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Review on: Safety and Efficacy of Doxycycline in the Treatment of Acne Vulgaris and Rosacea

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A B S T R A C T

Doxycycline have long been accustomed treat a large type of medical conditions, particularly within the field of medical specialty. sadly, safety issues, particularly canal (GI), have invariably been gift. alternative safety issues have enclosed tooth development in kids, moniliasis, proprioception issues, photosensitivity/phototoxicity, and more eerie adverse effects like uncontrolled high blood pressure. The goal of this review was to summarize the obtainable literature covering the protection profiles of oral antibiotic. antibiotic could be a member of the Achromycin category of antibiotics and has been used clinically for over forty years. it's a well-tolerated drug that's organic process and acts via the inhibition of microorganism ribosomes. it's typically given at a dose of 100-mg daily or doubly daily. it's well absorbed and has typically sensible tissue penetration. This review concentrate on study of acne and acne rosacea. acne rosacea could be a common, chronic, skin condition characterised by continual episodes of facial flushing, transient or persistent erythroderma, papules, pustules, and telangiectasias, in a very symmetrical facial distribution

Keywords: antibiotic, acne vulgarise, rosacea, doxycycline.

Introduction

Acne vulgarism could be a malady of follicle unit characterized by the formation of open and Closed comedowns, papules, pustules, nodules And cysts. it's the foremost common disorder treated By dermatologists. The term skin disorder comes from Greek word “acme” which suggests “prime of life”. though typically thought-about to be a benign, self limiting condition, skin disorder could cause severe psychological issues or disfiguring scars which will persist for a life.11 acne is that the most common chronic disease of the skin within the United States, touching around eightieth of persons at some purpose between eleven and thirty years of age.1 In one996 within the u. s., the National Health Interview Survey reported the prevalence of skin disorder was 26/1000 in persons <45years of age. Acne vulgarism and rosaceous present therapeutic challenges due to their chronicity, potential for disfigurement, and psychosocial impact. Although path physiological distinct, both conditions have major inflammatory components. Consequently, topical and systemic antimicrobial agents are routinely prescribed for extended periods. 2 Emergence of resistant strains of Propionibacterium acnes, adverse events, and compliance issues associated with chronic systemic tetracycline use have led toned treatment approaches. Doxycycline displays excellent activity against gram-positive and gram-negative aerobic and anaerobic pathogens. 3,4The oral absorption of doxycycline is rapid and virtually complete and is not significantly decreased by food. Moreover, serum concentrations ofdoxycycline following oral and in intravenous administration are comparable. Because of the prolonged half-life of doxycycline, once daily administration is possible.(1)Doxycycline is highly effective, inexpensive in with a broad therapeutic spectrum and exceptional bioavailability. However these benefits have been overshadowed by its classification alongside the tetracycline’s – class D drugs4

Rosacea is a common, chronic dermatologic condition, whose cause remains unknown. It has a higher prevalence in fair-skinned individuals and most commonly affects individuals between the ages of 30 and 50, women being more affected than men.5The diagnosis of rosaceous requires the presence of one or more of the following primary features concentrated on the central area of the face: flushing (transient erythematic), no transient erythematic, papules and pustules, and telangiectasia.Rosacea represents a therapeutic challenge because of its chronic nature, progression, potential for disfigurement, and psychological impact.(6). Doxycycline-treatable diseases area unit rising as leading causes of dedifferentiated symptom unwellness in geographic area. Rosacea is a common, chronic dermatologic condition, whose cause remains unknown.. The medical community often under recognizes the importance of drug induced esophageal lesions and fails to deliver proper advice and instructions related to drug ingestion. The diagnosis is usually clinical although endoscopy is the gold standard diagnostic tool. Treatment is symptomatic with discontinuation of the drug often being sufficient. Long-term squeal are infrequent and acute complications uncommon.7Doxycycline is a tetracycline-derived synthetic antibiotic with potent anti-inflammatory effects 8. Minocycline and doxycycline are.relatively well absorbed, even with simultaneous ingestion of food, including milk.9 High tissue levels have been reported following oral ingestion of these drugs, which is an advantage in the treatment of acne vulgaris.10The past twenty-five years have brought about significant changes in the treatment of acne. No other group of medications has altered the management of acne more than the retinoid. The topical retinoid became mainstream acne treatment in the early1980s, but problems with skin irritation limited their utility in some individuals. Adapalene, a topical retinoid by function, was introduced in the mid-1990s, followed quickly by formulations of tretinointouted to be less irritating. Tazarotene was

soon added to the list of topical retinoid effective in the treatment of acne. Topical retinoid have been well accepted as the treatment of choice for comedonalacne since their inception.

Pathogenesis of acne vulgarise:

Many questions remains unknown in our understanding of the pathogenesis of acne. What is the initial stimulus for follicular hyper proliferation? Why do some persons develop acne and others do not despite similar serum hormone levels and similar P acnes counts? What determines the severity of skin disorder Associate in Nursing exceedingly in a very} given patient? Is skin disorder primarily an inflammatory dermatitis? abundant progress has been created within the study of skin disorder, however several queries stay. maybe the foremost vital question is, however we have a tendency toucan we will we} treat our patients with skin disorder a lot of effectively and safely than we area unit now? the solution to the present question lies within the development of a deeper understanding of the pathological process of acne sebaceous glands and sebum The pilosebaceous unit consists of sebaceous glands and hair follicles. Sebaceous glands and hair follicles are physically connected and usually vary inversely in size. These units are located in all skin areas except the palms and soles. There are approx-irately 900 glands per square centimetre on the face, upper neck, and chest. The rest of the body averages fewer than 100 glands per squarecentimeter. “Free” sebaceous glands (those not attached to a hair follicle) that open to the surface of the skin are present in the meibomian glands of the eyelid, the areola of the nipples, and the labours vermilion borders of the lip and in the Mouth.(12)Sebum is secreted by the sebaceous gland and comprises an oily mixture of triglycerides, wax esters, squalling, free fatty acids and small amounts of cholesterol, cholesterol esters and triglycerides. Sebum production is regulated by many factors that activate pathways involved in cell proliferation differentiation, lip genesis, hormone metabolism, and cytokine and chemokine release.(13)Figure 1 | Acne formation. Schematic representation of the skin containing a sebaceous unit (part a) comprising the hair follicle and the sebaceous gland, which is responsible for sebumproduction. Acne formation starts when sebum and keratinous material shed from the skin clog up a pore and trigger bacterial colonization, leading to a closed or whitehead come done (part b). As the whitehead come done continues to expand, owing to more accumulation of sebum and keratinous material, the follicular orifice opens and forms an open or blackhead come done (part c). The black colour is the result of oxidized lipids and the skin pigment melanin. More distension of the come done results in follicular rupture and inflammatory lesions such as papules (part d), pustules (part e) and nodules or cysts (part f). Nodular acne is sometimes inaccurately referred to as ‘cystic’ or ‘nodulocystic’ acne. An acne cyst is not a true cyst as true cysts are lined by epithelium. Histological images of a pilosebaceous unit (part g), a comedone (part h)and an inflammatory lesion with rupture of the follicular walls (part i) are shown(.14)

Dietary lipids and inflammatory process in acne:

Topically applied linoleic acid was shown to induce an almost25% reduction in the overall size of microcomedones over a1-month treatment period. On the other hand, arachidonicacid, an essential, long-chain, pro-inflammatory o-6 fatty acid,stimulates IL-8 and IL-6 synthesis in cultured human sebocytes and enhances synthesis of sebaceous lipids. Natural cycling of the sebaceous follicle. Uncontrolled overstimulation or defect negative feedbackregulation lead to the development of clinically detectableacne lesions, such as comedones and inflammatory papules.(17)Hypercornification of the pilosebaceous ductObstruction of the pilosebaceous canal precedesthe development of acne lesions. The obstructionis produced by the accumulation of adherentkeratinized cells within the canal that form animpaction obstructing the flow of sebum. Causeis unknown but the process may be under theinfluence of androgens.It may also be due to anabnormality in the sebaceous lipids resulting in arelative hyperproliferation ofcorneocytes.Comedone formation may be due to a localizeddeficiency of linoleic acid in pilosebaceous duct.Linoleic acid is incorporated via plasma intosebaceous gland cells, where it is diluted due tolarge volume of sebumand the ductalcorneocytes are effectively bathed in aninadequately low level of linoleic acid.As the follicular lumenbecomes obstructed byabnormally desquamated follicular cells, sebumgets trapped behind the hyperkeratotic plugs, dilating the follicle. Sebaceousglands and hair follicles are physically connected and usually vary inversely in size.These units are located in all skin areas except the palms and soles. There are approx-imately 900 glands per square centimeter on the face, upper neck, and chest. The rest of the body averages fewer than 100 glands per squarecentimeter. “Free” sebaceous glands (those not attached to a hair follicle) that open to the surface of the skin are present in the meibomian glands of the eyelid, the areolae of the nipples, and the glabrous vermilion borders of the lip and in the Mouth.(12)Sebum issecreted by the sebaceous gland and comprises an oily mixture of triglycerides, wax esters, squalene, free fatty acids and small amounts of cholesterol, cholesterol esters and diglycerides. Sebum production is regulated by many factors that activate pathways involved in cell proliferation differentiation, lipogenesis, hormone metabolism, and cytokine and chemokine release.(13)Figure 1 | Acne formation. Schematic representation of the skin containing a sebaceous unit (part a) comprising the hair follicle and the sebaceous gland, which is responsible for sebumproduction. Acne formation starts when sebum and keratinous material shed from the skin clog up a pore and trigger bacterial colonization, leading to a closed or whitehead comedone (part b). As the whitehead comedone continues to expand, owing to more accumulation of sebum and keratinous material, the follicular orifice opens and forms an open or blackhead comedone (part c). The black color is that the results of oxidised lipids and also the skin pigment animal pigment. More distension of the comedone results in follicular rupture and inflammatory lesions such aspapules (part d), pustules (part e) and nodules or cysts (part f). Nodular acne is sometimes inaccuratelyreferred to as ‘cystic’ or ‘nodulocystic’ acne. An inflammatory disease cyst isn't a real cyst as true cysts square measure lined by animal tissue. Histological images of a pilosebaceous unit (part g), a comedone (part h) and an inflammatory lesion with rupture of the follicular walls (part i) are shown(.14)

Role of androgens:

Androgens are thought to play a crucial role in the pathogenesis ofacne . The relevance of hyperandrogenism in maleacne patients isoften not considered, whereas in women or prepubertal childrensuffering from acne, disorders of androgen metabolism are readily suspected. Extensive investigations have documented that in women,acne isaccompanied by hyperandrogenemia . This notion is alsosupported by clinical observation of acne onset around puberty andflare during menstruation or hyperandrogenic states.(13) Studies havealso shown a statistically significant increase in circulating androgenlevels in women with acne as compared to healthy controls. Thoughthe majorities ofthe female patients with acne have androgen levelswithin normal limits and do not have an underlying endocrinopathy.Nonetheless, the possibility of a hyperandrogenic state in female.patients with acne in certain clinical settings must be excluded.Suspicion should be high in women with signs of virilization andirregular menses. The most commonly considered endocrinopathiesin this setting are polycystic ovary syndrome .

Androgens influence acne development throughtheir impact on sebum production. As mentionedpreviously, androgens stimulate sebocytes toproliferate and produce more sebum.Sebumacts as a nutrient source for theskin colonizerP acnes.Lipases produced by P acnes hydrolyzesebum into proinflammatory free fatty acids.resultant inflammatory host response causes follicular Wall rupture and inflammatory lesion formation 15The role of androgen hormones in the pathogenesis of acne has also been carefully evaluated. Overall, circulating androgen hormone levels arenormal in individuals with acne who do not haveother signs or symptoms of hyperandrogenism. Theenzyme 5a-reductase type 1 has been studied inthose withand without acne. 5a-reductase type 1 ispresent in the sebaceous gland and converts testosteroneto the more potent androgen receptor ligand,dihydrotestosterone. It has been hypothe-sized that those with acne might have more active 5a-reductase type 1. However, no statistically significantdifference in enzyme activity has beenobserved todate between those with and without acne, butsubject numbers have been very low.(16)

Dietary lipids and inflammatory process in acne

Topically applied linoleic acid was shown to induce an almost25% reduction in the overall size of microcomedones over a1-month treatment period. On the other hand, arachidonicacid, an essential, long-chain, pro-inflammatory o-6 fatty acid,stimulates IL-8 and IL-6 synthesis in cultured human sebocytes and enhances synthesis of sebaceous lipids. Natural cycling of the sebaceous follicle. Uncontrolled overstimulation or defect negative feedbackregulation lead to the development of clinically detectableacne lesions, such as comedones and inflammatory papules.(17)Hypercornification of the pilosebaceous ductObstruction of the pilosebaceous canal precedesthe development of acne lesions. The obstructionis produced by the accumulation of adherentkeratinized cells within the canal that form animpaction obstructing the flow of sebum. Causeis unknown but the process may be under theinfluence of androgens.It may also be due to anabnormality in the sebaceous lipids resulting in arelative hyperproliferation ofcorneocytes.Comedone formation may be due to a localizeddeficiency of linoleic acid in pilosebaceous duct.Linoleic acid is incorporated via plasma intosebaceous gland cells, where it is diluted due tolarge volume of sebumand the ductalcorneocytes are effectively bathed in aninadequately low level of linoleic acid.As the follicular lumenbecomes obstructed byabnormally desquamated follicular cells, sebum gets trapped behind the hyperkeratosis plugs, dilating the follicle.

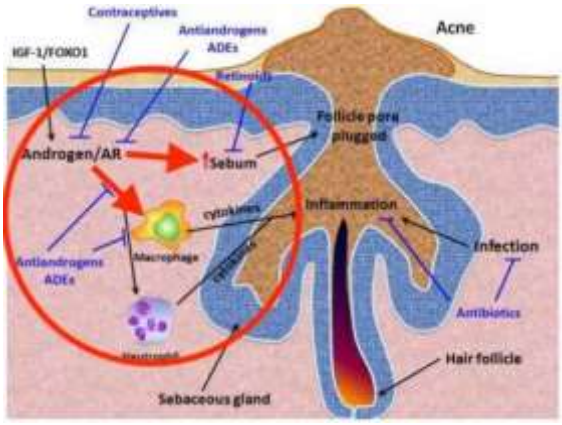


Figure 2: Androgens cause changes in the skin and directly drive

Inflammation Here are the three reasons why androgens cause acne;

1. The sebaceous glands are very rich in androgen receptors. As soon as androgens meet their receptors, the sebaceous glands produce more sebum. This causes greasiness of the skin and a build up of sebum in the pores. The sebaceous glands are also where the precursors are converted to Testosterone and DHT.

2. Androgens may also be important in ‘clogging’ hair follicles and causing comedowns to be formed.

HEA-S is a stimulator of inflammation. It causes T cells (a type of white blood cell) in the skin to produce IL2 and drives inflammation leading to acne spots

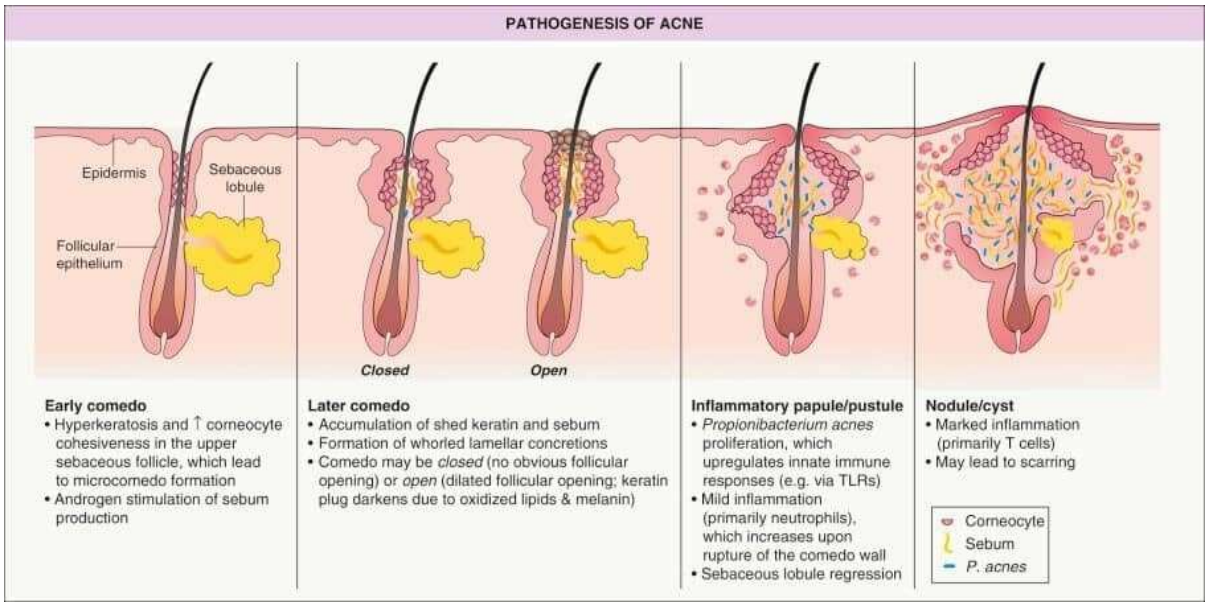


Fig. Acne formation. Schematic representation of the skin containing a sebaceous unit (part a) comprising the hair follicle and the sebaceous gland, which is responsible for sebum production. Acne formation starts when sebum and keratinous material shed from the skin clog up a pore and trigger bacterial colonization, leading to a closed or whitehead come done (part b). As the whitehead come done continues to expand, owing to more accumulation of sebum and keratinous material, the follicular orifice opens and forms an open or blackhead come done (part c). The black colour is the result of oxidized lipids and the skin pigment melanin. More distension of the come done results in follicular rupture and inflammatory lesions such as papules (part d), pustules (part e) and nodules or cysts (part f). Nodular acne is sometimes inaccurately referred to as 'cystic' or 'nodulocystic' acne. An acne cyst is not a true cyst as true cysts are lined by epithelium. Histological images of a pilosebaceous unit (part g), a comet done (part h)and an inflammatory lesion with rupture of the follicular walls (part I) are shown.

Diet:

The association between diet and skin disorder still must be elucidated. Studies are done showing a potential link between milk consumption and redoubled skin disorder lesions, however the info area unit weak. information examining chocolate and cooked food as potential triggers to skin acne are inadequate or conflicting. There appears to be an association between foods with high glycolic load and acne. It is propose that diets with high glycolic index can cause hypersinsulinemia, leading to increased androgen levels and sebum production.(18)

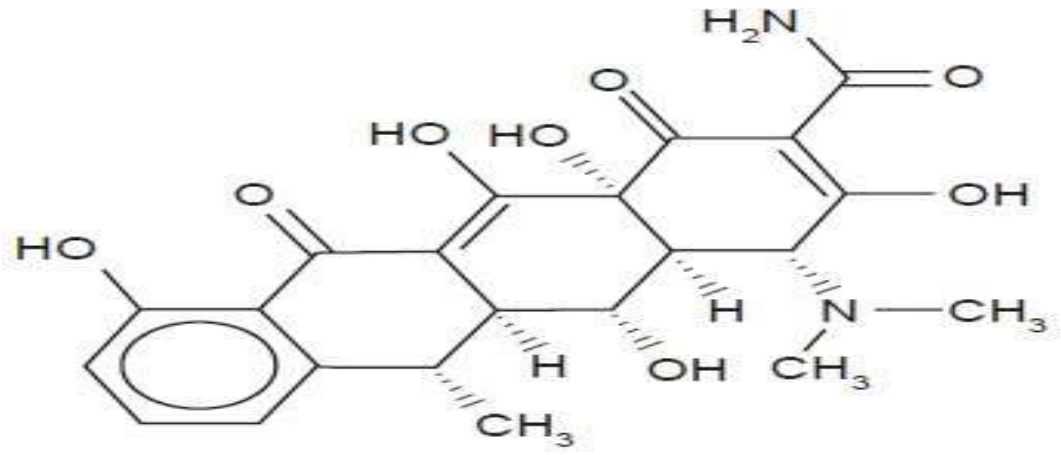
It has been proposed that milk also increasescomedogenicity through interactions with the IGF-1pathway. Milk, particularly skim milk, is positivelycorrelated with higher plasma IGF-1 levels.IGF-1 stimulates synthesis of androgens in both ovarian and testicular tissues and inhibits hepatic synthesis of sex hormone-binding globulin resulting in increased bioavailability of androgens. BothIGF-128 and androgens increase sebum production, which is implicated in acne. When broken down into categories of milk type, including whole, low fat, and skim, only skim milk showed a statistical correlation with acne. This may be surprising given that one might expect bovine hormones to be concentrated in the lipid fraction of milk.Theauthors hypothesized that the bioavailability of the factors responsible for comedogenicity of milk maybe increased by skim milk processing. (19)They also postulated that skim milk is more acnegenic because, in comparison with whole milk, skim milk contains less estrogens, a hormone known to reduce acne. It's unknown how processing affects hormone levels but it has been documented that fermentation that occurs with cheese production results in additional testosterone production from androgen precur-sBecause the association between milk and acne was more marked for skim milk, it was postulated that the fat content of milk itself was unlikely correlated to comedogenicity. In the study were also positive associations found between acne and instant breakfast drink, sherbet, and cottage cheese. These associations were attributed to the milk content of the foods.(20,21)However, dietary fish rich in omega-3 fatty acids can improve glycolic control, whereas processed meats can impair glycolic control. In addition, vegetable cooking technique can affect glycemicload. By focusing only on carbohydrates, the study failed to account for the impact of other foods. Interestingly, the levels of IGF-1 were significantly higher among patients with acne as compared with control subjects. Furthermore, the levels of IGFBP-3were significantly lower among patients with acne .(22)

Rosacea :

Rosacea may be a common condition characterised by transient or persistent central facial erythroderma, visible blood vessels, and sometimes papules and pustules. Because the facial skin is the predominant site of involvement, many patients sense that rosacea alters their social and professional interactions, leading to problems on the job, in their marriage, or in meeting new people. These common issues have led to the formation of a large active patient advocacy group, the National Rosacea Society, which produces newsletters, encourages research by offering grants, and distributes educational and supportive materials to professionals and patients. The expert panel recognized 4 subtypes of rosacea. The concept that patients present with a preponderance of one or a clustering of signs is most useful. Dermatologists recognize that some patients have solely persistent erythroderma cheeks while not papules and pustules. These patients often are the same ones who have dramatic histories of flushing to a wide variety of stimuli, who bitterly

complain of burning and stinging, and who often are intolerant of topically applied products. Contrast such patients with the sebaceous-skinned man with many papules, pustules, and even nodular erythematous lesions, and a background of central facial erythematic. Patients like him are often not ‘‘flushers and blushers,’’ have fewer, if any, symptoms of burning and stinging, and tolerate topical medications better than patients with ETR.[26,27]

Doxycycline in the treatment of Acne vulgarise and rosacea



Mechanism of Action

Doxycycline inhibits bacterial protein synthesis by reversibly binding to the 30S ribosomal subunit and preventing the association of aminoacyl-tRNA with the bacterial ribosome. Further inhibition of protein synthesis occurs in mitochondria through binding to the 70S ribosomes. It is therefore a bacteriostatic drug. Doxycycline enters the cell via hydrophilic pores in the outer cell membrane and a pH-dependent active transport system in the inner cytoplasm membrane. [29] It also inhibits apicoplast ribosomal subunits in *Plasmodium falciparum*, leading to impaired fatty acid synthesis and impaired heme biosynthesis late in the malarial cell cycle. [30]

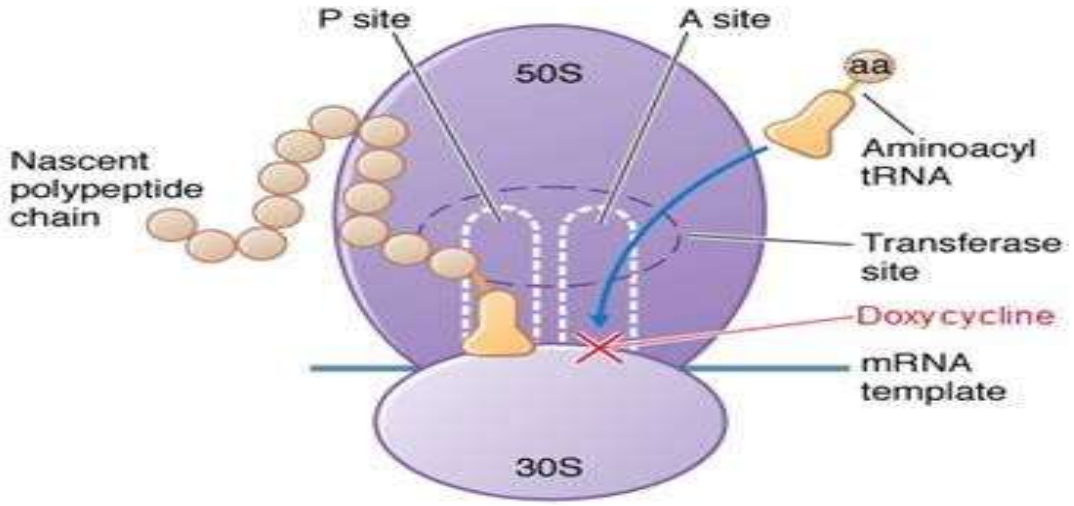


Figure 4: The doxycyclines combat two key factors in acne pathogenesis with their antimicrobial effect on C. acnes and their anti-inflammatory mechanisms. of the bacterial ribosome, which prevents acryl-transfer RNA from binding to the ribosome. Thus, protein synthesis is ceased which halts the growth.

Pharmacokinetic:

Doxycycline pharmacokinetics in the absence of renal function. Doxycycline is a new tetracycline that is now in widespread clinical use. It differs from the other tetracycline drugs in many important respects including small daily dosage schedules, essentially complete upper gastrointestinal absorption and excretory characteristics that are independent of renal function. Our studies demonstrate that in anaphoric patients and patients with varying degrees of renal function the plasma t½ of biologically active doxycycline is not significantly extended and that in such a clinical situation the usual therapeutic regimen of the drug is necessary. Clearance rate of the compound from the systemic circulation by haemodialysis is only 10ml/min or less. In addition, our investigations identify the importance of the nonhepatic gastrointestinal pathway of elimination of doxycycline from the systemic circulation. Doxycycline therefore appears to be unique among the tetracyclines in that it may be utilized as a drug of choice for the therapy of systemic infections when a tetracycline compound is indicated in the clinical setting of impaired renal function.[33]

Doxycycline Action

The first Achromycin by-product to come back to plug was antibiotic drug, approved by the agency in 1967 and still one amongst the foremost normally used antibiotics in clinical follow. Relative to its parent Achromycin, antibiotic drug is a lot of lip tropic, creating it optimum for penetrating and accumulating within the oily gland—where C. acnes resides and proliferates.[34] 2 formulations of antibiotic drug square measure available—doxycycline hyalite and antibiotic drug hydrate, that square measure completely different salt kinds of a similar active drug. antibiotic drug hyalite is a lot of soluble than antibiotic drug hydrate and may be a lot of ulcerogenic and prone to inflicting canal (GI)- associated facet effects.

Their differences are more relevant for manufacturing purposes than for assessing efficacy, however. The side effect profile of doxycycline is superior to that of tetracycline, although there are potential adverse events that should be.. Most of doxycycline's side effects are mild and/or can be prevented with proper measures. Doxycycline is frequently associated with phototoxicity; it interacts with ultraviolet (UV) rays, making an individual more susceptible to severe sunburn. Gastrointestinal disturbance is a common side effect of doxycycline treatment and might present as nausea, vomiting, and/or diarrhea.

Doxycycline is amenable to being loving food—which would possibly reduce GI discomfort— though its absorption is reduced by close to twenty % with food. once it's taken to treat skin disease, however, this reduction in absorption is believed to own bottom clinical connection. Pill esophagitis—inflammation or musculature ulcers—can occur once taking Vibramycin. Like alternative facet effects, however, it's mostly avertable if patients take medication with an outsized glass of water and don't lie shortly once ingesting medication. Lastly, there's the potential for tooth discoloration in people with developing teeth. this is often a facet result shared by all Achromycin derivatives that don't seem to be suggested for kids younger than eight years mature and ladies throughout physiological condition.

Comparison of Doxycycline and Minocycline

In 2005, Smith and Leyden systematically reviewed the literature on the adverse effects of doxycycline and minocycline (in all indications, not just acne).

Between 1966 and 2003 they identified 130 case reports on adverse events with doxycycline therapy and 333 case reports on adverse events with minocycline therapy. Since then, 13 further reports of minocycline and 1 report of doxycycline adverse events were added to. However, reports are not standardized, blinded, or controlled; they are biased, as severe or uncommon adverse events may be over-reported while common/well known effects may be under-reported. Furthermore, the relationship between a given adverse event and the drug of interest cannot be definitively determined if patients are taking multiple medications. Nevertheless, it appears that minocycline more often caused adverse effects of sufficient interest to justify publication. The adverse effects identified in case reports of doxycycline and minocycline are summarized in. In case reports, the most common adverse effects of doxycycline are phototoxicity and oesophageal erosions, which can be prevented by adequate behaviour, i.e. sun-protection measures and adequate fluid intake. Minocycline adverse effects, however, comprise a drug-specific hyper pigmentation and, especially, systemic immunologic reactions (hypersensitivity, hepatic dysfunction, and lupus-like syndromes) that cannot be prevented. Smith and Leyden also screened the published trials for adverse events of these two compounds. However, this approach also has limitations due to the inclusion of a controlled. There are no differences between doxycycline and minocycline with respect to gastrointestinal complaints. Doxycycline had a higher rate of phototoxicity and minocycline had a higher rate of CNS symptoms like dizziness. [44]

Patient Preference Doxycycline is inexpensive and available worldwide, and can be conveniently administered via oral or parenteral routes. This makes it practical for use in community and hospital settings. Excellent absorption and tissue distribution make it particularly useful for the severely ill patient compared with other antibiotics. Common adverse reactions such as gastrointestinal upset or oesophagi are can be prevented with careful attention to correct administration. Enteric-coated pellets have fewer gastrointestinal side effects. Photosensitivity can be prevented or ameliorated with adequate attention to sun protection. It is important to remind women that the efficacy of the contraceptive pill is reduced and that barrier methods of contraception are required during and after doxycycline therapy **[46]**

Dosage and Administration Doxycycline Is usually commenced with a starting dose of 200-mg daily, followed by a maintenance dose of 100-mg daily (or twice-daily for severe infections). It can be administered orally or intravenously. The oral dose should be taken with sufficient fluids and the patient should remain upright for 30 minutes following administration. The maximum recommended dose is 300-mg daily. In children, when doxycycline benefits outweigh the risks, a weight-adjusted dose of 2.2 mg/kg daily or twice daily is used. A higher loading dose of doxycycline, for example 200-mg twice daily for 72 hours, is recommended for optimal dose- dependent killing in serious infections. Variations exist with dosing and duration for specific indications, for example, malaria prophylaxis, syphilis, and scrub typhus. Lower doses, for example 20-mg twice daily, are used for acne

Gastrointestinal

Common symptoms include nausea, vomiting, diarrhoea and epigastria burning. More severe reactions include oesophagi is, oesophageal ulceration, and mediastinitis. The risk of oesophageal ulceration can be reduced with the use of enteric-coated preparations, and with the monohydrate (rather than hydrochloride) formulation. Patients should take doxycycline with sufficient fluids and remain upright for 30 minutes after administration to reduce symptoms. Doxycycline should be avoided in patients with oesophageal compression or obstruction. Other gastrointestinal effects include Clostridium difficult-associated diarrhoea, although this occurs less frequently than with other antibiotics such as clindamycin. Tetracycline-induced hepatotoxicity is increased in the presence of hepatic impairment, however the risk with doxycycline is lower or minimal compared with other tetracycline's. [47, 48]

Dermatological and hypersensitivity

Doxycycline may cause photosensitivity and photo-onycholysis. A wide variety of skin eruptions may occur, including erythematous, maculopapular and pustule rashes, prorates, urticaria and fixed drug eruptions. Rarely hypersensitivity and serum sickness reactions, Stevens-Johnson syndrome and toxic

epidermal necrolysis may occur. The Jarisch-Herxheimer reaction may occur when doxycycline is used for treatment of spirochete infections. Anaphylaxis has also been reported. [49, 50]

Bones and teeth

The accumulation of doxycycline in teeth and bones leads to discolouration of teeth and is more common in deciduous rather than permanent teeth. However if they are given to children whilst permanent teeth are still in development, this may lead to lifelong discolouration. Discolouration may also occur in permanent teeth, especially with concomitant poor dental hygiene and increased sunlight exposure. It may also cause enamel dysplasia and bone deformities and impairment in bone growth. Premature infants administered doxycycline demonstrated a 40% reduction in fibular bone growth that was reversible upon drug cessation

Pregnancy location and children

Doxycycline can be given during the first 18 weeks of pregnancy but is contraindicated after this time due to potential discolouration and malformation of fatal teeth. It is potentially teratogenic in animal studies. There was a minor increase in fatal abnormalities (odds ratio 1.6, 95% confidence interval 1.1–2.3) in a large survey of over 18,000 pregnancies; however another study of 1795 doxycycline-exposed pregnancies demonstrated no increased risk of fatal abnormalities. High doses of doxycycline have been associated with fatty necrosis of the liver in pregnant women, especially those with pyelonephritis. A short course of doxycycline for 7 to 10 days is considered safe during breast- feeding if there are no other alternatives available.

Conclusion

This review focus on safety and efficacy of doxycycline it is used to treat bacterial infections in many different parts of the body. Oral antibiotics have been used for the treatment of acne vulgarise for six decades. Among dermatologists, tetracycline represents at least three-fourths of the oral antibiotics prescribed in clinical practice. Unlike other specialties, antibiotic use in dermatology is predominantly for the treatment of non-infectious disorders, such as acne vulgarise and rosacea, which usually involves prolonged therapy over several weeks to months as compared to short courses used to treat coetaneous infections.

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