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CLINICAL REPORT

Usefulness of compounds with monacolin K in a case of statins intolerance

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Abstract Many patients with familial hypercholesterolaemia (FH) or in secondary prevention situations and with statin intolerance do not achieve LDL-C targets, and require treatment with PCSK9 inhibitors (iPCSK9) and ezetimibe. The case is presented on a patient with FH and total intolerance to statins. Treatment with iPCSK9 and ezetimibe failed to achieve her LDL-C target. A compound with red yeast rice derivatives containing 3 mg of monacolin K was added, with good therapeutic compliance, and a very good control of LDL-C. The addition of red yeast rice derivatives containing low doses of monacolin K, together with IPCSK9 in patients with total intolerance to statins, may open a new path to obtain LDL-C targets in patients with high/very high cardiovascular risk.

PALABRAS CLAVE
Inhibidores de PCSK9;
Monacolina K;
Intolerancia a las estatinas

Utilidad de los compuestos con monacolina K en un caso de intolerancia a estatinas

Resumen Muchos pacientes con hipercolesterolemia familiar (HF) o en situaciones de prevención secundaria con intolerancia a estatinas no logran objetivos a pesar del tratamiento con inhibidores de PCSK9 (iPCSK9) y ezetimiba. Presentamos el caso de un paciente con HF e intolerancia total a las estatinas. El tratamiento con iPCSK9 y ezetimiba no logró el objetivo lipídico. Se añadió un compuesto derivado de la levadura roja del arroz, que contenía 3 mg de monacolina K con una excelente tolerancia, lográndose un muy buen control de los objetivos de cLDL. La suma al tratamiento de IPCSK9 de un compuesto derivado de la levadura roja del arroz, con bajas dosis de monacolina K, abre una nueva puerta para lograr los objetivos de cLDL en pacientes de muy alto riesgo cardiovascular.

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Introduction

Variable doses of statins with diverse intensity are the first step in the treatment of hypercholesterolemia. Ezetimibe in addition to statins represents a second step in the approach of LDL-cholesterol (LDL-C) reduction. PCSK9 inhibitors, a new therapeutic group, allows additional declines in LDL levels up to 60% on top of goals achieved with statins+/− ezetimibe. PCSK9 inhibitors on top of statins+/− ezetimibe are able to bring almost all high risk and very high risk patients into their LDL cholesterol targets (100 mg/dL and 70 mg/dL respectively).[1] However, in some patients statins intolerance can represent a failure in the consecution of LDL-C goals. We present the case of a patient with this condition and outside of lipid targets despite iPCSK9 having to resort to other therapeutic alternatives.

Case report

We report the case of 47 years-old woman with a history of thyroidectomy 8 years before that was followed up in the outpatient clinic. Familial Hypercholesterolemia (FH) clinic. FH was diagnosed at the age of 18 years with a positive genetic study of the LDL receptor gene M079 (c134C > T, pGln427x) and with MedPED 23 without other cardiovascular risk factors or toxic habits.

In the beginning of follow-up in the absence of lipid-lowering treatment and despite good dietary compliance, the baseline lipid profile was: LDL-C cholesterol 363 mg/dL, total cholesterol 445 mg/dL, HDL-C 57 mg/dL, triglycerides 123 mg/dL. She was previously treated with different statins (atorvastatin, simvastatin, rosuvastatin, pitavastatin) requiring progressive decreases of the doses in all cases; all of them were discontinued as the patient referred intense myalgia without elevation in creatine phosphokinase (CK) or transaminases. She received ezetimibe 10 mg/day with improvement of her lipid profile: LDL-C 253 mg/dL (−30.3%), total cholesterol 327 mg/dL (−26.5%), HDL-C 58 mg/dL (+1.7%). After that, she started treatment with evolocumab 140 mg/2 weeks on top of ezetimibe achieving stable decrease of LDL-C 115 mg/dL (−53%) and total cholesterol down to 185 mg/dL (−41%).

As the LDL-C target in FH patients on primary prevention is 100 mg/dL,[1] an oral compound with red yeast rice was added, containing 3 mg of monacolin K, as well as 0.5 g of berberine, a natural plant derivative. An additional improvement on lipid profile was achieved: LDL-C 68 mg/dL, total cholesterol levels 143 mg/dL. She maintained these LDL-C values in further controls, with good tolerance and good therapeutic compliance without myalgias nor CK increases.

Discussion

In clinical practice, statin intolerance can present as several degrees of muscle aches, with a prevalence ranging from 7 to 29% in different registries and observational studies.[2] The STOMP Study, a randomized, double-blind, placebo-controlled study specifically designed to examine the effect of statins on skeletal muscle symptoms and performance, showed a considerably lower incidence of muscle complaints due to statins than that reported in observational studies: 9.4% in the statin-treated group (atorvastatin 80 mg daily) vs. 4.6% in the control subjects ($p = 0.054$).[3] Incidence of statin intolerance is more frequent in women and in the elderly.[4] Statin intolerance usually can be solved or improved with a change in the dose or type of statin. Due to this condition patient with familial hypercholesterolemia (FH) or with prior cardiovascular events and statin intolerance may not achieve their therapeutic goals even when receiving ezetimibe and in addition PCSK9 inhibitors.[5]

There are several pharmacological presentations on the market of red yeast rice (Monascus purpurea) containing low amounts of the original form of the statins, initially obtained from different kinds of fungi. The main metabolite present in red rice yeast is monacolin K,[6] identical in structure to lovastatin, the first statin introduced on the market to treat hypercholesterolemia in the 80s.[7] In the last years several clinical trials and a meta-analysis has shown how the nutraceutical combination containing berberine, policosanol, and red yeast rice is an effective product for the improvement of the lipid profile[8,9] with mild hypocholesterolemic effects but synergistic action to ezetimibe and IPCSK9.[10,11]

Conclusion

In patients with statins intolerance and out of LDL-C target despite iPCSK9, several pharmacological presentations on the market containing red yeast rice with monacolin K can help us to lead their LDL cholesterol goals avoiding the use of conventional statins.

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Authorship

All the authors mentioned have contributed to this manuscript, both by providing ideas as well as in preparing the draft and its final approval.

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