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Antidepressants Link to Antibiotic Resistance

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Abstract

Antidepressants and antibiotics are two of the most relevant medications in modern medicine today; antibiotics keep general infection at bay, and antidepressant prescriptions are on the rise. The study aimed to look at if antidepressants are having an impact on the recent increase in antibiotic resistance, as antidepressant prescriptions have been a common rise with antibiotic resistance. The study took three of the most commonly prescribed antidepressants (Fluoxetine, Sertraline, and Amitriptyline) and tested them against *Acinetobacter baumannii (A. Baumanni)*, an antibiotic resistance threat in the United States (1). The antibiotics were tested on *A. baumannii* isolates against Gentamycin, Imipenem, Colistin, and Ciprofloxacin. The study found an exciting link to some antidepressants causing resistance to certain antibiotics after varying exposure times. There is much to be investigated with this problem, as only a small number of antidepressants were tested on a small number of antibiotics with one antibiotic-resistant bacterium.

Key Words:
A,Baumanni, Minimum Inhibitory Concentration, Antibiotic, Antidepressant, PCR

Introduction

Antibiotic resistance is a growing modern-day problem. Antibiotics are frequently used in farming and are being overprescribed by physicians; a question arose over what else could be aiding in the rise of antibiotic resistance. Antidepressants are another prescription drug with a recent rising in prescription; the study looked if three commonly prescribed antidepressants led to antibiotic resistance in the bacterium *A. Baumannii*, which is becoming an antibiotic resistance problem. Overexpression of the efflux pump is a mechanism of antibiotic resistance; in a study by Gurpinar et. al (2022) efflux pumps arcB and arcD are measured for overexpression. Resistance was also measured over minimum inhibitory concentration (MIC) after being exposed to agar plates. Overall, various antibiotic resistance mechanisms were measured in increments of 5,10, and 30 days.

Recent Progress

Fluoxetine, Sertraline, and Amitriptyline are three commonly prescribed antidepressants; in a 2022 study, bacterium *A. baumannii* was grown in the presence of these three antidepressants for 30 days and then tested against four antibiotics (1). Resistance testing of each antibiotic was measured by the 5th, 10th, and 30th days with quantitative reverse-transcriptase PCR and minimum inhibitory concentration (MIC). *A. baumannii* isolates were taken from plates that were exposed to each antidepressant for 30 days. Isolates were placed in broth for 30 days and then on plates to test against antibiotics Gentamycin, Imipenem, Colistin, and Ciprofloxacin. The isolate testing examined PCR results for efflux pump and membrane porin target genes. Fluoxetine had no result on Imipenem resistance after the 5th, 10th, or 30th day, but after 30 days, each developed resistance to Ciprofloxacin and Gentamicin. Thirty days of exposure also increased Chloramphenicol, Amoxicillin, and Tetracycline resistance. Fluoxetine increased gene expression of efflux pumps arcB and arcD, allowing higher Ciprofloxin resistance. Sertraline showed Imipenem resistance after the 5th day of exposure and higher Colistin resistance after the 5th, 10th, and 30th days. Sertraline also increased gene

expression of efflux pumps arcB and arcD like Fluoxetine, leading to higher Ciprofloxin resistance. Amitriptyline yielded the most antibiotic resistance and higher MIC for all antibiotics tested by the 30th day and increased resistance to Colistin after the 5th, 10th, and 30th days. Resistance increased to Ciprofloxacin and Gentamicin by the 30th day; the MIC value of isolates for Gentamicin particularly increased after Amitriptyline exposure.

Discussion

Results indicated that antidepressants hold an impact on antibiotic resistance in as short of time as 30 days. The antidepressants tested showed multiple antibiotic resistance mechanisms; overexpression of membrane proteins was one large result found through PCR, and MIC showed the number of isolates grown on an antibiotic plate. Fluoxetine and Sertraline operate on the same mechanism of action as antidepressants, resulting in similar results to efflux pump overexpression and high resistance to Colistin on the 5th,10th, and 30th-day checks. Both increased Ciprofloxin resistance as well. Fluoxetine resistance to Chloramphenicol, Amoxicillin, and Tetracycline is a concerning result, as Amoxicillin is among the most commonly prescribed antibiotics today. Amitriptyline resistance was more widespread but was not surprising as it operates off a different mechanism than Fluoxetine and Sertraline. Amitriptyline's link to resistance increased for all antibiotics on the 30th day, with Colistin resistance on the 5^{th}, 10^{th}, and 30^{th} days. Ciprofloxacin and Gentamicin resistance was the most notable, with the MIC value rising in isolates after Amitriptyline exposure. Surprisingly, there was no result for protein porin overexpression in Amitriptyline.

Overexpression of porin proteins threatens antibiotic resistance as "known omp porin proteins found in the cell wall of A. Baumannii prevents the entry of some molecules into the cell while preventing the exit of others from the cell, giving the cell wall selectivity. For this reason, the loss of these proteins in the outer membranes plays an important role in the emergence of antimicrobial resistance" (1). Antidepressants allow the bacteria to hold more cell wall selectivity against antibiotics, leading to a rise in resistance. This study's results only validate a narrow spectrum of antidepressants and antibiotic resistance with extensive ranges existing for each. The study considered the results significant with P values better than 0.05. There remain unanswered questions on mechanisms of resistance that antidepressants may influence. The antidepressant-antibiotic resistance relationship has much more to be discovered with the research needed in more than one area, like the excretion of antidepressants in the urine of those that take a prescription antidepressant. Excretion of antidepressants potentially impacts resistance with minute amounts building in wastewater and dump sites. A link was found between antidepressants and antibiotic resistance from more than those prescribed antidepressants; more antibiotic-resistance genes were found circulating in domestic wastewater samples than in samples of wastewater from hospitals, where antibiotic use is higher (2). This same study also found that they can trigger SOS responses, making them better able to survive antibiotic treatment (2). With only one other study, it is evident that there is much more room for investigation and knowledge in the link between antidepressants and antibiotic resistance. A very narrow spectrum of antibiotics and antidepressants was tested leaving much room for improved research. The method of tracking porin protein genes also limits what has been studied, leaving many mechanisms of resistance open for study. Though studying membrane protein expression is a fairly new research technique, there is a wide range of research methods that can be applied. The study's research and results can be applied to the lives of those taking antidepressants or those that may not be overly cautious about taking antibiotics. Extensive research needs to be continued in this area, it has only been proven in one study that an antidepressants-antibiotic mix can cause small and varying resistance mechanisms in the narrow range of medications tested. Overall, the main study gave the first look into significant testing on the impact antidepressants have on growing antibiotic resistance.

References

1. Gurpinar, S.S., Kart, D. & Eryilmaz, M. The effects of antidepressants fluoxetine, sertraline, and amitriptyline on the development of antibiotic resistance in *Acinetobacter baumannii*. *Arch Microbiol* **204**, 230 (2022). https://doi.org/10.1007/s00203-022-02853-6

2. Drew, L. (2023, January 24). *How antidepressants help bacteria resist antibiotics*. Nature News. Retrieved February 6, 2023, from https://www.nature.com/articles/d41586-023-00186-y

