Research Article

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

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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. Most of the experimental evidence indicates that the aminoglycosides possess both pre- and postjunctional blocking actions. Patients receiving antibiotic medications for the treatment or prophylaxis of infection are often encountered during anaesthetic practice. The main concern for anaesthesiologist in this setting is the action of these antibiotics on the neuromuscular system. Most antibiotic depress neuromuscular conduction because they have pre and post synaptic inhibitory effects at the neuromuscular junction.

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. 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

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
钙化结合对神经肌肉活动的影响尚未被报道。因此，研究四环素对神经肌肉接头的影响是具有意义的。

**METHODS**

所有实验均在获得印第安纳大学及MGMO光学部门伦理委员会许可后进行，所有被试均签署知情同意书。实验前，志愿者被要求进行适当的练习，以便在实验过程中尽可能地输出力量。

**Drugs used**

所有药物均来自研究：氧四环素500mg（Pfizer Ltd. Bangalore, India）和多西环素100mg（Omega Biotech Ltd. Uttrakhand, India）。

**Grip strength test using jamar hand grip dynamometer**

平均握力下降了3.15%。多西环素组的右左手平均握力下降了4.11%和7.0%，而氧四环素组的右左手平均握力下降了4.41%和7.0%。所有结果均通过配对t检验进行分析。p值小于0.05被认为是具有统计学意义的。

**RESULTS**

平均握力下降了3.15%。多西环素组的右左手平均握力下降了4.11%和7.0%，而氧四环素组的右左手平均握力下降了4.41%和7.0%。所有结果均通过配对t检验进行分析。p值小于0.05被认为是具有统计学意义的。

**DISCUSSION**

四环素是针对广泛且广泛的革兰氏阳性细菌和革兰氏阴性细菌的抗菌药物。

四环素在治疗上呼吸道感染时被广泛使用，因为它能够与streptopyogens产生交叉耐药性。
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 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, actinimycosis 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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