the optic canal, corticosteroid treatment or observation alone is the most potentially effective[4,12,13]. In attempts to provide a means of establishing the best standardized treatment option for traumatic optic neuropathy, many investigators have proposed that an individual possibly requires a different appropriate therapy depending on the clinical basis of injury[13]. However, the evidence for benefit of corticosteroid over spontaneous resolution has been documented in several reports[5,6].

As in previous reports, the presented patients with traumatic optic neuropathy were mainly young men, and motor vehicle accidents were found to be the most common cause. The severity of injury correlated poorly with the level of consciousness following the injury and the presence of craniofacial fracture[4-6,11]. In addition, no correlation between interval from injury to treatment and final visual outcome was found in treatment using dexamethasone and methylprednisolone.

By comparing improvement in visual acuity in traumatic optic neuropathy following treatment between dexamethasone and methylprednisolone in the present study, it was found that dexamethasone was not significantly different compared with methylprednisolone between the initial and post-pulse outcome (p=0.77) or initial and final visual outcome (p=0.42). This finding agrees with the improvement in vision obtained in 7 of 9 patients (78 %) treated with dexamethasone and 12 of 13 (92 %) treated with methylprednisolone in the nonrandomized study by Spoor et al[11] which was also not statistically significantly different. Though treatment with methylprednisolone seemed to be useful in producing an improvement in vision more quickly than treatment with dexamethasone, the intervals from injury to the start of treatment and the initial visual acuity were quite different between the two groups.

With respect to the mean interval from injury to treatment in the study by Spoor et al, there was a considerable difference between the dexamethasone group at 17 hours compared with the methylprednisolone group at 4.2 days. In contrast to their study, the dexamethasone group in the present study received treatment only one day later than the methylprednisolone group. Instead of rapid visual improvement in the methylprednisolone group as demonstrated in their results, the present study inversely showed a slightly faster visual recovery in the dexamethasone group despite the much higher dosage of methylprednisolone. This might be due to the much higher mean initial visual acuity of the methylprednisolone group at 2.10 ± 1.23 logMAR than the dexamethasone group at 2.84 ± 0.91 logMAR in their study.

Basically, the dexamethasone is thought to have five times the anti-inflammatory effect of methylprednisolone. However, dexamethasone at a dose of 2 mg/kg/day in the present study was not comparable to methylprednisolone given at 30 mg/kg.

Interestingly, despite the differences in dosage between dexamethasone and methylprednisolone, the present study demonstrated that both types

of corticosteroids have similar efficacy with respect to improvement in vision. This might not result from the treatment but possibly from spontaneous improvement. Nevertheless, it is still uncertain whether corticosteroid treatment is of greater benefit than receiving no treatment. In order to obtain data on this, a further controlled trial with a larger sample size should be carried out.

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# การศึกษาสุ่มตัวอย่างเพื่อเปรียบเทียบระหว่างเด็กซาเมธาโซนขนาดสูง และเมธิล-เพร็ดนิโซโลนขนาดสูงมาก ในการรักษาโรคประสาทตาเสื่อมจากอุบัติเหตุ

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**วัตถุประสงค์** : เพื่อศึกษาเปรียบเทียบผลการรักษาโรคประสาทตาเสื่อมจากอุบัติเหตุด้วยยาเด็กซาเมธาโซนขนาดสูง และยาเมธิลเพร็ดนิโซโลนขนาดสูงมาก

**วิธีการ** : ทำการศึกษาในกลุ่มผู้ป่วยโรคประสาทตาเสื่อมจากอุบัติเหตุ จำนวน 44 ราย แบ่งเป็นผู้ป่วยกลุ่มแรกได้รับการรักษาด้วยยาเด็กซาเมธาโซนขนาดสูง และผู้ป่วยกลุ่มที่ 2 ได้รับการรักษาด้วยยาเมธิลเพร็ดนิโซโลนขนาดสูงมาก ผู้ป่วยทั้งสองกลุ่มได้รับการรักษาภายในระยะเวลา 2 สัปดาห์ภายหลังอุบัติเหตุ และทำการเปรียบเทียบอายุ เพศ สาเหตุของอุบัติเหตุ ระยะเวลาตั้งแต่ได้รับอุบัติเหตุจนได้รับการรักษา และระดับสายตาก่อนและหลังการรักษา

**ผล** : ผู้ป่วยในกลุ่มที่ได้รับยาเด็กซาเมธาโซน จำนวน 24 ราย มีระดับสายตาที่วัดด้วย Snellen chart ดีขึ้นอย่างน้อย 2 แถว จำนวน 10 ราย คิดเป็นร้อยละ 50 และกลุ่มที่ได้รับยาเมธิลเพร็ดนิโซโลน จำนวน 20 ราย มีระดับสายตาดีขึ้นอย่างน้อย 2 แถว จำนวน 9 ราย คิดเป็นร้อยละ 37.5 ผลการรักษาในผู้ป่วยทั้งสองกลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ

**สรุป** : การรักษาผู้ป่วยโรคประสาทตาเสื่อมจากอุบัติเหตุด้วยยาเด็กซาเมธาโซนขนาดสูง และยาเมธิลเพร็ดนิโซโลนขนาดสูงมากได้ผลใกล้เคียงกัน

**คำสำคัญ** : โรคประสาทตาเสื่อมจากอุบัติเหตุ, เด็กซาเมธาโซน, เมธิลเพร็ดนิโซโลน

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