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PSEUDOMEMBRANOUS COLITIS RESULTING FROM THE USE OF ANTIBACTERIALS: A SYSTEMATIC REVIEW

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Abstract: Pseudomembranous colitis is an inflammatory condition of the colon characterized by raised whitish-yellow plaques that coalesce to form pseudomembranes on mucosal surfaces. Antibacterial treatment is the main risk factor for the development of pseudomembranous colitis through the interruption of resistance to colonization of the intestinal microbiota, which favors colonization by the *Clostridium difficile*. This article is a systematic review of the literature, using the PubMed database. Were selected 14 articles using the descriptors: *"pseudomembranous enterocolitis AND antibacterials"*. Studies have shown that under normal conditions, this human gut microbiota can prevent the colonization of pathogens through general mechanisms, such as direct inhibition by bacteriocins, nutrient depletion, or stimulation of the host's immune defenses. However, treatment with broad-spectrum antibacterials preceding C infection. *difficile* disturbs the normal balance of the colonic microbiota, creating a more hospitable environment for the growth of C. *difficile*. Therefore, the use of antibacterials is the main responsible for the disruption of the intestinal microbiota and, consequently, for the reduction of resistance to colonization, which favors the infection by C. *difficile* and the development of pseudomembranous colitis.

Keywords: Pseudomembranous colitis, antibacterial, *Clostridium difficile*

INTRODUCTION

Pseudomembranous colitis is an inflammatory condition of the colon characterized by raised whitish-yellow plaques that coalesce to form pseudomembranes on mucosal surfaces. Endothelial damage from the initiating event or disease process causes small areas of necrosis in the surface epithelium, and the eruption

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of neutrophils, nuclear debris, and other inflammatory elements lead to the formation of pseudomembranes. These can be up to two centimeters in diameter, spread over areas of normal or erythematous mucosa; however, confluent pseudomembranes covering the entire mucosa may be seen in severe disease.

Antibacterial treatment is the main risk factor for the development of pseudomembranous colitis through the interruption of resistance to colonization of the intestinal microbiota, which favors colonization by the *Clostridium difficile*. Although nearly all antibiotics have been associated with C. *difficile*, clindamycin, third-generation cephalosporins, penicillins, and fluoroquinolones have traditionally been considered the most at risk. Not just the choice of antibiotic, but the number and duration of antibiotics also increase the risk of developing pseudomembranous colitis. Therefore, the aim of this article is to analyze the relationship between the use of antibacterials and the development of pseudomembranous colitis.

METHODOLOGY

This is a systematic literature review, using the PubMed database. Were selected 14 articles using the descriptors: *"pseudomembranous enterocolitis AND antibacterials"*, and as a filter: review articles and systematic reviews published in the last 5 years, available for free. As an inclusion criterion, 12 articles dealing with the topic of pseudomembranous colitis associated with the use of antibacterials were considered eligible, and as an exclusion criterion, 2 articles that differed from the topic in question were disregarded.

RESULTS AND DISCUSSION

The selected articles highlighted that the resident intestinal microbiota is a complex community of microorganisms that populate the gastrointestinal tract in a healthy person, being a micro ecosystem that plays a crucial role in the protection of the intestine, providing resistance to colonization and infection by pathogenic organisms, in addition to to have immeasurable effects on host homeostasis. Under normal conditions, this human gut microbiota can prevent the colonization of pathogens through general mechanisms, such as direct inhibition by bacteriocins, nutrient depletion, or stimulation of the host's immune defenses. However, broad-spectrum antibacterial treatment that precedes C. difficile infection disrupts the normal balance of the colonic microbiota.

The ability of C. difficile to cause colitis depends on a number of virulence factors, including toxins, which are encoded at the pathogenicity locus, and adherence and motility factors. In response to limited nutrient availability, C. difficile produces toxins that primarily target intestinal epithelial cells. After endocytosis of the toxin and activation in the cytosol, epithelial cells undergo necrosis, which leads to loss of intestinal membrane integrity, exposure of the host to intestinal microorganisms, and activation of the host's inflammatory response.

Studies have shown that in the healthy colon, sialidase-producing commensal bacteria cleave sugars from glycosylated proteins that are bound to the epithelial cell membrane releasing free sialic acid into the lumen, and primary fermenters break complex carbohydrates into succinate, both metabolites being rapidly consumed as energy sources by commensal bacteria. However, antibacterial treatment can deplete competing commensal bacteria, which leads to an abundance of sialic acid and succinate, allowing C. difficile to use this excess to colonize the intestine, releasing toxins that primarily target intestinal epithelial cells, which after endocytosis of the toxin and activation in the cytosol undergo

necrosis, which leads to loss of integrity of the intestinal membrane, exposure of the host to microorganisms and activation of severe inflammation of the colonic mucosa through the formation of the pseudomembrane composed of fibrin, mucus, necrotic epithelial cells and leukocytes.

CONCLUSION

The use of antibacterials is the main responsible for the disruption of the intestinal microbiota and, consequently, for the reduction of resistance to colonization, which favors the infection by C. *difficile* and the development of pseudomembranous colitis. Therefore, regulating the use of broad-spectrum antibiotics, preventing long-term antibiotic therapy, reducing polymedication, avoiding incorrect prescription and using probiotics during antibiotic therapy are important measures in preventing the disease.

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