

ORIGINAL ARTICLE

INTRAVENOUS METHYLPREDNISOLONE EFFECTS ON RECTUS MUSCLES IN THYROID EYE DISEASE

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ABSTRACT

Introduction: Intravenous methylprednisolone has been used in management of Thyroid Eye Diseases (TED) which was an autoimmune inflammatory disease of the orbital tissues and the eyes. Previous study has shown benefits of intravenous methylprednisolone therapy on TED but there was need of quantitative measure to assess the effect of intravenous methylprednisolone therapy on extraocular rectus muscles. This study aimed to report the effect of high-dose intravenous methylprednisolone pulse therapy on inferior, medial, superior, and lateral rectus muscles and providing data distribution of active TED before and after therapy.

Case Report: Retrospective analyses were used in the data collection of patients with active Thyroid Eye Disease (TED) underwent high-dose intravenous methylprednisolone pulse therapy regiment 500mg every week for six consecutive weeks at Sardjito Eye Centre between January 2022 and December 2022. Ophthalmological investigation and quantitative computed tomography (CT) scan of the orbit were performed before and after methylprednisolone pulse therapy and demographics data were presented in tables and graphs.

Discussion: This study included 62 eyes of 31 patients (61,3% female) with mean age of 37.8 ± 13.47 years old. The mean thickness of Superior Rectus (SR) muscle before therapy were 4.12 ± 2.20 mm and significantly decreased to 3.70 ± 1.54 mm post therapy. There was no significant difference in delta mean Inferior Rectus (ΔIR) -0.18 ± 1.69 ($p=0.381$), Medial Rectus (ΔMR) -0.34 ± 1.68 ($p=0.116$), and Lateral Rectus (ΔLR) -0.33 ± 1.94 ($p=0.188$).

Conclusion: The treatment of Thyroid Eye Disease (TED) with high dose intravenous corticosteroid is safe and effective in reducing extraocular muscle tissue thickness with minimal side effects.

Keywords: Thyroid Eye Disease, Extraocular Muscle, Intravenous Methylprednisolone Therapy.

INTRODUCTION

Thyroid eye disease (TED) is a chronic immune-mediated inflammation of the orbital and periorbital tissues. The aetiology of thyroid eye disease is commonly associated with complex immune-mediated cycle of orbital adipose tissue and fibroblast as target cells. In hyperthyroidism state, fibrocytes infiltrate the orbit and express elevated levels of thyroid-

stimulating hormone (TSH) receptors and recruiting inflammatory cytokines such as interleukins (IL-6). These cells can differentiate into adipose and myofibroblast and caused phenotypic clinical manifestation of TED.^{1,2}

Corticosteroid therapy is a common and well-established method of treatment of active TED, due to its anti-inflammatory and immunosuppressive actions. In previous study, intravenous steroids in the form of methyl prednisolone (IVMP), within safe dosage and the length of time is effective for TED. Therefore, this therapy is considered cost effective and relatively safe with minimum side effects.^{3,4} In other study, the usage of Rituximab (RTX) as monoclonal antibody had more pronounced improvement than that observed after IVMP therapy and seemed to appear earlier. Interestingly, the Clinical Activity Score (CAS) continued to decline in patients treated with RTX even after the first 5 months of follow-up, when B-cells returned, whereas same results were not observed in patients after IVMP therapy.⁵

Therefore, the aim of our study is to report the effect of high-dose IVMP pulse therapy on inferior, medial, superior, and lateral rectus muscle and providing demographic data and laboratories parameters of active TED patients before and after therapy.

METHODS

This was a retrospective hospital-based study conducted at RSUP DR. Sardjito Hospital in the Yogyakarta from January 2022 and December 2022 after ethical approval by the institutional review committee. All patients diagnosed with Thyroid Eye Disease and underwent high dose IVMP therapy were included in the study. Patients with incomplete data were excluded. History and routine eye examinations findings before therapy including visual acuity, tonometry, and slit lamp evaluation were collected from medical record. The procedure processes were fully explained to each patient and written informed consent was obtained as documented on medical records. Laboratories data including Thyroid Stimulating Hormone (TSH), Free Triiodothyronine (FT3), and Free thyroxine (FT4) were also collected from medical records. The patients were divided into groups based on age (<40 years old and \geq 40 years old), gender (male and female), and Laboratories parameters group (Lab hyperthyroid and Lab normal). All patients underwent standard protocol of High Dose Intravenous Methylprednisolone (IVMP) 500mg dose regiment per injection every week for six consecutive weeks. The extraocular muscle thickness data were measured using Contrast Head MSCT Scan measured before and after injection. Scans were analysed by consultant radiologist in RSUP DR. Sardjito hospital and then uploaded in electronic medical records. Complications during and following procedure were noted in medical records. Continuous variables were expressed

as the mean \pm standard deviation for those displaying normal distribution. Paired t-test was applied to compare before and after procedure parameters. We also evaluate association between nominal and interval data using Eta coefficient value and bivariate analysis. All the statistical analysis was performed using SPSS software. P-values less than 0.05 were considered statistically significant.

RESULTS

This study included 62 eyes of 31 patients with mean age of 37.8 ± 13.47 years old. The male to female ratio were 1:1.58 (61,3% female). Laboratories parameters that were analysed in this study were TSH (mean 0.49 ± 0.96 μ IU/L), FT3 (mean 5.53 ± 5.12 pg/ml), FT4 (3.36 ± 4.70 ng/ml)

Table 1. Profile Cases of IV MP Pulse Therapy TED Patients

Age (years)	Frequency	Percentage (%)	Mean \pm SD	Range
<40	16	51.6	37.8 ± 13.47	20 - 61
≥ 40	15	48.4		
Gender			M:F ratio	
Male	12	38.7	1:1.58	
Female	19	61.3		
Affected eye			OD:OS ratio	
OD	31	50.0	1:1	
OS	31	50.0		
Hyperthyroid Lab group			Lab (+): Lab (-) ratio	
Lab Hyperthyroid	22	71.0	2.44:1	
Lab Normal	9	29.0		
Lab Parameters	Frequency	Normal Value	Mean \pm SD	Range
TSH	31	0.27-4.20	0.49 ± 0.96	0.005- 4.30
FT3	31	2.20-4.40	5.53 ± 5.12	0.93 -24.01
FT4	31	0.93-1.70	3.36 ± 4.70	0.60 -26.18

Table 2. Age and Gender Wise Distribution of Baseline Extraocular Muscle Thickness, UCVA and IOP

Age (yr.)	Frequency	IR	MR	SR	LR	UCVA	IOP
<40	32	4.30 ± 1.74	3.93 ± 1.05	3.76 ± 1.45	3.49 ± 1.04	0.21 ± 0.24	15.59 ± 3.19
≥ 40	30	4.61 ± 1.87	4.36 ± 1.97	4.50 ± 2.76	4.41 ± 1.96	0.36 ± 0.33	14.40 ± 3.43
p-value	0.505	0.283	0.190	0.025	0.041	0.161	
Gender	Frequency	IR	MR	SR	LR	UCVA	IOP
Male	24	5.16 ± 2.36	4.44 ± 2.20	4.40 ± 2.98	4.05 ± 2.30	0.27 ± 0.20	17.75 ± 2.95
Female	38	4.00 ± 1.16	3.95 ± 0.97	3.87 ± 1.50	3.86 ± 0.98	0.33 ± 0.37	13.84 ± 2.81
p-value	0.013	0.234	0.275	0.671	0.583	0.003	

The findings in our study shows majority of the cases were in age group <40 (51.6%) and female (61.3%) in accordance with the previously known studies that TED commonly occurred in female, age before forty.⁶ Previous study shows that the thickness of the extraocular

muscles increases up to the middle age, then it starts decreasing, there was slight difference between the genders as males have thicker muscle than females.⁷

There were significant differences between baseline data for the LR thickness and UCVA in age group, and IR thickness and intraocular pressure (IOP) in gender group. This study shows females have thinner IR and in accordance with the previous studies shown that females have thinner IR than males. [7] The IOP difference in gender group in our study shows that males have higher IOP contrary to previous study that stated females have higher IOP than males.⁸ This result can be caused by the geographical difference of the population that was sampled.⁹

Table 3. Comparative Analysis Baseline and After IVMP Pulse Therapy

Parameters	Mean		Mean Δ	P-value
	Pre IVMP	Post IVMP		
UCVA	0.28 \pm 0.29	0.246 \pm 0.292	-0.08 \pm 0.34	p=0.206
IOP	15.01 \pm 3.33	15.53 \pm 4.71	0.51 \pm 4.48	p=0.369
IRMT	4.45 \pm 1.80	4.33 \pm 1.67	-0.18 \pm 1.69	p=0.381
MRMT	4.14 \pm 1.57	3.80 \pm 1.22	-0.34 \pm 1.68	p=0.116
SRMT	4.12 \pm 2.20	3.70 \pm 1.54	-0.47 \pm 1.84	p=0.046
LRMT	3.93 \pm 1.61	3.61 \pm 1.57	-0.33 \pm 1.94	p=0.188

Table 4. Association and Correlation of Age Group, Gender, and Lab Group in IV MP Pulse Therapy Results

	Δ IR	Δ MR	Δ SR	Δ LR	Δ UCVA	Δ IOP
Age	0.015	-0.148	0.019	-0.49	0.392	0.266
p-value	0.906	0.250	0.882	0.051	0.029	0.149
Gender	0.156	0.290	-0.066	0.195	0.124	0.075
p-value	0.225	0.022	0.612	0.293	0.507	0.689
Lab Group	0.112	0.082	-0.105	-0.005	0.156	0.169
p-value	0.388	0.527	0.418	0.968	0.401	0.364

Comparative analysis shows no significant differences between UCVA and IOP before and after treatment procedures. Even though the results showed a slight increase of UCVA and IOP meaning the visual acuity benefit and IOP side effects were low. We analyse the delta extraocular muscle thickness, UCVA, and IOP with each sub-groups to find eta association and correlation significance and found delta UCVA showed weak association and was significantly correlate in age group. Another parameter that showed weak association was Δ MR in gender group while other parameters revealed no significant results.

DISCUSSION

TED leads to extraocular muscle oedema, which can restrict motility and cause diplopia. Increased orbital fat and immune cells infiltration increase the volume of orbital soft tissue,

leading to venous congestion and proptosis. Worsening congestion can compress the optic nerve, leading to neuropathy and permanent vision loss. Elevated orbital pressure can lead to forward protrusion of the eye, known as exophthalmos.¹¹ IVMP is the well choice of the treatment due to its anti-inflammatory and immunosuppressive actions.^{1,12}

Δ SR muscle thickness were significantly decreased, while Δ IR, Δ MR, and Δ LR were not, this supported previous study that stated SR muscle thickness were more significantly decreased than other rectus muscles thickness after IVMP therapy.¹³

IOP were not significantly differ before and after the therapy even though previous study stated that IVMP could result in the increase IOP of both eyes.¹⁴ UCVA tend to increase but not significantly in this study. Previous study reported that patients that were treated with IVMP had significant improvement in the quality of life related to the vision or any alteration of the vision¹⁵, therefore the side effect of this research is guarded.

There were 5 cases (8.06%) of high IOP (>20 mmHg) after IVMP therapy, however 4 out of 5 patients had already high baseline data and only one patient (1.67%) had elevated IOP due to the side effect of IVMP. All patients with high IOP then referred to glaucoma subdivision and received glaucoma medication according to the standard operational procedures. Previous study reported that side effects of high dose IVMP were acute liver damage, cardiac and cerebrovascular events. Other side effects include osteoporosis, avascular necrosis, hyperglycaemia, cardiovascular disease, Cushing's syndrome, secondary adrenal insufficiency, and susceptibility to infections.¹⁰

Limitations of this study were the lack of data about the severity TED based on European Group of Grave's Orbitopathy (EUGOGO) or CAS score and the duration hyperthyroidism in subjects, therefore we could not analyse data in further details.

CONCLUSION

The treatment of high dose intravenous methyl prednisolone is effective in reducing rectus muscles thickness in Thyroid Eye Disease (TED) patients with minimal side effects. Further study is recommended to investigate the effect of IVMP therapy on TED severity group.

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