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EFFECT OF OMEGA-3 FATTY ACIDS TREATMENT ON INSULIN RESISTANCE

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Abstract

Background and aims*: Insulin resistance (IR) is a common pathogenic factor of several diseases: diabetes mellitus, the metabolic syndrome, arterial hypertension, atherosclerosis, dyslipidemia, etc. There are many therapeutic factors involved in decreasing IR. Among them we mention metformin, pioglitazone, physical activity, weight loss, diet, etc. In the last decade, there are more observations of the influence of poly-unsaturated fatty acids on IR. The most powerful seem to be omega-3 fatty acids. In our study, we wanted to asses if the administration of omega-3 fatty acids is involved in modifying IR.* ***Materials and methods****: We evaluated 126 diabetic patients with IR from January 2011 until July 2014. The study was open-label and non-randomized. For the determination of IR we used the HOMA-IR method.* ***Results:*** *For both males and females there was a regression of HOMA-IR during the 4 weeks of treatment with omega-3 and also after 2 weeks after stopping the administration of these fatty acids. The decrease of HOMA-IR was statistically significant ($p<0.05$). The statistic result observed in the next 2 weeks after stopping administration of omega-3 was also significant ($p<0.05$).* ***Conclusion****: The results of the study showed that the omega-3 fatty acids can reduce IR. The greater the IR, the smaller the results for the same dose of omega-3. The effect of these fatty acids on IR continues after the end of treatment.*

key words: *insulin resistance, metabolic syndrome, omega-3 fatty acids*

Background and aims

Nowadays, insulin resistance represents one of the most dangerous biological aspects of health deterioration [1,2]. IR is the common starting point of different syndromes that can modify the normality of the biological status [3,4]. Among these, we stress on the metabolic syndrome, dyslipidemia, acute coronary syndrome, hypertension, diabetes mellitus, some hereditary metabolic diseases, etc.

In fact, IR alters the entire organism in different ways. Some diseases associated with IR can be present in the same time. For example, hypertension can be associated either with the metabolic syndrome, dyslipidemia or acute coronary syndrome. The more diseases that are associated, the greater the risk of morbidity and mortality.

Sometimes a single disease induced by IR is enough to lead to serious complications (including death) [5]. This is why, in the present,

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in our clinic we use many medications to reduce the intensity of IR: metformin, pioglitazone, fenofibrate, insulin, Ringer solutions, etc. [6]. In the same time, if the patient is able to have physical activity, we must encourage him to increase it, up to the point it doesn't damage his health.

Some authors consider that the reduction of IR could prevent or at least delay the decline of cognitive functions [7,8]. This is a good point for having in attention the methods that could reduce IR as possible interventions for the prevention of Alzheimer's disease [9-11].

In that context, the fact that in the specialized literature there are several reports that in communities that use a diet rich in fish-oil (from ocean fish) IR is in general on a lower level than in normal conditions made us take into consideration that some components from fish-oil could be useful in reducing IR [12].

There are some data suggesting that omega-3 fatty acids could be involved in the mechanism of reducing IR [13,14]. Or study was aimed to clarify if administration of omega-3 fatty acids could induce a decline in IR or not.

Materials and methods

Our study was carried out on 126 diabetic and non-dislypidemic patients treated only with diet, with IR, admitted in the metabolic emergency department of "Prof. N.C. Paulescu" National Institute of Diabetes, Nutrition and Metabolic Diseases, Bucharest, from January 2011 till July 2014. Most of the subjects were female (74), the rest of the subjects being males (52). The mean age was 52 ± 12 years. The mean BMI of the female group was 32.4 ± 4 kg/m^2 and for the male group 29.9 ± 5 kg/m^2 ($p<0.05$). None of these subjects had any other co-morbidities. All the patients had the same level of physical activity and approximately a similar diet. No other medication was given in the period in which the study was conducted, other than the omega-3 fatty acids.

For every patient we determined IR using the HOMA-IR method. This one was calculated using the formula: basal insulinemia (μU/mL) x FPG (mg/dl)/405.

We separated the study group in 5 subgroups based on their BMI. For the females, the 5 subgroups were: 25.5-27.9 kg/m^2, 28-29.9 kg/m^2, 30-31.9 kg/m^2, 32-33.9 kg/m^2, 34-36 kg/m^2, respectively for the males: 25-26.9 kg/m^2, 27-29.9kg/m^2, 30-30.9 kg/m^2, 31-32.9 kg/m^2, 33-35 kg/m^2.

To all these patients we administered 4 g of omega-3 fatty acids per day, for a period of four weeks. We monitored the level of HOMA-IR every week.

For both males and females we compared the values of mean HOMA-IR from a week to another, for every category of BMI. We stress that IR was also determined in some subjects after two weeks from stopping the administration of omega-3 fatty acids.

Statistical analysis: Statistical analysis was performed on patients that completed the study using IBM SPSS v20 software. Comparisons between groups were performed using ANOVA parametric (Tukey test). Data were considered significant if $p<0.05$. Results are given as mean ± standard deviation.

Table 1. HOMA-IR reduction from one week to another for different categories of BMI in women.

BMI (kg/m^2)	Initial	Week1	Week 2	Week 3	Week 4
34 - 36	4.8 ± 1.36	4.7±1.4	4.2±1.38	4.0±1.41	3.9±1.39
32 - 33.9	4.4 ± 1.5	4.1±1.58	3.7±1.49	3.3±1.53	3.05±1.48
30 – 31.9	4.0 ± 1.4	3.7±1.46	3.5±1.51	3.1±1.43	2.8±1.4
28 - 29.9	3.6 ± 1.4	3.4±1.41	3.1±1.48	2.7±1.47	2.3±1.37
25.5 -27.9	3.2 ± 1.5	3.0 ± 1.49	2.7 ± 1.37	2.3 ± 1.52	2.0 ± 1.46

Results

Progression of IR (expressed by HOMA-IR) during the 4 weeks of omega-r fatty acid treatment for every category of BMI in females and in males is given in Tables 1 and 2.

Table 2. HOMA-IR reduction from one week to another for different categories of BMI in men.

BMI (kg/m^2)	Initial	Week1	Week 2	Week 3	Week 4
33 - 35	4.7 ± 1.5	4.5 ± 1.48	4.3 ± 1.51	4.0 ± 1.39	3.7 ± 1.38
31 - 32.9	4.3 ± 1.6	3.9 ± 1.53	3.6 ± 1.5	3.1 ± 1.46	2.7 ± 1.49
30 – 30.9	3.9 ± 1.54	3.4 ± 1.48	2.9 ± 1.5	2.5 ± 1.49	2.1 ± 1.36
27 - 29.9	3.6 ± 1.5	3.05 ± 1.37	2.6 ± 1.52	2.2 ± 1.4	1.8 ± 1.51
25 – 26.9	3.2 ± 1.6	2.7 ± 1.42	2.4 ± 1.35	2.05 ± 1.39	1.7 ± 1.47

Table 3. HOMA-IR in the next 2 weeks after stopping treatment with omega-3 in different categories of BMI in women.

BMI (kg/m^2)	Week 4	Week 5	Week 6
34 - 36	3.9 ± 1.39	3.85 ± 1.34	3.8 ± 1.35
32 – 33.9	3.05 ± 1.48	3.0 ± 1.45	3.0 ± 1.42
30 – 31.9	2.8 ± 1.4	2.7 ± 1.3	2.65 ± 1.35
28 – 29.9	2.3 ± 1.37	2.2 ± 1.34	2.15 ± 1.34
25.5 – 27.9	2.0 ± 1.46	1.9 ± 1.44	1.9 ± 1.44

Table 4. HOMA-IR in the next 2 weeks after stopping treatment with omega-3 in different categories of BMI in men.

BMI (kg/m^2)	Week 4	Week 5	Week 6
33 - 35	3.7 ± 1.38	3.65 ± 1.37	3.6 ± 1.36
31 – 32.9	2.7 ± 1.49	2.6 ± 1.5	2.55 ± 1.48
30 – 30.9	2.1 ± 1.36	2.05 ± 1.34	2.0 ± 1.32
27 – 29.9	1.8 ± 1.51	1.75 ± 1.49	1.7 ± 1.47
25 – 26.9	1.7 ± 1.47	1.68 ± 1.45	1.65 ± 1.43

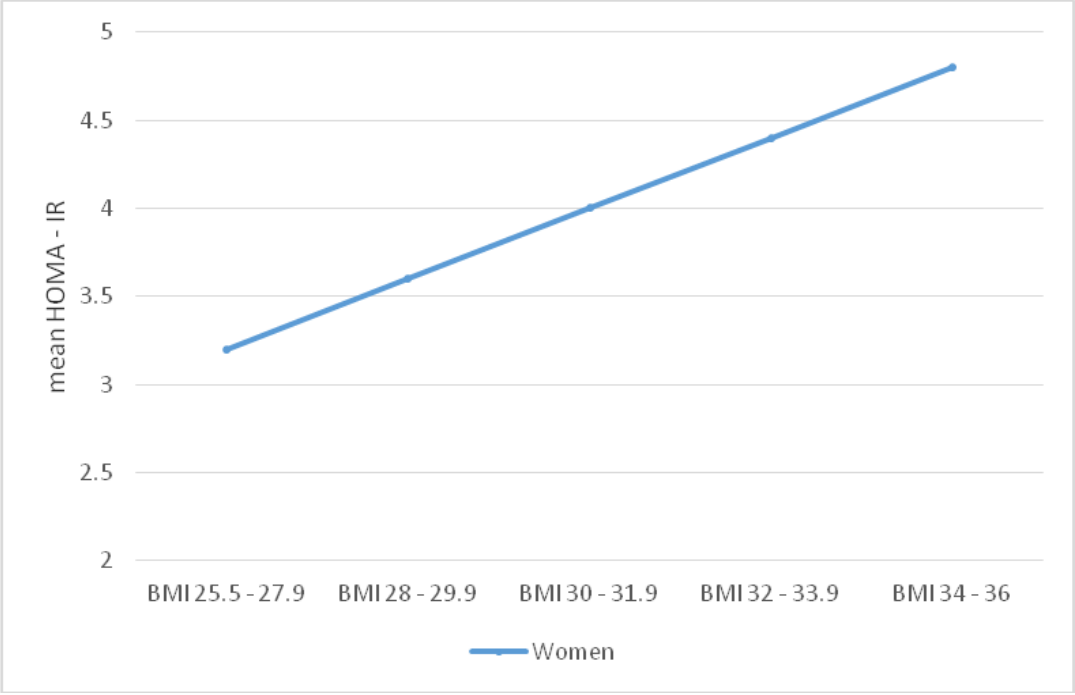

Figure 1. *Initial mean HOMA-IR according to BMI in the 5 female subgroups.*

In Tables 3 and 4 we see the progression of IR during the 2 weeks after stopping the administration of omega-3 fatty acids.

If we compare the baseline HOMA-IR value according to BMI subgroup in males and females, we observe that there is a positive correlation between the corresponding values (Figs. 1 and 2). This is consistent with the results shown in the specialized literature. That is why one of the most important therapeutic methods to reduce IR is weight loss.

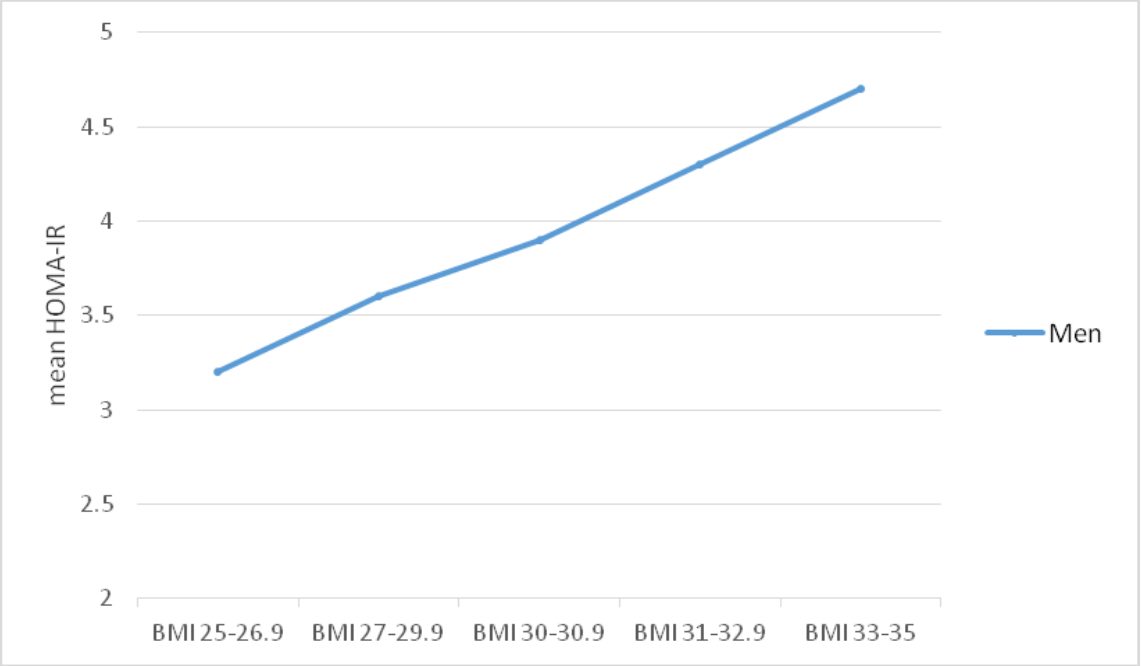

Figure 2. *Initial mean HOMA-IR according to BMI in the 5 male subgroups.*

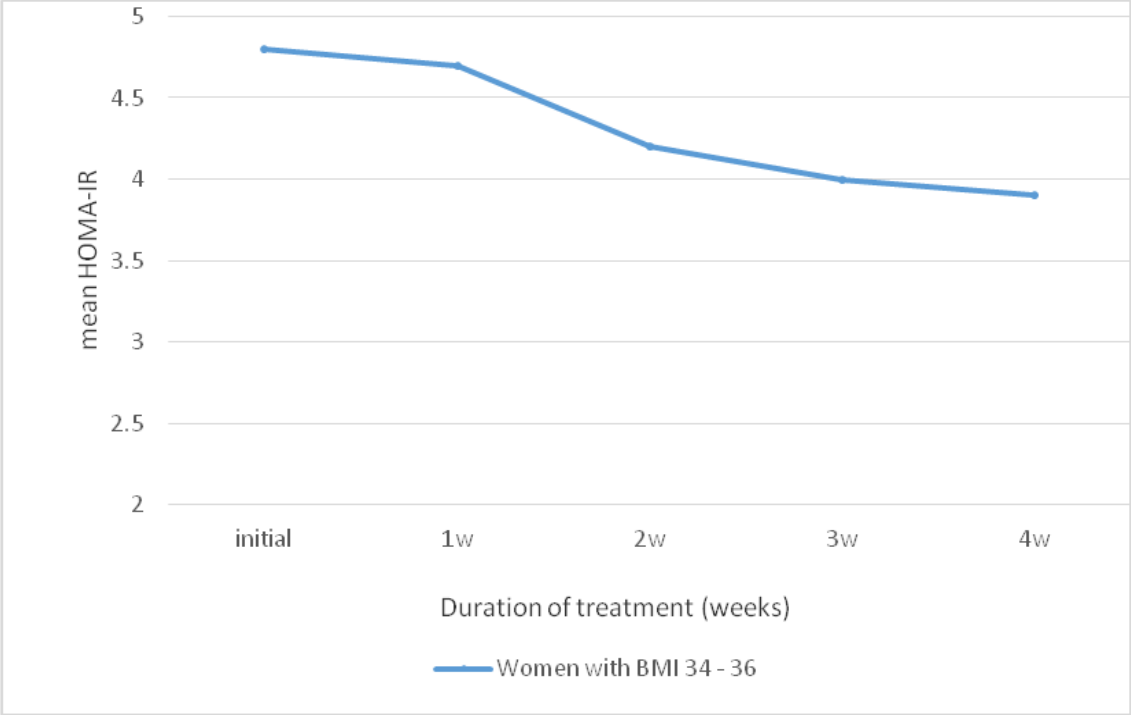

Figure 3. *Decrease in HOMA-IR in the female subgroup with BMI 34 – 36.*

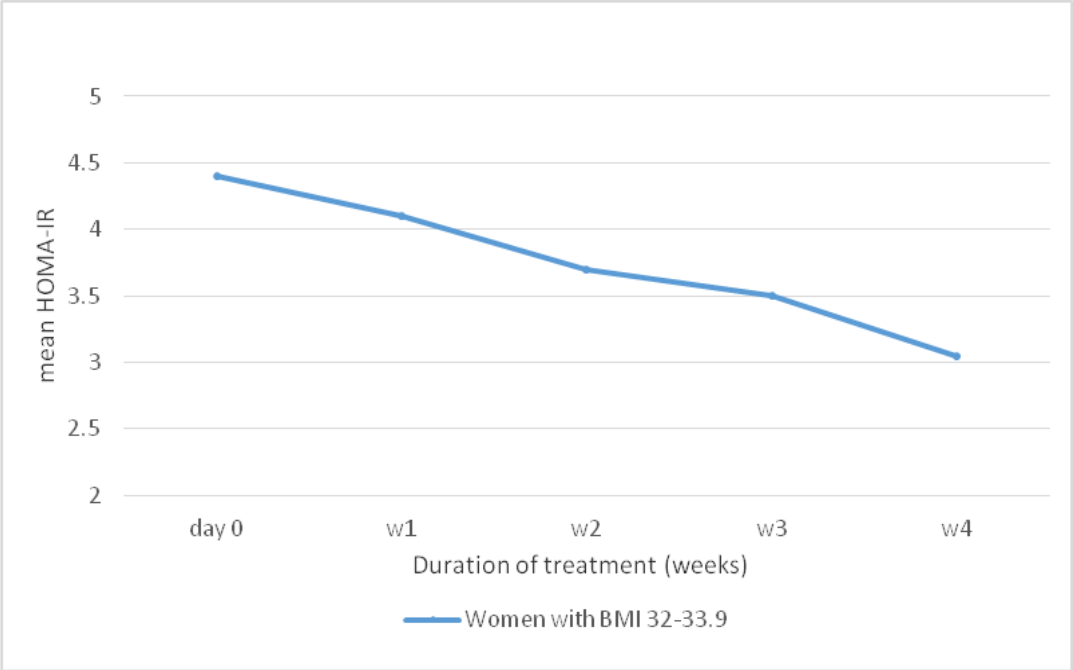

Figure 4. *Decrease in HOMA-IR in the female subgroup with BMI 32 – 33.9.*

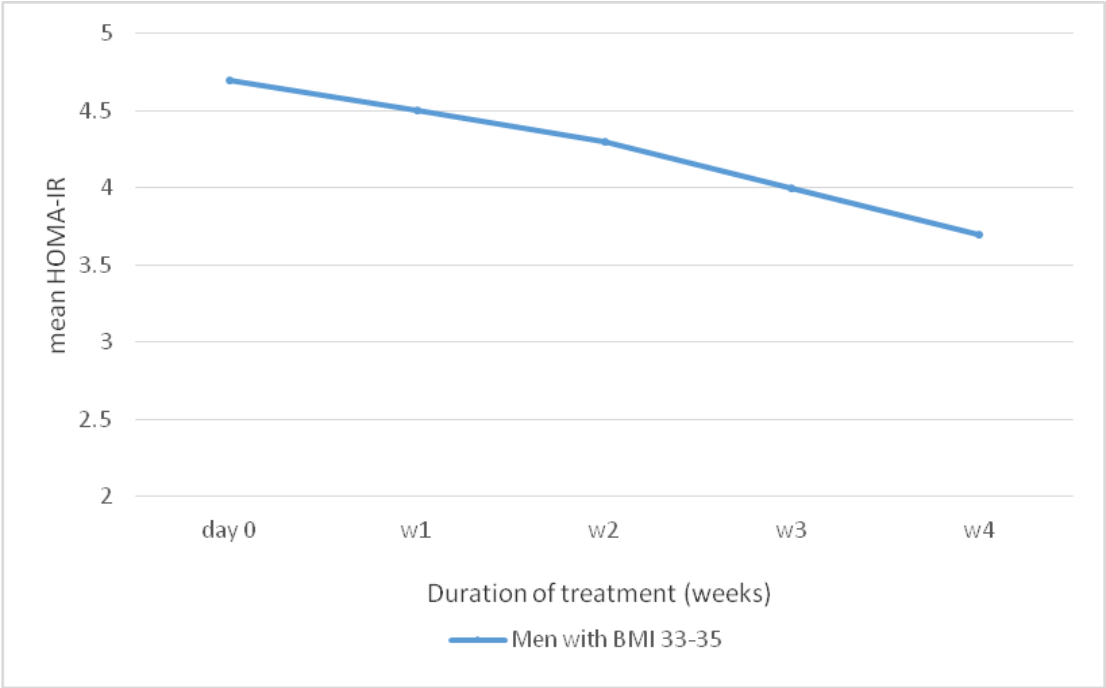

Figure 5. *Decrease of HOMA-IR in the male subgroup with BMI 33-35.*

Another observation was the fact that for every BMI subgroup, both in females and males, IR can be reduced with omega-3 fatty acids treatment. It is interesting that the greater BMI is, the less improvement of HOMA-IR can be observed, using the same quantity of omega-3 fatty acids. This is illustrated in Figs. 3 and 4 for females.

If we compare these two figures, one can notice that in Fig. 3 the decrease in IR from one week to another was of approximately 0.2 while in Fig. 4 this is about 0.3/week ($p<0.001$). The same observation was valid in the male group, as shown in Figs. 5 and 6.

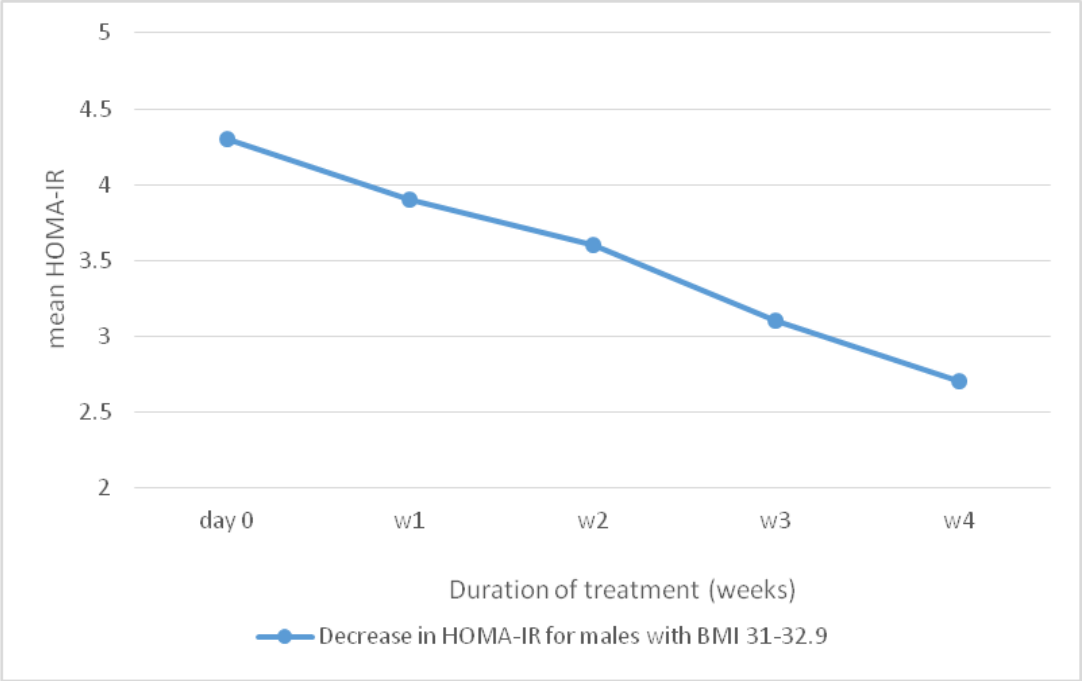

Figure 6. *Decrease of HOMA-IR for the male subgroup with BMI 31-32.9.*

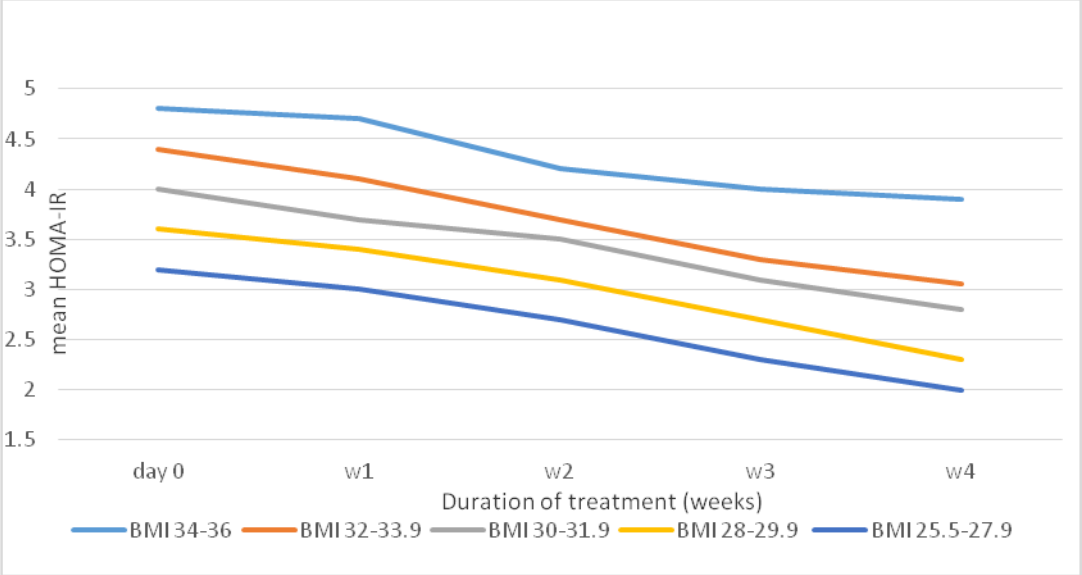

Figure 7. *Decrease of HOMA-IR for the female subgroups during the 4weeks of treatment.*

Analyzing Tables 1 and 2, it can be noticed that the degree of decrease in IR is influenced by BMI and not so evident by the sex of the analyzed subjects. We observed that with the same quantity of omega-3 fatty acids, the improvement of IR is different from a category of BMI to another. This is illustrated in Figs. 7 and 8.

Discussions

Our study showed it seems to be easier to obtain an improvement in IR with omega-3 fatty acids treatment when the patient is only overweight, than in the obese. The IR improvement decreased progressively with the rise of the obesity level, which is concordant with the results of other studies [12].

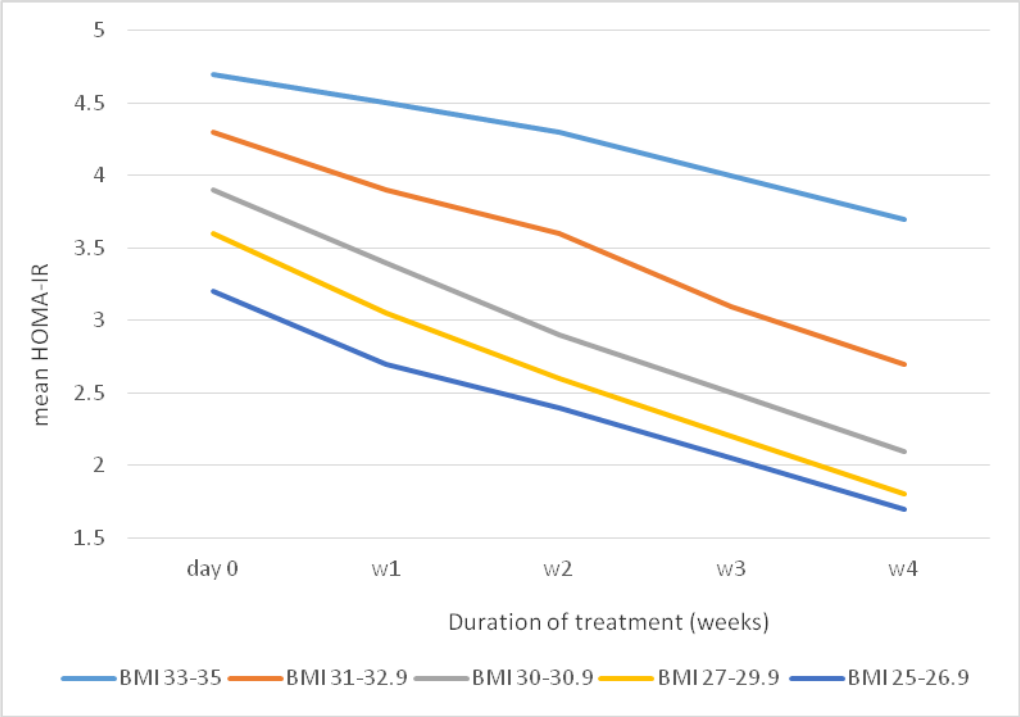

Figure 8. *Decrease of HOMA-IR for the male subgroups during the 4weeks of treatment.*

On the other hand, we observed that with 4 grams of omega-3 fatty acids, given to overweight subjects, the IR can decrease quite well, the HOMA-IR returning to near normal range. This is a very important aspect that can be used as a treatment tool for reducing the risk for hypertension, metabolic syndrome, acute coronary syndrome, dyslipidemia, diabetes mellitus and so on [2,3].

We must stress that the decrease in IR is not present only during the treatment with omega-3 fatty acids, but this phenomenon also continues at least 2 weeks after we cease their administration (as shown in Tables 3 and 4). For people who take omega-3 fatty acids on a long-term basis for various diseases (to activate the action of lipoprotein-lipase involved in reducing hypertriglyceridemia and indirectly in rising HDL-cholesterol; to improve spermatogenesis; to maintain skin beauty and elasticity), the incorporation of these unsaturated acids in the cell membranes makes it possible to have a long, efficient and complex effect on reducing IR. In contrast, those who do not take nutritive supplements with omega-3 fatty acids seem to be exposed to a greater risk of having an increased IR (and all the consequences which could derive from this phenomenon).

Taking into account this observation, we plan to start another study in which to adapt the dose of omega-3 fatty acids to match the degree of IR. We want to see if this can be possible and to evaluate its cost-efficiency. The last aspect is very important because not only overweight or obese people need to reduce their IR since this can sometimes be increased even in normal and underweight persons.

Normally, for the prophylaxis of the IR-dependent diseases, it is much cheaper to raise the level of physical activity. In certain circumstances when this is not a viable solution, we can use the beneficial effects of supplementary nutrients containing omega-3 fatty acids.

Conclusions

The results of this study indicate that treatment with omega-3 fatty acids can help a lot

of diabetic patients with IR since this reduced insulin sensibility predisposes to severe co-morbidities and mortality.

As expected, we confirmed that IR rises with the increase of BMI. So, to prevent a lot of diseases linked to IR like diabetes mellitus, metabolic syndrome, arterial hypertension, atherosclerosis, dyslipidemia and so on, we have to reduce the IR. Our study also showed that treatment with omega-3 fatty acids can decrease IR. The greater the BMI, the more difficult is to improve IR with the same quantity of poly-unsaturated fatty acids. After stopping of administration of omega-3 fatty acids, the decrease of IR is maintained for at least 2 weeks.

In conclusion, we consider that omega-3 fatty acids treatment represents a possible solution which can be added to the other methods used for decrease IR.

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