Efficacy of PCSK9 Inhibitors Compared to Standard of Care in Improving the Low-density-lipoprotein Cholesterol and Lowering the Risk of Cardiovascular Events in Patients with Familial Hypercholesterolemia.

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Abstract

Familial hypercholesterolemia is an inherited condition that causes patients to have significantly increased levels of LDL cholesterol, which often leads to coronary artery disease. Statin medications are typically prescribed to treat this condition, however these medications have adverse side effects and often subpar efficacy in this patient population. Evidence collected in this literature review yielded evidence that the use of PCSK9 inhibitors in the treatment of patients with familial hypercholesterolemia may be efficacious. Many of these studies were able to show statistically significant improvement of LDL-C and decrease in cardiovascular risk when compared to placebo. In addition, this medication was found to be tolerated well without adverse side effects, most notably in patients with a statin intolerance. Although more research is needed, PCSK9 inhibitors seem to be efficacious compared to standard of care in improving LDL-C and lowering the risk of cardiovascular events in patients with familial hypercholesterolemia.

Introduction

OVERVIEW: Familial hypercholesterolemia

• autosomal dominant inheritance - 10 million people living with FH
• causes high plasma levels of LDL cholesterol - regardless of their lifestyle & diet habits
• 20-fold increase in premature coronary artery disease
• 20% of myocardial infarctions under age 45 & 5% of myocardial infarctions under age 60 due to FH

STANDARD OF CARE:

• first line treatment: lifestyle & diet modifications
• those with FH often still have high cholesterol
• first line medications: statins
• highest dose often does not bring down LDL-C in pts with FH
• Side Effects: muscle aches/weakness, neuro-cognitive impairments, liver damage, GI upset

Methods

A literature search was performed in October 2019 in PubMed, GoogleScholar, and ClinicalKey. A total of 12 articles were selected that were published within 5 years and included clinical trials, controlled clinical trials, and randomized controlled trials with subjects. The study design and results of six of these studies were evaluated and compared.

Results

• 5/6 found % of LDL-C reduction of 50% or more
• 2/4 achieved patients LDL-C goals
• 2/2 of the studies looking at the reduction of cardiovascular events found a statistically significant reduction.
• 3/6 found at least 5% of participants had reported significant side effects
• injection site reactions, GI side effects, or transaminase elevation.
• 2/2 of the studies that evaluating the non-adherence due to cost, the cost was found to be a significant barrier for patients.

Discussion

PCSK9i are effective in lowering LDL-C & cardiovascular risk in patients with familial hypercholesterolemia

• Strengths:
  • recruitment methods: use of healthcare professionals to recruit patients with existing FH diagnosis or statin intolerant patients
  • observer bias unlikely in most of the studies

• Weaknesses:
  • short study duration with no long term follow-up
  • small sample size - highest at 511
  • low diversity in terms of race & country of administration
  • no research on use in pediatric population

Future Focus

• Further research into this topic is warranted to address the shortcomings of current studies and confirm current research findings. In addition, studies including cost analysis and real world use as a therapy need to be assessed since cost is a big factor in patient adherence.

Further research will hopefully demonstrate the long term effectiveness vs cost of the medication and its use in clinical practice as a standard treatment of familial hypercholesterolemia.

Conclusion

PCSK9i should be considered as a possible therapeutic treatment in the management of patients with familial hypercholesterolemia, especially if the patient is statin intolerant. These medications are effective in lowering the patients LDL-C and cardiovascular risk as evidenced by the six studies selected for review. Although study designs and observer bias prevents these results from achieving clinical significance, there is promising evidence.

References: