TWELVE WEEKS TREATMENT OUTCOME OF OMEGA-3 FATTY ACID IN COMPUTER VISION SYNDROME DRY EYE: AN OPEN LABEL, RANDOMIZED, CONTROLLED PILOT STUDY

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ABSTRACT

BACKGROUND
The incidence of Computer Vision Syndrome Dry Eye is on an increase. This study was targeted to evaluate the effect of Omega 3 Fatty Acids on this particular segment of population.

METHODS
A prospective, open label, randomized controlled trial was conducted on 67 male professional computer users aged 25-45 years who used computer for 8-10 hours a day. All the patients were subjected to OSDI questionnaire and patients with moderate-to-severe Dry Eye were included in the study. They were clinically monitored by TBUT, Rose Bengal Staining and Schirmer’s Test with an anaesthesia on Day 1 and after 12 weeks of treatment. The patients were randomly divided into two groups. Group 1 (Prescribed only lubricant drops) consisted of 33 patients. Group 2 (Prescribed lubricant drops along with commercially available Omega 3 fatty acids with EPA 180 mg and DHA 120 mg 2 capsules a day for twelve weeks) consisted of 34 patients.

RESULTS
Statistical Software SPSS 21.0 was used to analyse the results. In Group 1, the mean OSDI, TBUT, RBS, Schirmer’s Test parameters before treatment were 32.42 5.52, 6.25 1.32, 3.72 2.47, 6.03 1.40 and after treatment were 28.38 5.81, 7.06 2.03, 4.22 2.43, 5.62 1.58 and after treatment were 14.76 6.59, 9.12 1.47, 0.88 1.04, 9.15 1.65 respectively. Whereas in Group 2 before treatment they were 33.09 5.89, 5.26 1.56, 4.24 2.43, 5.62 1.58 and after treatment were 30.73 5.78, 7.06 2.03, 3.22 2.34, 5.63 1.61 respectively.

CONCLUSION
The comparison of the scores of two Groups revealed an undeniably positive role of Omega 3 Fatty Acids in Dry Eye of Computer Vision Syndrome.

KEYWORDS
Dry Eye, Computer Vision Syndrome, Omega 3 Fatty Acids.


INTRODUCTION
The incidence of dry eye is as high as 90% in persons using computer for only 3 hrs. a day for a year.1,2 The magnitude of the problem is going to increase by leaps and bounds as our requirement for the use of computers has no limits. Dry eye has far reaching effects on our lifestyle.

A number of studies have made it abundantly clear, now that inflammation and disorder of immune system are the root causes responsible for reduction in tear secretion.3,4,5,6 It is not only the quantity of tear secretion, but also abnormalities of its quality that are responsible for the symptoms of dry eye.7,8 Thus, we need a strategy that should maintain the inflammatory and immune status of the ocular surface apart from maintaining the trilaminar lubrication barrier; its volume, stability and chemical composition, i.e. maintain and repair the ocular surface round the clock without any untoward side effects.

Lubricants, our mainstay of treatment for Dry Eye with their short duration of action cannot prevent and halt the progress of the disease. Omega 3 fatty acids (PUFA Fatty Acids) with their anti-inflammatory, immuno-modulator and anti-apoptotic properties can be of great help in addressing this problem.9,10

Mechanism of action of EPA (Essential Fatty Acids) is better understood by their interactions (Figure 1).11,12,13 Short chain EPA-Omega6, Linoleic Acid) and Omega 3 (Alpha linolenic acid) with the help of enzymes desaturase and elongase are converted to Long Chain Fatty Acids, AA-Arachidonic Acid, GLA-Gamma linolenic acid, DGLA-Dihomo-GLA, EPA-Eicosapentaenoic Acid, DHA- Docosahexaenoic Acid which are further converted to eicosanoids (PG-Prostaglandins, PGI-Prostacyclins, TX-Thromboxane by the enzyme Cyclooxygenase and LT-Leukotrienes by the enzyme15-Lipoxygenase). Eicosanoids of AA (PGE 2, LT-B4) result in pain and inflammation and act as messengers for the immune system to protect the body from further damage. Once the message is conveyed the messengers are turned off by
Eicosanoids from GLA, EPA and DHA (PGE 1, PG1 3 and LT-B5) that are less inflammatory, inert or anti-inflammatory. Less dietary intake of GLA, EPA and DHA leads to chronic inflammation. This inflammation can also be ameliorated by stepping up the intake of these fatty acids, which interact with AA at 3 levels.14

1. Displacement – Increased dietary intake of omega 3 displace LA and thereby AA.
2. Competitive inhibition – EPA and DGLA compete for COX and LOX, thereby reducing the output of AA eicosanoids.
3. Counteraction – DGLA and EPA derived eicosanoids directly counteract their AA derived counterparts.

**Fig. 1: Mechanism of Action**

EFA-Essential Fatty Acids, LA-Linoleic Acid, ALA-Alpha Linolenic Acid, AA-Arachidonic Acid, GLA-Gamma Linolenic Acid, DGLA-Dihomo-GLA, EPA-Eicosapentaenoic Acid, DHA-Docosahexaenoic Acid, COX-Cyclooxygenase, LOX-Lipoxygenase, PG-Prostaglandins, PGI-Prostacyclins, TX-Thromboxane, LT-Leukotrienes.

Apart from Eicosanoid dependent mechanism, EFA also affects cellular signalling by making lipid rafts and altering gene expression by their effect on transcription factor and blockage of TNF α (Tumour Necrosis Factor), IL (Interleukin) and LT (Leukotrienes), which is responsible for improved lacrimal secretion (Figure 2).15,16

**Fig. 2: Mechanism of Action**

*EFA-Essential Fatty Acids, NF-kB-Transcription Factor, TNF-Tumour Necrosis Factor, IL-Interleukin, LT-Leukotrienes*

### RESULTS

A total of 67 men with computer vision syndrome were studied for the efficacy of Omega 3 Fatty Acids prescribed for 12 weeks. All the patients abided by the requirement of our study except for 1 from the control group who was lost for follow-up. Thus, Group 1 and Group 2 consisted of 32 and 34 patients respectively.

The mean age of the patients of the control group, i.e. Group 1 was 35.6 years and treatment group i.e. Group 2 was 35.8 years which was comparable.
All the patients filled OSDI questionnaire before and after twelve weeks of treatment and objective parameters studied for efficacy of treatment were TBUT, Rose Bengal Staining and Schirmer I Test with anaesthesia.

The Statistical Analysis was performed using SPSS Software 21.0 version. Paired 't' test was used to compare the pre- and post-treatment values, which are statistically significantly different in both the groups as shown in Table 1. We have also compared the change in the response parameters in the two groups. This has also been found to be statistically significantly different.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>N</th>
<th>Pre-Treatment</th>
<th>Post-Treatment</th>
<th>Change in Mean</th>
<th>Paired t</th>
<th>p</th>
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<tbody>
<tr>
<td>OSDI</td>
<td>1</td>
<td>32</td>
<td>32.42±5.52</td>
<td>28.38±5.81</td>
<td>4.04</td>
<td>19.40</td>
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<td>2</td>
<td>34</td>
<td>33.09±5.89</td>
<td>14.76±6.59</td>
<td>18.33</td>
<td>36.96</td>
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<td>TBUT</td>
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<td>32</td>
<td>6.25±1.32</td>
<td>7.06±2.03</td>
<td>0.81</td>
<td>4.60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>34</td>
<td>5.26±1.56</td>
<td>9.12±1.47</td>
<td>3.86</td>
<td>32.00</td>
<td></td>
</tr>
<tr>
<td>RBS</td>
<td>1</td>
<td>32</td>
<td>3.72±2.47</td>
<td>3.22±2.34</td>
<td>0.5</td>
<td>5.57</td>
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<tr>
<td></td>
<td>2</td>
<td>34</td>
<td>4.24±2.43</td>
<td>0.88±1.04</td>
<td>3.36</td>
<td>10.82</td>
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<tr>
<td>ST</td>
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<td>32</td>
<td>6.03±1.40</td>
<td>6.53±1.61</td>
<td>0.5</td>
<td>4.98</td>
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<tr>
<td></td>
<td>2</td>
<td>34</td>
<td>5.62±1.58</td>
<td>9.15±1.65</td>
<td>3.53</td>
<td>23.89</td>
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</tr>
</tbody>
</table>

**Table 1: Master Table showing Change of Values for All the Parameters**

OSDI questionnaire revealed a change in the mean score of 18.33±2.89 in Group 2 as compared to 4.04±1.18 in Group 1 (Table 2), as reported by the patients. It is very highly statistically significant (p<0.001). This implies that treatment protocol in both the groups reduced the symptom severity, but the advantage gained in Group 2 is statistically significantly higher as compared to Group 1.

<table>
<thead>
<tr>
<th>OSDI</th>
<th>N</th>
<th>Change in Mean</th>
<th>SD</th>
<th>Mean Difference</th>
<th>95% Confidence Interval of the Difference</th>
<th>t</th>
<th>p</th>
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<td></td>
<td></td>
<td></td>
<td>Lower</td>
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</tr>
<tr>
<td>Group 1</td>
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<td>4.04</td>
<td>1.18</td>
<td>14.28</td>
<td>13.19</td>
<td>25.99</td>
<td>0.000</td>
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<tr>
<td>Group 2</td>
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<td>18.32</td>
<td>2.89</td>
<td></td>
<td>15.38</td>
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</tbody>
</table>

**Table 2: Comparison of Change in OSDI Score**

Similar outcome was observed in analysis of objective parameters.

TBUT showed a mean change of 3.86±.70 in Group 2 (Table 3) as compared to a mean change of .81±.99 in Group 1. This again was statistically significant (p<0.001).

Mean change in RBS Score was 3.36±1.80 in Group 2 (Table 4) and .5±.51 in Group 1, which is also very highly significant in Group 2 (p<.001).

<table>
<thead>
<tr>
<th>TBUT</th>
<th>N</th>
<th>Change in Mean</th>
<th>SD</th>
<th>Mean Difference</th>
<th>95% Confidence Interval of the Difference</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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<td></td>
<td>Lower</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>32</td>
<td>0.81</td>
<td>.99</td>
<td>3.04</td>
<td>2.62</td>
<td>14.38</td>
<td>0.000</td>
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<td>Group 2</td>
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<td>3.85</td>
<td>.70</td>
<td></td>
<td>3.46</td>
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</tbody>
</table>

**Table 3: Comparison of Change In TBUT**

Schirmer Test values showed a mean change of 3.53±.86 mm in Group 2 (Table 5) and 0.5±.57 mm in Group 1 with a highly significant p value of <0.001.

<table>
<thead>
<tr>
<th>ST</th>
<th>N</th>
<th>Change in Mean</th>
<th>SD</th>
<th>Mean Difference</th>
<th>95% Confidence Interval of the Difference</th>
<th>t</th>
<th>p</th>
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<td></td>
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<td></td>
<td>Lower</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>32</td>
<td>0.50</td>
<td>.57</td>
<td>3.03</td>
<td>2.67</td>
<td>16.76</td>
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<tr>
<td>Group 2</td>
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<td>3.53</td>
<td>.86</td>
<td></td>
<td>3.39</td>
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</tbody>
</table>

**Table 5: Comparison of Change in Schirmer’s Test Values**
DISCUSSION
DEWStudy has demonstrated how dry eye limits and degrades visual performance including the conduct of common vision-related daily activities; apart from causing repetitive strain disorder and profound ocular morbidity. We have not yet found the optimum treatment options for different types and severity of the disease. A serious effort needs to be done to treat it at war footing.

Promising results are pouring in regarding the role of Omega-3 fatty acids in dry eye of different aetiologies. Although, it is not yet clear whether it works best on aqueous tear deficiency dry eye or lipid tear deficiency dry eye. However, it is amply clear that Omega 3 fatty acids have a softening role on inflammation of the ocular surface and immune-modulator properties, which may be responsible for improved tear production and its stability. EFAs are important constituents of cell membranes and influence the behaviour of membrane bound enzymes and receptors. Therefore, the membrane fatty acid composition can affect cell and organ functions.

To consolidate this hypothesis, the role of Omega-3 fatty acids in ever increasing aetiology of dry eye, i.e. Computer Vision Syndrome was studied.

Miller et al recommended an MCID (Minimum Clinically Important Difference) of 7.0 to 9.9 for all OSDI categories (4.5 to 7.3 for mild or moderate disease and from 7.3 to 13.4 for severe disease). A significant improvement in OSDI Scores in our study was found to be very encouraging. A mean difference of 18.33 in Group 2 in pre- and post-treatment scores was higher than MCID. This was statistically as well as clinically significant. It is also demonstrated by Kangari et al who found a difference of 9.4 in OSDI scores after 1-month treatment. A difference in the mean score in Group 1 was only 4.04, which is even lesser than the lowest value of MCID. An improvement in subjective and objective parameters has also been reported by a number of researchers in different aetiologies of Dry Eye. To consolidate this hypothesis, the role of Omega-3 fatty acids in dry eye of different aetiologies of Dry Eye.

This difference in subjective scores also reflected in objective tests.

TBUT showed a drift towards normal values with a mean of 9.12 sec. and a change in mean of 3.86 sec. Bhargava R. et al demonstrated a change in mean of 3.3 sec after 3 months treatment (325EPA+125DHA), Kangari et al demonstrated a change in mean of 1.7 sec after only a month’s treatment. Although supplementation duration and its quantity varies in these studies, but there is a definite agreement about the beneficial effect of Omega 3 on this parameter. In Group 1, a change in mean was .81, which was hardly a deviation from baseline value as compared to Group 2.

A significant change in Rose Bengal Staining indicates a healthier ocular surface. A change in mean of 3.36 was highly significant (p <.001). A statistically significant relation was also found by Bhargava et al.

A very significant change mean Schirmer values of 4.2 was found by Wojtowicz et al [Fish oil (EPA 450+DHA300) + flaxseed oil 1000 mg for 3 months], whereas a very insignificant change in mean of .62 was found by Bhargava et al. Although, Schirmer test is an unreliable indicator of tear secretion, but in this study the mean change in Schirmer of 3.53 (p <.001) was commensurate with the changes in other indicators.

REFERENCES