Chapter 4: Pharmacological cholesterol-lowering treatment in children

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4.1: In children less than 18 years of age with CKD (including those treated with chronic dialysis or kidney transplantation), we suggest that statins or statin/ezetimibe combination not be initiated. (*2C*)

RATIONALE

Clinical trials of dyslipidemias are limited in the pediatric CKD population given the rapid transitions from CKD to dialysis and/or transplant, which complicates trial design, recruitment and analyses (Supplemental Table 32 online). Accurately predicting CVD risk is also not possible in the pediatric CKD population given the limited data available; scores commonly used in adults have not been validated in the pediatric population. Nonetheless, young adults ages 20–24 treated with dialysis or kidney transplantation have significantly lower expected survival compared to an age-matched group in the general population.[66]

Treatment for dyslipidemia in children should first include nutrition and dietary counseling, and address obesity with weight loss regimens if necessary. Recent studies in the general population have shown that dietary fat restriction is safe in children.[67–70] In particular, there have been no adverse effects on growth and development, or nutrition.[67–70] Diets, however, should be used judiciously, or not at all, in children who are malnourished. Secondary causes of dyslipidemias should also be treated first (Table 1). Therapeutic lifestyle changes (TLC) should be adopted among all children with CKD.

Statin therapy has been shown to reduce LDL-C in children and adolescents ages 8–18 years with no adverse effects on growth, development or sexual maturation reported.[7] However, the follow-up time of the studies was quite variable and safety data in children with CKD are very limited. Data on the benefits of treating LDL-C in children aged <10 years are extremely limited, and chiefly include patients with severe familial hypercholesterolemia or cardiac allografts. In the US, statins are approved for use among adolescent boys and post-menarchal girls ages 10–18 years (age 8 and older for pravastatin) for treatment of elevated LDL-C among those with familial dyslipidemias, family history of premature heart disease and 2 or more cardiovascular risk factors.[7]

Four randomized trials have examined drug treatment of dyslipidemia in children with CKD, primarily in children with nephrotic syndrome.[71–74] The trials demonstrate that statins lower LDL-C over 7 months to 5 years. No randomized trials have studied clinically relevant outcomes such as cardiovascular events or mortality.

There have been 13 statin trials in 1683 children with dyslipidemias and normal kidney function. These trials have demonstrated that statins lower LDL-C by 17-50% (depending on dose) and have modest effects on TGs or HDL-C.[75–87] There were only two studies that studied statins in combination with a second drug such as colestipol or ezetimibe.[81,85]

This is a weak recommendation that reflects the lack of evidence for benefit and safety associated with long-term use. As for all weak recommendations, practitioners should consider the clinical circumstances and the patient's preferences when considering an individual patient. The Work Group further suggests that the patient's age could also be considered when applying this recommendation.

Due to the very limited available data, the Work Group does not recommend the use of statins in children with CKD aged <10 years. Patients (boys aged >10 years and post-menarchal girls, together with their parents) with severely elevated LDL-C who place a higher value on the potential for preventing cardiovascular events and are less concerned about adverse events from statin use might be candidates for statin use – especially those with multiple additional risk factors such as family history of premature coronary disease, diabetes, hypertension, smoking and ESRD.

If a statin is prescribed, the Work Group suggests the lowest dose available. There are no data on the appropriate target for LDL-C in children (with or without CKD), extremely limited long-term safety data in pediatric CKD populations, and no dose escalation studies in children with CKD to confirm the safety of higher statin doses even over the short term.

Given the lack of evidence for the benefit and safety of combination therapy with bile acid resins, colestipol and ezetimibe in pediatric CKD populations, the Work Group does not recommend the use of such multi-drug regimens even in children with severely elevated LDL-C.

Suggested Audit Criteria

- Determine the number of children treated with statins (and statin type) and other lipid-lowering therapies by CKD severity.
- Document the number of children with intolerance and/or non-compliance to statins or other lipid-lowering treatment.
- Document the number of children that receive statin therapy for primary prevention.

KEY POINTS

- TLC should be recommended to all children with CKD and dyslipidemia.
- Statins are not recommended for children with CKD and dyslipidemia.

RESEARCH RECOMMENDATIONS

Future studies should be conducted to assess short- and long-term association between lipids and CVD, using surrogate outcomes such as carotid intima-media thickness and clinically relevant outcomes such as MI and stroke.

DISCLAIMER

SUPPLEMENTARY MATERIAL

Supplemental Table 32: Summary table of RCTs of statins vs. placebo in children with CKD without DM [continuous outcomes]

Supplementary material is linked to the online version of the paper at http://www.kdigo.org/home/guidelines/lipids