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Antibiotics Interaction with Dairy products - Exploring Health Impacts and Treatment Consideration

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ABSTRACT

Antibiotics were recognized as naturally occurring substances produced by specific microorganisms with the capability to harm others. Dairy products such as milk, cheese, yogurt, and butter are carefully crafted to preserve the nutritional benefits of milk, highly valued worldwide for their nutritional richness, culinary versatility, and integral role in various dietary traditions. The interaction between antibiotics and dairy products is a critical consideration in clinical settings. This review examines the mechanisms underlying these interactions, emphasizing the impact of calcium on antibiotic bioavailability. Clinical implications are discussed, highlighting the importance of separating antibiotic administration from dairy consumption to optimize treatment outcomes.

Keywords- Antibiotics, Milk, Yogurt, Tetracycline and Fluoroquinolones.

I. INTRODUCTION

Infections remain a leading cause of mortality in developing countries worldwide, with bacterial infections being a significant contributor to illness and death globally[1]. Antibiotics are compounds with antimicrobial properties, derived either naturally, partially synthetically, or fully synthetically, and can be administered through injections, orally, or topically. The term "antibiotic" originates from "antibiosis," meaning "against life"[2]. Historically, antibiotics were recognized as organic substances produced by one microorganism that can harm others. An antibiotic is defined as a substance that halts bacterial growth or completely eradicates bacteria[3]. They are specifically designed to treat bacterial infections within or on the body. Antibiotics that kill bacteria are known as bactericidal, while those that only slow their growth are termed bacteriostatic. Sir Alexander Fleming discovered penicillin in September 1928 while studying the fungus Penicillium notatum[2]. Officially announced in 1929, penicillin underwent human trials starting in 1940. By 2018, global antibiotic consumption had risen significantly, with a consumption rate of 14.3 defined daily doses (DDD) per 1000 people per day, marking a 46% increase from 2000[4]. Dairy products, also known as lacticinia, are a variety of foods made from milk and found worldwide in grocery stores. They include basics like milk, cheese, yogurt, and butter, each made using specific methods to capture milk's nutritional benefits. While widely available, some people avoid dairy due to dietary choices like lactose intolerance or veganism. Despite this, dairy products are important for providing key nutrients like calcium, crucial for bones and overall health[5].

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Antibiotics are invaluable in combating bacterial infections, but their effectiveness can be compromised by dietary choices. One such commonly overlooked concern is the consumption of dairy products during antibiotic treatment. While dairy is needed for many, its interaction with antibiotics can pose significant risks and diminish treatment efficacy. Understanding this interaction is crucial for maximizing the benefits of antibiotics and maintaining optimal health. This article explores why healthcare providers advise against consuming dairy products with antibiotics, offering insights into how this simple adjustment can enhance treatment outcomes and promote overall wellness.

II. TETRACYCLINE

Since the 1950s, tetracyclines have been widely used to treat a broad spectrum of bacterial infections, including both gram-positive and gram-negative species. They are effective against intracellular pathogens such as chlamydiae, mycoplasmas, rickettsiae, and certain protozoan parasites, as well as for managing non-infectious conditions and potential biological warfare agents[6]. They are prescribed for infections such as Rocky Mountain spotted fever, Lyme disease, and respiratory infections, and are used in acne treatment and as an alternative for penicillin-allergic individuals. Naturally occurring drugs in this class are tetracycline, chlortetracycline, oxytetracycline, and demeclocycline. Semi-synthetic tetracyclines are lymecycline, methacycline, minocycline, rolitetracycline, and doxycycline. There is one glycylcycline subclass agent named tigecycline[7-8]. Tetracycline and oxytetracycline are examples of antibiotics that interact with dairy products.

Bacterial resistance to tetracyclines emerged soon after their introduction, driven by mechanisms like gene acquisition, efflux pump mutations, and changes in cell permeability. Notably, resistance has not been observed in protozoa or other eukaryotic organisms. Its mechanism of action is it enters bacterial cells via passive diffusion and inhibit protein synthesis by binding to the 30S ribosomal subunit[9].

Mechanism behind the interaction of tetracycline:

The effectiveness of tetracyclines can be significantly diminished by the presence of divalent and trivalent cations like calcium, magnesium, and iron. These elements are commonly found in antacids, iron supplements, dairy products such as milk, and other medications. When tetracyclines are taken alongside these substances, they can form complexes known as chelates in the stomach and small intestine. These chelates are insoluble and cannot be absorbed effectively across the intestinal lining, leading to lower levels of the antibiotic in the bloodstream[10].

Clinical management:

To minimize this interaction, it's recommended to administer tetracyclines and products containing these cations (milk, antacids) at least 1 to 3 hours apart. This timing helps minimize interference and chelation, which otherwise lead to poor absorption of the antibiotic[10].

Pharmacokinetics:

When tetracycline interacts with dairy products, it significantly reduces the drug's absorption in the bloodstream, typically by 20% to 75%. This interaction is considered moderately severe, with effects appearing rapidly[11].

III. LITERATURE REVIEW

Welling PG et al.1977, comparative study conducted to evaluate the influence of various test meals and fluid volumes on the relative bioavailability of commercial formulations of doxycycline hyclate and tetracycline hydrochloride was studied in healthy human volunteers. Subjects were four male and two female healthy volunteers and advised to take no drugs for 1 week preceding the study and no drugs other than the required doses of doxycycline and tetracycline during the study. Subjects were fasted overnight before each treatment and were permitted to eat no food, apart from test meals, until 4 h after dosing. On the morning of a treatment, subjects drank 250 ml of water on arising, at least 1 h before dosing. Drugs were administered at 8 a.m., and blood samples (-4 ml) were taken from a forearm vein into vacutainers containing no anticoagulant immediately before and at 0.5, 1, 2, 3, 4, 6, 8, 24, and 32 (tetracycline) or 48 (doxycycline) h after dosing. Serum was separated and deep-frozen until assayed. Assays were done within 48 h of sampling. Serum levels of tetracycline were uniformly reduced by approximately 50% by all test meals, whereas serum levels of doxycycline were reduced by 20%. The reduction of tetracycline serum levels will likely be of clinical significance. The rate of doxycycline absorption was reduced when capsules were administered with a small volume of water, but the overall efficiency of absorption of both drugs was essentially independent of co-administered fluid volume. The study concluded that 8-h serum data provides a reliable estimate of drug bioavailability for tetracycline and, to a lesser extent, for doxycycline[12].

IV. FLUOROQUINOLONES

Fluoroquinolones, a class of broad-spectrum bacterial agents, demonstrate strong effectiveness against a wide variety of aerobic Gram-positive and Gram-negative bacteria. Gram-positive organisms susceptible to fluoroquinolones include both penicillinase-producing and non-penicillinase-producing staphylococci, Streptococcus pneumoniae, Streptococcus viridans, Enterococcus faecalis, Listeria monocytogenes, and Nocardia species. Among Gram-negative bacteria, fluoroquinolones target pathogens such as Neisseria meningitis, Neisseria gonorrhoea, Haemophilus

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influenzae, most species of Enterobacteriaceae, Pseudomonas aeruginosa, and Vibrio species[13].

Nalidixic acid, the first clinically useful quinolone, was discovered in 1962 by Lesher[15]. In 1980, enoxacin, an analog of nalidixic acid, was developed, broadening its spectrum of activity to encompass a wider range of Gram-negative and Gram-positive bacteria[17]. Subsequently, ciprofloxacin was introduced to the market in 1986 due to its enhanced pharmacokinetic properties and potent activity against diverse pathogens[14-18].

Ciprofloxacin and ofloxacin are examples of antibiotics that interact with dairy products. Fluoroquinolones function by inhibiting the bacterial enzyme DNA gyrase, which is crucial for nicking double-stranded DNA, introducing negative supercoils, and resealing the nicked ends. This mechanism prevents excessive positive supercoiling of DNA strands during replication and transcription[18-19].

Mechanism behind the interaction of fluoroquinolones:

Ciprofloxacin is known to interact with dairy products due to the formation of insoluble complexes between ciprofloxacin and divalent cations (such as calcium, magnesium, aluminum, and iron) present in dairy products. Concurrently consuming ciprofloxacin and dairy products may reduce ciprofloxacin levels in the body due to calcium chelation[10].

Clinical management:

The Clinical Management is Ciprofloxacin can be taken irrespective of meals. However, it is advisable to avoid taking ciprofloxacin with dairy products (like milk or yogurt) or calcium-fortified juices alone, as this could significantly decrease ciprofloxacin absorption. To minimize this interaction, it's recommended to administer ciprofloxacin and products containing these cations (milk, antacids) at least 1 to 3 hours apart [20].

Pharmacokinetics:

The administration of ciprofloxacin with calcium or products containing high quantities of calcium (milk, yogurt, antacids) may cause reductions in ciprofloxacin peak plasma concentrations and the area under the plasma concentration-time curve when these two agents are the only ones administered together. These two agents should not be administered concurrently[20-21].

Literature review:

Neuvonen PJ et al.1991, randomized crossover trial conducted to analyze the effects of milk and yogurt on the bioavailability of ciprofloxacin were studied in Four female and three male volunteers. After an overnight fast, they were given 500 mg ciprofloxacin. Immediately after the ciprofloxacin tablet, 300 ml water, 300 ml whole milk was ingested. No other food or drinks were ingested during the next 3 hours. Timed venous blood samples were collected until 24 hours after drug ingestion. Plasma was separated within 30 minutes. Plasma ciprofloxacin concentrations were significantly lower during the 70% by milk and by 92% by yogurt. Milk reduced the peak plasma concentration. The extent of bioavailability, measured as the total area under the plasma concentration-time curve and 24-hour urinary excretion of ciprofloxacin, was reduced by 30% to 36% by milk and yogurt. This study concluded that the absorption of ciprofloxacin can be reduced by concomitant ingestion of milk or yogurt[20].

V. CONCLUSION

In conclusion, the interaction between antibiotics and dairy products poses a significant consideration in clinical practice. The presence of dairy products, particularly those rich in calcium, can reduce the absorption and efficacy of antibiotics. Healthcare providers should educate patients on the importance of timing antibiotic doses separately from dairy consumption to maximize therapeutic benefits. Understanding and managing these interactions are crucial steps in ensuring effective treatment and patient safety.

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