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The impact of antibiotic usage on normal flora in the gastrointestinal tract

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ABSTRACT

Antibiotics are agents that help to handle infection in humans. The impact of using broad-spectrum antibiotics and uncontrollable is resistance. Besides resistance, the use of antibiotics also disturbs normal flora in the human body. The impact of normal flora disruption is diarrhea, constipation, and even cancer on the gastrointestinal. The gastrointestinal normal flora alteration can happen even antibiotic was given from another route as intravenous. This research aimed to get information about the impact of using antibiotics on gastrointestinal normal flora. This research is qualitative research with a narrative review approach. From 64 journals 5 journals appropriate with criteria. The data obtained was analyzed with a narrative description. This result suggests that there is a relationship between using antibiotics to gastrointestinal normal flora. The impact of using antibiotics can be profitable or damaging. Profitable impacts include antibiotics in cognitive function, but damage impacts emerge in *Candida albicans* growth and *S.aureus* and *E.coli* that are high in gastrointestinal so that can disturb gastrointestinal normal flora.

Keywords: antimicrobial, normal flora, gastrointestinal

INTRODUCTION

Antibiotics are agents that can help deal with infections in humans. Although it has been regulated in the policy on the use of antibiotics and information on surveillance results in hospitals, it has not been socialized and implemented properly (Rukmini et al., 2019). The impact of widespread and uncontrolled use of antibiotics is the emergence of resistance.

Normaliska et al., (2019) reported that ESBL-producing E. coli isolates isolated from environmental samples at RPH-R Bogor City were resistant to penicillin and amoxicillin by 100%. Furthermore, there are case reports of infection-causing bacterial resistance in urine, sputum, feces, and blood samples of pediatric patients to ampicillin, erythromycin, and amoxicillin (Novard et al., 2019).

In addition to having an impact on the emergence of resistance, the use of antibiotics can also disrupt the normal flora in the human body including the oropharynx, vagina, and normal intestinal microflora/flora (Sullivan et al., 2002). Normal flora in the gastrointestinal tract plays a role in the immune system, helps the absorption of food nutrients, slows down the natural degenerative process due to the development of harmful bacteria in the digestive system, and helps intestinal function (Wahyuningsih, 2018).

There are several theories about the impact of antibiotics, the most frequent report being the use of broad-spectrum antibiotics in infectious disease conditions such as sepsis. On the other hand, there is an impact that cannot be ignored, namely the disruption of the normal flora of the gastrointestinal tract due to the use of antibiotics. The impact caused by the disruption of the normal intestinal flora can cause diarrhea, constipation, and even cancer in the gastrointestinal tract (Konain et al., 2018). Changes in the normal flora of these channels can occur even though the administration of antibiotics is done through other routes such as intravenously. Until now there have been no reports on the impact of antibiotics on the normal flora of the gastrointestinal tract, so this study is important to do. This study aims to obtain information on the impact of antibiotic use on the normal flora of the gastrointestinal tract. It is hoped that this study can reveal the relationship between antibiotic use, antibiotic resistance, and its impact on the normal flora of the gastrointestinal tract.

METHODS

The research conducted is qualitative research with a narrative review approach. The library search process is carried out using the PUBMED database and the keywords "antimicrobial", "normal flora" and "gastrointestinal" combined with the Boolean operator namely "AND". Data was retrieved in March - November 2020. The scientific articles obtained then sorted lead to the negative impact of antibiotic use on normal flora and gastrointestinal diseases. The inclusion criteria were antibiotic usage on gastrointestinal tract infection, and the impact of antibiotics on flora normal. The analysis was conducted in a narrative descriptive manner. Discussions between researchers are carried out to find systematic and comprehensive study.

RESULT AND DISCUSSION

Based on the results of online searches, 64 journals were obtained that matched the keywords. Then sorting journals was carried out, 8 journals were obtained that had digests following inclusion criteria. After a thorough screening, 5 journals were obtained that discussed the impact of antibiotic use on the normal flora of the gastrointestinal tract.

Normal flora has an important role in maintaining a healthy body, one of the places in our body that is an important place for normal flora is the digestive tract. The health of the gastrointestinal tract and its physiological function will be disrupted by changes. Jandhyala et al., (2015) mentioned several factors that influence in formation of normal floral intestines, including the mode of birth (normal or cesarean), diet during growth (breast milk or formula food), and adulthood (vegetable or meat-based ingredients), as well as the use of several antibiotics or prebiotics resulting from the normal intestinal flora environment.

In addition, metformin is also known to have a significant impact on gastrointestinal microbiota. Mentioned Sun et al., (2018), oral administration of metformin can regulate gastrointestinal microbiota and bile acid metabolism in individuals with type 2 diabetes mellitus. The impact of gastrointestinal microbiota is a significant decrease of *Bacteroides fragilis*, accompanied by an increase in glycoursodeoxy-cholic acid (GUDCA), a bile acid after metformin therapy. Metformin shows inhibition of signals from intestinal farnesoid X receptor (FXR), (Sun et al., 2018).

Table 1. The results of characteristics and phytochemical screening assay

No	Author and year	Title	The impact of antibiotics on flora normal in the gastrointestinal tract
1	Krueger *et al*., (1997)	Influence of Intravenously Administered Ciprofloksasin on Aerobic Intestinal Microflora and Fecal Drug Levels When Administered Simultaneously with Sucralfate	Detrimental, *E. coli, S. aureus and Candida albican* thrive
2	Tansho *et al*., (2004)	Production Of Anti-Candida Antibodies In Mice With Gut Colonization Of Candida Albicans	Detrimental, *Candida albican* thrives
3	Alam *et al*., (2014)	Intestinal Alkaline Phosphatase Prevents Antibiotic-Induced Susceptibility to Enteric Pathogens	A solution to the negative impact of antibiotics, namely CIF oral supplementation to prevent the emergence of antibiotic resistance
4	Möhle *et al*., (2016)	Ly6C^{hi} Monocytes Provide a Link between Antibiotic-Induced Changes in Gut Microbiota and Adult Hippocampal Neurogenesis	Detrimental on gastrointestinal, positive impact on neurological function
5	Angelucci *et al*., (2019)	Antibiotics, gut microbiota, and Alzheimer's disease	Detrimental on gastrointestinal, positive impact on cognitive function

Research conducted by Möhle et al., (2016) states that in conditions of no microbes, monocytes will drop due to inactive bone marrow which has an impact on nerve development. This can happen with broad-spectrum antibiotics for 7 days. So to increase monocytes again due to long-term antibiotic therapy can be done by giving probiotics and exercise.

The main focus of antibiotic use is the length of change from the normal intestinal flora and the horizontal transfer of resistant genes that can result in the location of organisms with antibiotic-resistant gene groups (Jandhyala et al., 2015). Antibiotics cause dysbiosis (a condition in which there is an imbalance in the number of microorganisms in the human digestive tract), because antibiotics act to kill bacteria, however, the type and extent of dysbiosis depends on the microbial target of the specific antibiotic (Alam, 2014). Antibiotics are strongly associated with dysbiosis, which leads to susceptibility to pathogenic bacterial infections.

Alam (2014) tested the effect of oral supplementation of the enzyme in intestinal Intestinal Alkaline Phosphatase (IAP) for the prevention of antibiotic-related infections of *Salmonella enterica, S. typhimurium,* and *Clostridium difficle* in mice. As a result, oral supplementation with calf intestinal alkaline phosphatase (CIF) during antibiotic administration protected mice from antibiotic-related infections. Alam (2014) concluded that oral IAP supplements may show new therapies to protect against resistance to antibiotic-related infections, in this case *Clostridium difficile*, and other enteric infections in humans.

Broad-spectrum antibiotics can have a major effect on the composition of normal flora in the intestine, reduce the diversity of normal flora, and inhibit colonization for a long period after antibiotic use (Angelucci et al., 2019). Although broad-spectrum antibiotics are successful in treating many infections, their use should not be arbitrary, the potential of narrow-spectrum antibiotics or therapeutic targets needs to be considered, as well as broad-spectrum antibiotics which generally must have detrimental effects on normal flora in the intestine (Vemuri et al., 2018). The use of antibiotics to fight the normal intestinal flora, especially those related to Alzheimer's disease, may be beneficial. Treatment of chronic infections caused by *H. pylori* or HSV1 virus may bring benefits to disease prevention, or also positive effects on cognitive function (Angelucci et al., 2019).

Krueger et al., (1997) conducted a study on the effect of ciprofloxacin administration on the normal flora of the gastrointestinal tract on eight volunteers who received 400 mg of ciprofloxacin intravenous infusion twice daily for 4 days. The bacteria members of the *Enterobacteriaceae* family found are *E. coli. Staphylococcus aureus* disappeared completely after 2 days of ciprofloxacin administration, but the amount fluctuated and returned to normal on the tenth day after the last ciprofloxacin administration. *Candida sp* counts increased more than 100-fold in two volunteers and dropped back when ciprofloxacin was given.

The presence of *Candida sp* is reduced during ciprofloxacin administration (Kruege et al., 1997). Therefore, intravenous administration of ciprofloxacin infusion eliminates the normal flora of the gastrointestinal tract from the *Enterobacteriaceae* family rapidly and selectively. Another study conducted by Tansho et al., (2004) on the effect of ampicillin and kanamycin administration with the results of the persistence of high concentrations of *Candida albicans* for more than 2 weeks in mice.

Based on the results of this review, people should always take antibiotics following the doctor's recommendations. Improper use of antibiotics can cause resistance and even trigger the growth of other microorganisms that can threaten the normal flora of the digestive tract. The results of this review can be used as study material to improve the use of antibiotics that are not appropriate. In this review, there are still limitations to articles that discuss the use of gastrointestinal antibiotics that affect normal flora. Limited literature also influenced the conclusion of this review.

CONCLUSION

Based on the results of the review, it can be concluded that there is a relationship between the use of antibiotics to the normal flora of the gastrointestinal tract. The impact of antibiotic use can be both beneficial and detrimental. Beneficial effects include its role in cognitive (neuro)function but adverse effects also appear on the high growth of *Candida albican, S. aureus,* and *E. coli* in the gastrointestinal tract which can disrupt the normal flora of the gastrointestinal tract.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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