DAV131, an Oral Adsorbent-Based Product, Fully Protects Hamsters Against Clostridium difficile Infection

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Abstract

Background. Antibiotic treatments greatly impact gut microbiota which can result in potentially severe, sometimes lethal Clostridium difficile infection (CDI) prevention. C. difficile is an opportunistic infectious agent that can cause severe, even lethal, disease. CDI is associated with antibiotic use and can cause serious illness. The ORAL product DAV131 is a novel adsorbent-based product, which provides protection against CDI in hamsters.

Methods. Syrian hamsters were administered 30 mg DAV131 subcutaneously once per day for 5 days, and infected orally at day 3 with 10^7 C. difficile ATCC 700684. Subsequent administrations were given at 24 and 48 hours after infection. The fecal levels of oxalate and viable C. difficile were respectively measured.

Results. Animals administered DAV131 alone exhibited rapid mortality upon injection of C. difficile spores, with 60% survival at day 1. In contrast, 7% of day 6, 5% of day 7, and 0% of day 7 in both DAV131 treated groups exhibited 100% survival until the end of the experiment at day 12, with no signs of morbidity. Fecal titers of C. difficile surviving animals were measured after infection as compared to DAV131 alone and were undetectable at 72 hours. Recombinant oxalate levels were assessed in hamsters treated with DAV131 over the course of the study.

Conclusion. Oral DAV131 fully prevented DAV131-induced lethal C. difficile with both regimens tested, the protective effect of DAV131 most probably results from the effective adsorption of residual antigen in the gut, and prevention of gut microbiota disruption. This is, to our knowledge, the first demonstration that a protective strategy can prevent CDI if applied concurrent with the causative C. difficile infection. The development of this promising strategy for the prevention of CDI in humans (code name DAV131) is underway.

Introduction

When patients are treated with antibiotics, either orally or parenterally, part of the gut microbiota reaches its active form, and can impact the bacterial population of the gut. This may result in the colonization of the intestine, and in its proliferation of undesirable and potentially lethal bacteria. Such is the case with the anaerobic toxic bacterium Clostridium difficile, which is responsible for diarrheal or pseudomembranous colitis (Pseudomycotic) which may progress into severe and potentially lethal conditions such as pseudomembranous colitis or toxic megacolon.

Methods

DAV131 is a novel oral adsorbent-based product, which binds to the causative agent C. difficile to prevent its adsorption to the gut wall, which should prevent its colonization and absorption.

Fig. 1: Induction of CDI in hamsters by oxalate and oxalate treatment. A: Growth of C. difficile spores in the colon. B: Oxalate concentrations in the feces. C: Oxalate concentrations in the feces.


References