Evaluating the Role of Nutraceuticals in Primary Prevention

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ABSTRACT

Prevention has become a main factor in the management of cardiovascular diseases. There are many options to control the LDL-Cholesterol levels, which reduction has been widely proved to diminish cardiovascular events rate. Despite the many pharmacological options, an important percentage of the patients do not reach the control target. Among other factors, the available drugs present tolerance problems that limit their use, emerging the necessity to develop new options of treatment that combine efficacy and security. In this field arise the nutraceuticals, which may become an alternative, especially in primary prevention, where the necessity of LDL-cholesterol reduction is not so ambitious, and tolerance and security are essential to achieve the patient adherence to the treatment.

The objective of the study is to demonstrate that the new formulation of Lipok® (a nutraceutical based in red yeast rice and berberine) adapting the guidelines objective (116 mg/dL) where included. Security and effectiveness of adding Lipok® 6 months to the treatment was evaluated. We observed a statistically significant reduction in the TCH values (-34.3 mg/dL), LDL-C (-33.8 mg/dL) and triglycerides (-29.3 mg/dL) at 6 months’ treatment. No variation in the levels of HDL-C was observed. No relevant side effects were reported (constipation <2%, no myalgias). There were mild reductions (that even reached statistical significance) in creatinine, GPT and glycosylated hemoglobin. No patient discontinued treatment in the 6 months. NO patient discontinued the treatment during the study.

New formulation of Lipok® has proved to be effective in the control of the LDL-Cholesterol levels without relevant side effects. Considering the significant reduction shown in this study, it may become an alternative to other pharmacological treatments in the management of dyslipidaemia in primary prevention where adherence to the treatment is fundamental.

Keywords: Dyslipidaemias, nutraceuticals, primary prevention, red yeast rice.

I. INTRODUCTION

Prevention has become a key factor in managing cardiovascular diseases. Multiple studies conducted demonstrate the impact of controlling the risk factors in the development and evolution of cardiovascular disease and is therefore a matter of priority in patient treatment.

Within the controllable risk factors, there is no doubt that cholesterol is one of the major ones. There are multiple options for controlling the levels of LDL cholesterol in the blood, the reduction of which has proven to diminish the rate of cardiovascular events and consequently cardiovascular mortality [1].

However, despite the different drug options available,
there is an important percentage of patients who fall short of the control objectives, either in primary or in secondary prevention. Among other factors, the drugs available have tolerance problems in a significant percentage of patients [2]. This limits their use, especially of statins, which are undoubtedly the cornerstone in the treatment of dyslipidaemia.

In this context, the need arises for treatment options that provide efficacy and tolerance in achieving the ambitious control goals and thus prevent the emergence or evolution of cardiovascular disease.

Functional, or nutraceutical, foods are an alternative for certain patients, especially in primary prevention where the need to reduce LDL is not as high and tolerance and safety are fundamental in achieving patient loyalty to the treatment [3], [4].

Prominent within this group is red yeast rice and berberine. Social and healthcare interest in prevention has led to a clear increase in their use in recent years, and clinical practice guidelines recognize their growing importance among the available therapeutic options. In fact, the increasingly widespread use of red yeast rice, whose active ingredient is monacolin K, has led to European-wide standardization, limiting its concentration to 2.99 mg [5], [6].

II. STUDY OBJECTIVES

In order to comply with the new regulations and maintain its nutraceutical status, Lipok® has been reformulated by adjusting the total monacolin dosage and increasing the proportion of berberine.

The study’s goal is to demonstrate that the new formulation is efficacious in controlling the lipid profile, especially in the reduction of LDL cholesterol, in uncontrolled patients in primary prevention.

The secondary goal pursues confirming the product’s safety in this group of patients, where tolerance and treatment adherence are crucial.

III. MATERIAL AND METHOD

It is an observational prospective study. 97 patients were included, who met the inclusion criteria and were valid for the statistical analysis. We collected variables at the start, at 3 and at 6 months of treatment. It included patients in primary prevention (who had not presented any cardiovascular events at the time of inclusion) who presented LDL cholesterol levels above the objective set in the cardiovascular prevention guidelines (LDL≥116 mg/dL).

Using a set of analytical variables, we assessed the efficacy and safety of adding Lipok® to the treatment. We collected the emergence of secondary effects in these patients.

We proceeded to an analysis using the non-parametric Wilcoxon signed-rank test (WSR), set at a significance level of 95% (i.e., p-value < 0.05), to evaluate whether there is a significant difference after 3 and 6 months per monitored variable in average. All statistical tests were and performed with scipy1.7.3 library in Python3.8.

IV. RESULTS

We assessed the efficacy and safety of adding Lipok® to the treatment. Fig. 1 shows the results grouped in boxplots of the samples obtained from patients at each visit stratified by each of the monitored variables.

Total Cholesterol (TCH) values, HDL cholesterol (HDL-C), LDL cholesterol (LDL-C) and triglycerides (Trig) as well as the rest of the variables analyzed, basal, at 3 months and at 6 months, are shown in Table I.

We observed a statistically significant reduction in the TCH values (-34.3 mg/dL), LDL-C (-33.8 mg/dL) and triglycerides (-29.3 mg/dL) at 6 months’ treatment. No variation in the levels of HDL-C was observed (Fig. 1 and 2).

As for secondary effects, no myalgia was reported (constipation in <2%). There were mild reductions (that even reached statistical significance) in creatinine, GPT and glycosylated hemoglobin. No patient discontinued treatment in the 6 months.

V. DISCUSSION

While the importance of cholesterol control has always existed in secondary prevention (both for patients and for doctors), it has notably grown at societal level in recent years in patients in primary prevention. This awareness of the need for control comes up against the difficulty of finding drugs that are free of secondary effects (disease awareness clashes with the lack of symptoms and the refusal to initiate treatments that can certainly be uncomfortable). In this context, the use of nutraceuticals has gained in popularity given that they are free of any relevant secondary effects, are easier to accept by patients and more readily recommended by doctors. In regard to this increase in their consumption, European authorities have regulated the use of monacolins which, despite being sourced from a natural ingredient (red yeast rice), closely resemble lovastatin, which already exists as a drug. So in order to retain its denomination as a nutraceutical, the dosage has had to be adjusted, in this case to below 2.99 mg daily. In conducting this study, the aim was to confirm the efficacy of the Lipok® nutraceutical in the control of the lipid profile after adapting its concentration to this new regulation. The results of this study confirm its efficacy while maintaining its fundamental value, tolerance.

Fig. 1. Boxplots per variable at start, 3 and 6 months.
TABLE I: MEAN VALUE PER VARIABLE AT START, 3 AND 6 MONTHS. DECREMENT PERCENTAGE PER VARIABLE AFTER 3 AND 6 MONTHS SINCE THE BEGINNING

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean at start</th>
<th>Mean at 3m</th>
<th>Mean at 6m</th>
<th>% decrement at 3m</th>
<th>% decrement at 6m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chol</td>
<td>234.81</td>
<td>212.70*</td>
<td>200.42*</td>
<td>-9.41%</td>
<td>-14.65%</td>
</tr>
<tr>
<td>LDL-C</td>
<td>152.71</td>
<td>130.35*</td>
<td>118.89*</td>
<td>-14.64%</td>
<td>-22.15%</td>
</tr>
<tr>
<td>HDL-C</td>
<td>52.36</td>
<td>54.01</td>
<td>54.33</td>
<td>+3.15%</td>
<td>+3.77%</td>
</tr>
<tr>
<td>trigl</td>
<td>137.90</td>
<td>125.12*</td>
<td>108.56*</td>
<td>-9.26%</td>
<td>-21.28%</td>
</tr>
<tr>
<td>creat</td>
<td>1.01</td>
<td>0.89*</td>
<td>0.85*</td>
<td>-11.05%</td>
<td>-15.25%</td>
</tr>
<tr>
<td>gluc</td>
<td>96.86</td>
<td>94.88</td>
<td>93.18</td>
<td>-2.05%</td>
<td>-3.80%</td>
</tr>
<tr>
<td>gpt</td>
<td>27.10</td>
<td>24.40*</td>
<td>24.33*</td>
<td>-9.97%</td>
<td>-9.93%</td>
</tr>
<tr>
<td>Hb1ac</td>
<td>5.84</td>
<td>5.77*</td>
<td>5.69*</td>
<td>-1.16%</td>
<td>-2.59%</td>
</tr>
</tbody>
</table>

*WSR significance at level .05 (p-value<.05)

VI. LIMITATIONS OF THE STUDY
Although the cholesterol reduction obtained is greatly consistent in all patients, the discrete n sample of the study and the non-randomization of the sample limit the mainstreaming of the conclusions.

VII. CONCLUSION
The new Lipok® formulation adjusted to the monacolin levels (2.99 mg) of the new European regulations, in which the proportion of berberine has been increased, is efficacious in reducing LDL cholesterol without presenting any significant secondary effects. Given the considerable reduction shown in the study, it can represent an alternative to other drug treatments in primary prevention where adherence to treatment is crucial given the lower perception of cardiovascular risk they present (primary prevention).

CONFLICT OF INTEREST
Authors declare that they do not have any conflict of interest.

REFERENCES