

## Dyslipidemia drugs used in Pediatrics. Unitary dose

(Fármacos para dislipidemias en Pediatría. Dosis unitarias)

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### SUMMARY

Pharmacological treatment of dyslipidemia in children is an option for reducing the prevalence of this metabolic disease, it is therefore necessary to expand the research studies on this type of drugs in children affected with this disease: because the medicines available have been developed for adult patients.

**Key words:** Dyslipidemia, drugs, children.

### RESUMEN

*El tratamiento farmacológico de las dislipidemias en niños es una opción para disminuir la prevalencia de esta enfermedad metabólica, es por eso necesario ampliar los estudios de investigación acerca de este tipo de fármacos en los niños afectados por esta enfermedad, debido a que los medicamentos disponibles han sido desarrollados para los pacientes adultos.*

**Palabras clave:** Dislipidemia, fármacos, niños.

The high triglyceride/low high-density lipoprotein cholesterol phenotype is a component of the metabolic syndrome. The obesity epidemic has increased the prevalence of this abnormality, and recognition of this dyslipidemia is increasingly common in pediatric practice. Dyslipidaemia may require early diagnosis and management, especially when it is familial with elevated cholesterol levels from birth onwards. If target goals for low-density lipoprotein reduction cannot be reached with lifestyle modification, drug therapy can be considered.<sup>1</sup> The treatment of hypercholesterolaemia in children is often discussed as part of the primary prevention strategy for premature coronary disease in adults. Cholesterol-lowering drugs are appropriate in children with hereditary autosomal dominant diseases such as

familial hypercholesterolaemia, familial Apo B100 deficiency, or combined familial dyslipidaemia. Children suffering from these diseases, cholesterol-lowering drugs are considered when the plasma low density-lipoprotein (LDL)-cholesterol concentration remains above 190 mg/dL after a 6-month dietary treatment. The drug of first choice remains bile acid-binding resins (colestyramine) because their efficacy and safety are well documented in children.<sup>2</sup> Colestyramine treatment with long-term tolerance is unknown, and currently this drug and others Cholesterol-lowering drugs have been used to treat dyslipidemia in practical clinical (*Table 1*).

The understanding of the molecular basis of inborn errors of LDL metabolism –such as familial hypercholesterolemia due to a defect of the LDL receptor– provided us new insights in physiology and pathophysiology of LDL metabolism. Most recently we have learned much about the vasoprotective HDL cholesterol. HDL is the major player in reverse cholesterol transport and some of its receptors such as ABCA1 and SR-BI.<sup>3</sup> The risk of developing the cardiometabolic syndrome is likely triggered or exacerbated by concurrent obesity, unhealthy lifestyle/eating habits, and hormonal changes (puberty). Limiting assessments as measurement of blood pres-

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**Table 1.** Drugs prescribed for dyslipidemia treatment in pediatric unitary dose in a hospital of third level.

Drugs	Pharmacological activity	Years and doses		
		2002-2003	2006-2007	2008-2009
Colestiramine	Hypolipidemic	29	6	0
L-carnitine	Lipotropic	13	0	0
Ursodesoxycolic ac.	Litolitic	377	0	13

sure, fasting insulin and glucose, and total cholesterol, underestimates cardiometabolic risk in overweight youth, particularly minorities. Early identification of cardiometabolic risk in its incipient stages may justify early and more aggressive intervention to prevent progression and complications.<sup>4</sup>

Some studies suggest that treatment with atorvastatin for 12 months was effective and safe for pediatric subjects with known familial hypercholesterolemia or severe hypercholesterolemia. These subjects (n = 187) were randomly assigned to 26 weeks of treatment with atorvastatin (10 mg) or placebo. Dosage was increased to 20 mg if LDL cholesterol (LDL-C) levels remained > 3.4 mmol/L (130 mg/dL), at week 4.<sup>5</sup>

Respect diet or supplementation with docosahexaenoic acid (DHA) with the diet, affects endothelial function in children with familial hypercholesterolemia (FH), this supplementation has been associated with increased levels of total cholesterol.<sup>6</sup>

Phytosterols daily into margarine, mayonnaise, orange juice, olive oil, low-fat milk, yogurt, and tablets is associated with significant reductions in low-density-lipoprotein (LDL) cholesterol from baseline or high cholesterol, in children. Indeed, phytosterol dosages of 1.6-3 g daily have been shown to reduce LDL cholesterol by 4.1-15%.<sup>7</sup>

Simvastatin has been shown to restore endothelial function in children with familial hypercholesterolemia after 28 weeks of treatment. Eighteen hypercholesterolemic patients (HC group) and 18 healthy controls, aged 6-18 years, were studied with medical history, physical examination, full lipid profile, serum apolipoprotein B (apo B), fibrinogen, hepatic transaminases, and creatine kinase concentrations. After treatment, significant reduction in total cholesterol (TC) (29%), low-density lipoprotein cholesterol (LDL-C); (37%), apo B concentrations (36%) and Flow-mediated dilatation restoration (mean,  $12.94 \pm 7.66\%$ ), were observed. Children and adolescents with hypercholesterolemia present endothelial dysfunction, and simvastatin, in addition to significantly reducing TC, LDL-C and apo B concentrations, restores endothelial function with

1-month treatment.<sup>8</sup> The addition of phytosterols to statin therapy has been associated with reductions of 7-20% in LDL cholesterol for up to 1.5 years. Overall, phytosterols are useful for reducing LDL cholesterol in patients who cannot reach their treatment goal by diet alone or who are taking maximum tolerated doses of statins. These products offer an alternative to statins in patients who cannot take statins or whose statin dosage is restricted because of potential drug interactions or concomitant diseases.<sup>7</sup>

Despite, the American Academy of Pediatrics released an updated policy statement recommending more frequent screening to detect dyslipidemia in childhood and the first-line use of statins in children with dyslipidemia who did not respond to lifestyle intervention and who were more than 8 years of age.<sup>9</sup> These recommendations have caused a lot of controversy within the medical community.

Strategies to prevent dyslipidemia related to cardiovascular disease should be implemented at an early age, especially in populations at high risk. However, if target goals for low-density lipoprotein reduction cannot be reached with lifestyle modification, drug therapy can be considered.

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