

Effect of oxytetracycline and doxycycline on muscle tone in healthy human volunteers

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ABSTRACT

Background: Reduced grip strength is associated with adverse health consequences, and therefore there is interest in identifying modifiable influences. Tetracyclines are commonly used antibiotics, but their effect on muscle strength is unclear.

Methods: We investigated associations between oxytetracycline, doxycycline and grip strength among 15 healthy human volunteers pre and post administration of test drug. The test drugs were administered at doses of oxytetracycline 500 mg and doxycycline 100 mg and the effect of test drugs on grip strength using jamar hand grip dynamometer was assessed.

Results: Oxytetracycline was associated with a significant decrease in average grip strength of both right and left hand.

Conclusions: Use of oxytetracycline is associated with reduced grip strength in healthy human volunteers. These findings have potential implication on the functional ability of muscle.

Keywords: Tetracyclines, Oxytetracycline, Doxycycline

INTRODUCTION

Neuromuscular blockade is a recognized clinical side effect of the use of aminoglycoside antibiotics, and prolonged respiratory depression may occur when aminoglycosides are used in conjunction with anaesthetic agents or neuromuscular blocking drugs.¹ Most of the experimental evidence indicates that the aminoglycosides possess both pre- and postjunctional blocking actions.^{2,3} Patients receiving antibiotic medications for the treatment or prophylaxis of infection are often encountered during anesthetic practice.⁵ The main concern for anaesthesiologist in this setting is the action of these antibiotics on the neuromuscular system.⁶ Most antibiotic depress neuromuscular conduction because they have pre and post synaptic inhibitory effects at the neuromuscular junction.^{7,8}

Doxycycline and oxytetracycline are broad spectrum antibiotics use to treat many types of bacterial infection, gram negative and gram positive microorganisms. Doxycycline is the new generation tetracycline widely used clinically as compared to older counterpart oxytetracycline. They differ in their pharmacokinetic profiles (bioavailability, elimination, plasma half life, potency and toxicity profile). Tetracyclines are known to be 'calcium chelators' resulting in deformation of bone and teeth.

As tetracyclines, chelates calcium there may be chances of relaxation of the contracting muscles as muscles require calcium for contraction.⁹ Oxytetracycline is the first generation tetracycline which is still used in the therapy. Doxycycline is second generation tetracycline which is more commonly used in therapy therefore these two drugs were taken for comparison. The effect of

calcium chelation on neuromuscular activity has not been reported. Therefore, it would be meaningful to study the effect of tetracycline on neuromuscular junction.

METHODS

All the experiments were performed after permission from the Institutional ethics committee, MGM Medical College Kamothe, Navi Mumbai, Maharashtra, India. Informed consent was taken from volunteers prior to the study.

Drugs used

The following drugs were used in the study: oxytetracycline 500 mg (Pfizer Ltd. Bangalore, India) and doxycycline 100 mg (Omega Biotech Ltd. Utrakhhand, India).

Grip strength test using jamar hand grip dynamometer

Study participants comprise of 15 healthy volunteers for each drug. For measuring the grip strength, the subjects were asked to sit on a chair with their hip joint flexed at 90 degree, and shoulder joint in a neutral position. The elbow was fixed at 90 degree flexion, forearm in a neutral position, and wrist at 0 degree to 15 degree radial deviation.¹⁰ Grip strength was measured three times on each side using a Jamar handgrip dynamometer, before and after administration of drug. The volunteers were given drug orally with a glass of water and the best of the average was used to characterise maximum muscle strength. The subjects were allowed a rest time of more than 5 minutes after the first measurement to avoid examiner bias and to decrease physical stress.

Statistical analysis

All the results were expressed as mean±SEM and the data were analysed using paired t test. A p value of <0.05 was considered as the level of significance.

RESULTS

Table 1: Effect of oxytetracycline and doxycycline on grip strength.

Treatment	Dose	Right Hand		Left Hand	
		Pre	Post	Pre	Post
Oxytetracycline	500 mg	27.48±5.8	24.41±7.0*	26.48±6.6	24.12±7.8*
Doxycycline	100 mg	31.28±6.7	31.15±8.3	28.75±7.1	28.57±7.4

*p<0.05 versus Baselines values.

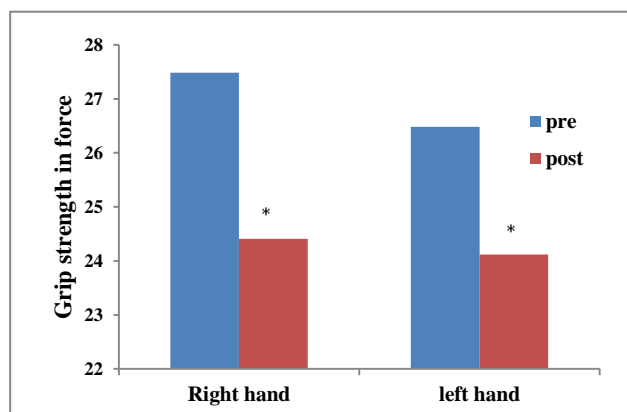


Figure 1: Effect of oxytetracycline on grip strength.
*p<0.05 versus baselines values.

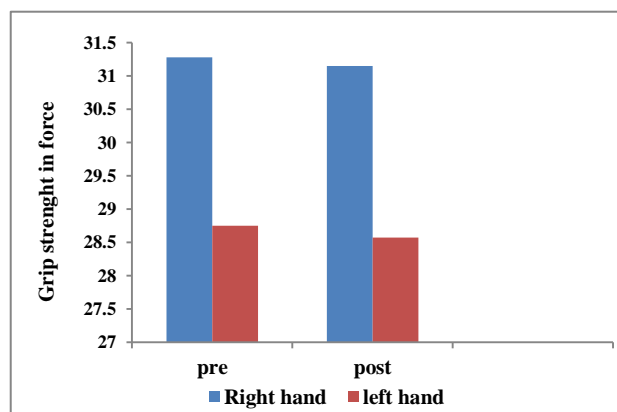


Figure2: Effect of doxycycline on grip strength.

Average grip strength reduced post administration of drug in both right hand as well as left hand with oxytetracycline but in case of doxycycline there was no difference in relation to post administration of the drug in both the hands. Oxytetracycline was associated with reduction in grip strength (p=0.04) in right hand, (p=0.07) in left hand. There was no significant association between grip strength and doxycycline (Table 1).

DISCUSSION

Tetracycline is active against a wide range of gram negative and gram positive organism.⁹ The drugs in the tetracycline class have closely similar antimicrobial spectra, and cross resistance among them is common.

Tetracycline is indicated in the treatment of upper respiratory tract infections caused by streptopyogens,

streptococcus pneumonia, and hemophilus influenza. Lower respiratory tract infections caused, skin and soft tissue infections. Infections caused by rickettsia including rocky mountain spotted fever, typhus group infections, Q fever, rickettsialpox. Psittacosis of ornithosis caused by chlamydia psittaci. Infections caused by chlamydia trachomatis such as uncomplicated urethral endocervical or rectal infections, inclusion conjunctivitis, trachoma and lymphogranuloma venerum. Granuloma inguinale, relapsing fever caused by borrelia species. Chancroid, trulaemia, plague, cholera, brucellosis, infections due to campylobacter fetus. As adjunctive therapy in intestinal amebiasis caused by entamoeba histolytica. Urinary tract infections caused by susceptible strains of escherichia coli, klebsiella.¹¹ Other infections caused by susceptible gram negative organism. In severe case of acne adjunctive therapy with tetracycline is useful. When penicillins are contraindicated tetracyclines are alternative drugs in the treatment of syphilis, vincent's infection, anthrax, infection due to listeria, actinomycosis caused by actinomyces species, Infections due to clostridium species. The drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines.

Doxycycline is more potent, well absorbed, highly plasma protein bound, excreted in faeces as conjugate hence safe in renal diseases. Whereas oxytetracycline is eliminated from kidney. Markedly alter intestinal flora, incidence of diarrhoea, phototoxicity is high as compared with doxycycline. Plasma half-life of doxycycline is 18-24 hours that of oxytetracycline is 6-10 hours. Bioavailability of oxytetracycline is 75% and that of doxycycline is 95%. Oxytetracycline is given in the dose of 500 mg whereas doxycycline 100-200 mg.

This study demonstrated that the use of oxytetracycline is associated with reduced grip strength in healthy human volunteers. These findings may reflect a direct adverse effect of oxytetracycline on muscle function. These findings have potential implication on the functional ability of muscle.

The reduction in grip strength associated with oxytetracycline in the study is clinically relevant. Ensurd et al have shown that 5 kg reduction in grip strength is associated with an odds ratio of 1.5 for other functional limitations associated with reduced grip strength include walking impairment, lower self-reported physical function.¹² Alternatively these medications may only have an appropriate effect on muscle of lower strength.

Tetracyclines are primarily bacteriostatic and exert their antimicrobial effect by the inhibition of protein synthesis. Tetracyclines have chelating property, hence are deposited in growing bones and teeth and form tetracycline calcium orthophosphate. Calcium chelation of tetracycline may be reason of decrease muscle tone or may relax muscle as calcium is important part of muscle contraction. In our study we found that oxytetracycline

significantly decreases average grip strength of both right and left hand.

It has been known for more than 20 years that certain antibiotics can induce neuromuscular paralysis.¹³ Prolonged neuromuscular blockade is well known adverse drug reaction that follows administration of antibiotics. It is likely; the neuromuscular effects of antibiotics will be accentuated when they are used in combination with muscle relaxants. The adverse effect at neuromuscular junction of certain antibiotic like aminoglycoside, fluoroquinolones, polymixin and antimalarial drugs like chloroquine, quinine, mefloquine has already been reported.

If at all these antibiotics have any effect on neuromuscular junction in situations where a neuromuscular blocker has been previously administered to patient, it can produce drug interaction or potentiate neuromuscular blocker.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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