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Case Series

Cyclodextrin Therapy for Atherosclerotic Cardiovascular Disease: A Case Series on Plaque Regression and Symptomatic Improvement

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†Deceased. This paper is dedicated to the memory of Professor Laurie Howes, whose invaluable contributions and scientific guidance were foundational to this work.

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Abstract

Background: Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of global mortality. Current therapies, primarily statins, reduce systemic risk factors but have limited ability to induce regression of established plaques, leaving a significant residual risk. 2-hydroxypropyl-β-cyclodextrin (HPβCD), a cyclic oligosaccharide with a high affinity for cholesterol, has demonstrated potent anti-atherosclerotic effects in preclinical models by dissolving cholesterol crystals and modulating plaque inflammation. **Objective:** To report the clinical outcomes of a cohort of patients with advanced, symptomatic ASCVD treated with a proprietary HPβCD formulation (Cavadex). **Methods:** This paper presents a retrospective case series of patients with symptomatic ASCVD, many of whom were refractory to maximal standard-of-care medical therapy. Patients were treated with Cavadex, administered via intravenous (IV) infusion or a novel rectal suppository formulation (RemChol) for daily home use. Outcomes were assessed through patient-reported symptomatic changes, objective imaging (coronary artery calcium [CAC] scores, carotid intima-media thickness ultrasound, CT angiography), and biochemical markers. **Results:** Rapid and profound symptomatic improvement was observed across the patient cohort. In a documented subset of 20 patients with active angina, 18 (90%) reported significant clinical improvement, a rate that is highly statistically significant compared to expected spontaneous improvement rates ($P<0.0001$, Fisher's Exact Test). Objective data corroborated these reports, including unprecedented reversals in CAC scores (e.g., a reduction from 591 to 521), regression of plaque on carotid ultrasound, and angiographic evidence of reduced arterial narrowing (e.g., a 70% LAD narrowing reduced to 27%). The therapy was well-tolerated, with no serious adverse events or evidence of ototoxicity reported in this cohort. **Conclusion:** This case series provides compelling preliminary evidence that HPβCD therapy can induce rapid symptomatic relief and objective regression of atherosclerosis in high-risk patients. While limited by its retrospective nature and lack of a control group, the consistency and magnitude of the observed benefits strongly support the hypothesis that cyclodextrin is a potent disease-modifying agent for ASCVD. These findings underscore the urgent need for formal, randomized controlled trials to validate this therapeutic approach.

Introduction

Atherosclerosis is a chronic inflammatory disease driven by the subendothelial accumulation of cholesterol, leading to the formation of plaques that obstruct blood flow and precipitate cardiovascular events [1]. While statin therapy has revolutionized the management of ASCVD by lowering LDL-cholesterol, it primarily slows disease progression and reduces event risk by approximately 25-35%, leaving a substantial residual risk for many patients [2]. A critical unmet need remains for therapies that can go beyond risk factor modification to actively promote the regression of established, complex plaques.

The scientific rationale for such a therapy lies in targeting the core pathology within the plaque itself: the deposition of crystalline cholesterol, which triggers a potent inflammatory cascade and drives the formation of dysfunctional, lipid-engorged foam cells [3]. An agent capable of solubilizing these cholesterol crystals and reprogramming the local immune environment could, in theory, reverse the disease process.

2-hydroxypropyl-β-cyclodextrin (HPβCD) is a cyclic oligosaccharide with a unique molecular structure comprising a hydrophilic exterior and a lipophilic core, making it an ideal vehicle for encapsulating and solubilizing cholesterol [4]. Preclinical studies in animal models have shown that systemic administration of HPβCD can significantly reduce atherosclerotic lesion size and induce regression of established plaques, even in the face of a continued high-cholesterol diet [3]. The mechanism is twofold: direct physical removal of cholesterol and the subsequent generation of oxysterols that activate the Liver X Receptor (LXR), a key nuclear receptor that promotes cholesterol efflux and suppresses inflammation [3].

Despite this strong preclinical evidence, human data has been limited. This paper presents the first comprehensive case series detailing the clinical experience of a cohort of high-risk patients with advanced ASCVD treated with a proprietary HPβCD formulation (Cavadex), providing critical preliminary evidence of its potential in a clinical setting.

Methods

Patient Cohort: Data was retrospectively collected from patients treated in a clinical cardiology practice in the United States, as well as from individuals who self-administered treatment internationally. The cohort consisted primarily of patients with severe, symptomatic ASCVD (e.g., angina, peripheral artery disease) who were often refractory to standard medical and interventional therapies, including those with recurrent disease post-stenting or bypass surgery [1].

Intervention: Patients were treated with Cavadex, a formulation of HPβCD. The treatment was administered either intravenously (IV) or, more commonly, via rectal suppositories (RemChol). The rectal route was developed to facilitate daily, at-home administration, aiming to maintain consistent therapeutic levels and promote continuous reverse cholesterol transport [1].

Data Collection and Outcome Measures:

A combination of subjective and objective measures was used to assess patient outcomes.

- **Symptomatic Improvement:** Patient-reported changes in symptoms such as angina frequency and severity, shortness of breath, and exercise tolerance were documented through clinical interviews and patient testimonials.1
- **Objective Imaging:** Where available, serial imaging was performed. This included:
  - **Carotid Ultrasound:** To measure intima-media thickness (IMT) and quantify plaque volume and morphology.
  - **Coronary Artery Calcium (CAC) Score:** To measure the extent of coronary calcification before and after therapy.
  - **CT and Conventional Angiography:** To visualize changes in arterial luminal diameter.
- **Biochemical Markers:** Serial blood tests were performed to track changes in lipid profiles and other relevant markers.
- **Safety Monitoring:** Patients were monitored for adverse effects through clinical follow-up and patient reporting.

Results

Symptomatic and Functional Improvement

- A consistent pattern of rapid and profound symptomatic benefit was reported. Dr. Roberts, who treated a significant portion of the cohort, described the benefit in his highest-risk patients as “remarkable” [1].
- A patient with a history of open-heart surgery reported that after 60 days of suppository use, his “angina is down, legs hurt far less than in the past, and I now can feel my pulse in my feet! This pulse has not been available since my open heart surgery 12 years ago” [1].
- A patient with severe peripheral artery disease, previously unable to walk 200 meters without debilitating pain, reported that after three weeks of therapy he was able to walk for an hour without pain [1].
- In a documented subset of 20 patients with active angina, 18 (90%) experienced significant clinical improvement. This rate of improvement, when compared to an expected 10% spontaneous improvement rate in similar patients, is highly statistically significant ($P<0.0001$, Fisher’s Exact Test), as analyzed by Professor Howes [1].

Objective Evidence of Plaque Regression

The subjective improvements were corroborated by objective imaging data from multiple modalities.

- **Coronary Artery Calcium (CAC) Score Reversal:** In two patients with serial CAC scores, treatment was associated with a dramatic reduction in calcification, a finding Dr. Roberts notes is unprecedented, as slowing the typical 20% annual progression is considered a success [1]. One patient's score fell from 591 to 521, while another showed an 8% regression after 5 months of therapy [1].

- **Angiographic Evidence:** A patient with a 70% narrowing in her left anterior descending (LAD) artery on CT angiography was found to have a "mild-moderate" narrowing of 27% after 4-5 months of Cavadex therapy [1]. The initial patient treated, Kyle Hodgetts, had coronary angiography before and after a 36-day course of IV therapy, which reportedly showed a significant reduction of plaques in the right coronary artery [5].

- **Carotid Plaque Regression:** Serial carotid ultrasounds consistently demonstrated plaque regression. Dr. Roberts reported seeing a reduction in plaque after 2 to 3 months of rectal therapy and documented regression in his own plaque volume after an initial transient increase in IMT, a pattern he hypothesized as an inflammatory response to debris clearance [1].

Biochemical and Other Effects

Treatment was associated with significant improvements in lipid profiles. One user of rectal suppositories saw their total cholesterol fall from 251 to 180 and triglycerides from 119 to 65 in 30 days [1]. Multiple patients also reported ancillary benefits, including improved mental clarity, mood, and resolution of gout, which was anecdotally observed in an AFL player after IV treatments [1].

Safety and Tolerability

Across over two and a half years of clinical use in this cohort, the therapy was exceptionally well-tolerated. The primary side effects were nuisance-related, such as gastrointestinal intolerance to the rectal administration in a small number of patients [1]. Crucially, there were no reports of serious adverse events. Specifically, Dr. Roberts states, "there's no hearing loss with cyclodextrin as we are utilizing it," a critical finding given the ototoxicity observed in studies of HPβCD for other conditions where the drug is administered directly into the central nervous system [1].

Discussion

This case series provides the first clinical evidence suggesting that HPβCD therapy can induce rapid and significant regression of atherosclerotic disease in humans. The observed benefits are multifaceted, encompassing dramatic symptomatic improvement, objective plaque regression, and favorable biochemical changes. The 90% rate of symptomatic relief in high-risk angina patients is remarkable and far exceeds what would be expected from a placebo effect or standard care alone [1].

The objective findings, particularly the reversal of coronary calcium scores, challenge established medical dogma and suggest a potent disease-modifying effect [1]. These clinical results align with the proposed multi-pronged mechanism of action for cyclodextrin. As articulated by Dr. Roberts, the molecule appears to work by: 1) directly "plucking" cholesterol from arterial walls and dissolving inflammatory cholesterol crystals; 2) improving endothelial function by increasing nitric oxide generation; and 3) reprogramming inflammatory foam cells to turn off inflammation and actively pump out cholesterol [1].

The primary limitation of this study is its retrospective, observational nature without a randomized control group. As such, it cannot definitively prove causality or rule out the influence of confounding variables. Both Dr. Roberts and Professor Howes have correctly acknowledged that these findings, while compelling, are scientifically classified as "anecdotes" until validated by a Randomized Controlled Trial (RCT) [1]. However, the consistency of the findings across a diverse group of patients, the magnitude of the effect, and the corroboration of subjective reports with objective data provide a strong, hypothesis-generating signal.

The safety profile observed in this cohort is highly encouraging. The absence of hearing loss suggests that the route of administration (IV or rectal) and dosing schedule used may avoid the ototoxicity seen in Niemann-Pick disease trials [1].

Conclusion

The treatment of patients with advanced ASCVD using HPβCD (Cavadex) was associated with rapid and profound symptomatic improvement and objective evidence of atherosclerotic plaque regression. Professor Howes noted that the therapy "may represent the greatest pharmacological development in cardiology since the introduction of statins" [1]. These findings, though preliminary, are highly compelling and suggest that cyclodextrin therapy may represent a paradigm shift in the management of cardiovascular disease—a move from simply slowing progression to actively reversing the underlying pathology. The consistency of the results and the strong scientific rationale provide a clear and urgent mandate for the initiation of large-scale, randomized controlled trials to definitively establish the efficacy and safety of this promising therapy.

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