

The clinical efficacy (reduction of symptoms, global assessment by patient and physician) was similar between the two treatment groups.

**Conclusion:** The IPD meta-analysis using objective parameters (elimination of bacteriuria) demonstrated equivalent efficacy (non-inferiority) of nitroxoline with the controls tested (cotrimoxazole, norfloxacin) in the treatment of uUTI. With a five (sporadic uUTI) or ten day (recurrent uUTI) therapy elimination of bacteriuria can be achieved in over 90% of the patients. Considering the good safety and efficacy of nitroxoline and the world wide increase of resistance of uropathogens against cotrimoxazole and fluoroquinolones, but not against nitroxoline within the last 20 years, nitroxoline should be reconsidered as one of the first line antibiotics for the treatment of uUTI.

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#### Repurposing avermectins as new potential TB therapies



S. Ramon-Garcia<sup>1,\*</sup>, G. Sweet<sup>1</sup>, A. Lenaerts<sup>2</sup>, C. Thompson<sup>1</sup>

<sup>1</sup> The University of British Columbia, Vancouver, BC, Canada

<sup>2</sup> Colorado State University, Ft. Collins, CO, USA

**Background:** Tuberculosis (TB) is a major cause of morbidity and mortality worldwide. Co-infection with HIV and the emergence of drug-resistant *Mycobacterium tuberculosis* strains (MDR- and XDR-TB) has reaffirmed TB as a global public health threat. New therapies are urgently needed. An alternative approach to generate new TB treatment options in a timely and cost-effective manner is “repurposing” clinically used drugs with known pharmaceutical properties. In the course of a screening program [PMID: 21576426], we identified the *in vitro* anti-tuberculosis activity of the anthelmintic avermectins (ivermectin, selamectin, moxidectin and doramectin) [PMID: 23165468].

**Methods & Materials:** We performed a literature search on the pharmacological properties of the avermectins. We integrated this information with our *in vitro* data and calculated a theoretical pharmacodynamic value (AUC/MIC; a measure of drug exposure) to define potential *in vivo* efficacy. We validated our analysis by evaluating avermectins in an *in vivo* model of *M. tuberculosis* infection.

**Results:** An AUC/MIC ratio of 10 to 15 was calculated for bactericidal activity of the avermectins. Due to tolerability and pharmacokinetic issues the low maximal plasma concentrations of ivermectin (ng/mL range) resulted in a low calculated exposure (AUC/MIC < 1). Moxidectin had a longer half-life than ivermectin and, therefore, the calculated AUC/MIC ratios increased. However, this was still not enough to provide theoretical *in vivo* activity. In contrast, selamectin’s pharmacokinetic properties suggest that it might be effective *in vivo* against *M. tuberculosis*; high plasma concentrations (μg/mL range), low toxicity (LD<sub>50</sub> >1,600 mg/kg bw), and theoretical AUC/MIC ratios are consistent with potential *in vivo* activity. Interestingly, reported concentrations of selamectin in the lungs (the main site where *M. tuberculosis* resides) were ca. 2-fold higher than in plasma, suggesting even higher AUC/MIC ratios at

the site of infection. We therefore tested ivermectin and selamectin for *in vivo* activity against *M. tuberculosis*. Our predictions were consistent with the *in vivo* data; while ivermectin at the highest possible safe dose did not have anti-mycobacterial activity *in vivo*, selamectin was active.

**Conclusion:** This theoretical data analysis supports the potential of selamectin for TB therapy, including MDR- and XDR-TB, and warrant further *in vivo* testing in mouse infection models.

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#### The life saving little tip: Intraosseous gas



A. Kivrak<sup>1,\*</sup>, S. Sumer<sup>1</sup>, N. Aktug Demir<sup>1</sup>, B.K. Aydin<sup>1</sup>, S. Ozcimen<sup>2</sup>

<sup>1</sup> Selcuk University, Faculty of Medicine, Konya, Turkey

<sup>2</sup> Konya state hospital, Konya, Turkey

**Background:** Emphysematous osteomyelitis is a rare but fulminant disease. Therefore, radiologists should be aware of the implication of intraosseous gas signs for quick diagnosis.

**Methods & Materials:** Case: A 55-year-old woman with diabetes mellitus and hypertension was admitted to the emergency department and presented with high fever (40°C), nausea, and pelvic pain. Physical examination revealed pelvic and pubic tenderness on deep palpation. Laboratory data included leukocytosis (12390/mm<sup>3</sup> with 85.5% neutrophils), high procalcitonin (33.8 ng/ml), C-reactiveprotein (211 mg/dl) levels, a high sedimentation rate (80 mm/h), also elevated blood sugar (290 mg/dl), and elevated hemoglobin A1C level (13.4%). Blood cultures were obtained prior to the initiation of antimicrobial therapy.

Abdominal ultrasonographic examination revealed cholelithiasis without gallbladder wall thickening and a small amount of isolated pelvic free fluid. A subsequent CT of her abdomen and pelvis showed multiple gas bubbles in the medullary cavity of the bilateral pubic bones, extending into the anterior acetabulum. A moderate amount of gas was seen in the soft tissues surrounding the pubis. Also, marked subcutaneous reticulation and low attenuation areas of subcutaneous gas were detected in the right gluteal region. MRI confirmed the CT findings and provided clearer images of the small abscess formations and the peripubic soft tissue component of the infection. CT-guided biopsy of prepubic soft tissue collection was performed, and *Escherichia coli* was cultured from the diagnostic specimen.

**Results:** Intravenous (IV) imipenem cilastatin (4 × 500 mg) and vancomycin (2 × 1 g) was started as an empirical treatment. The patient underwent urgent surgical debridement of the soft tissue abscess. All samples (biopsy-surgical specimens and blood cultures) revealed a monomicrobial growth of *E. coli*. Intravenous ciprofloxacin (2 × 400 mg) was started based on the antibiogram results. The first 3 weeks of treatment was completed as IV therapy. The patient was discharged with oral antibiotic treatment (ciprofloxacin 2 × 750 mg). The patient’s treatment was completed in 6 weeks. No complications were seen and she continues to be followed up.

**Conclusion:** In conclusion, we want to emphasize two points. First, emphysematous osteomyelitis is a rare but fulminant disease. Second, infections in diabetic subjects will be more serious than in non-diabetic patients.

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**A novel therapeutic approach in tetanus: Botulinum toxin**



N. Aktug Demir<sup>1,\*</sup>, S. Ozturk<sup>1</sup>, S. Sumer<sup>1</sup>, O. Ural<sup>1</sup>, J.B. Çelik<sup>1</sup>, S. Ozcimen<sup>2,\*</sup>

<sup>1</sup> Selcuk University, Faculty of Medicine, Konya, Turkey

<sup>2</sup> Konya state hospital, Konya, Turkey

**Background:** Here, we presented a tetanus case treated with botulinum toxin, which is reported in a small number of cases in the literature.

**Methods & Materials:** A 73-year-old male patient had a puncture wound to the sole of his left foot caused by a wood splinter 10 days earlier. Patient received tetanus shot the same day but did not have wound care or immunoglobulin administration. On day 7 of the injury, the patient sought medical attention from a number of medical care facilities for trismus and presented to our Outpatient Clinic on day 10. Physical examination showed trismus, risus sardonicus and a wound with necrotic crust on the sole of the left foot measuring 1x1 cm. Laboratory findings were unremarkable besides elevated creatinin phosphokinase of 967 U/L (N: 30-200 U/L). The patient was admitted with tentative diagnosis of tetanus.

**Results:** Surgical drainage and debridement was carried out and tetanus toxoid and tetanus immunoglobulin was administered. Patient was placed on intravenous metronidazol 500 mg QID empirically. The patient was transferred to Anesthesiology and Reanimation Unit when contractions started 6 hours after being admitted. Sedation was achieved by Phentanyl and Dormicum. Upon development of severe contractions and signs of autonomic dysfunction, sedation was increased and the patient was placed on mechanical ventilator. Sedation was reduced intermittently but could not be discontinued due to ongoing contractions. Patient did not experience an alleviation in contractions even after a week of treatment and on day 8 of admittance, a total of 300 units of botulinum toxin was administered bilaterally into the masetter, trapezius, quadriceps and rectus abdominis muscles. By this, we aimed to prevent the complications of tetanus, especially respiratory failure. Following the administration, reduction in contractions were observed and the patient is currently under follow-up.

**Conclusion:** Tetanus is a serious infectious diseases characterized by complications secondary to contractions. Botulinum toxin is a new therapeutic modality tried in a limited number of cases to prevent many complications including respiratory failure.

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**Evaluation of urinary infections in elderly patients**



S. Ozcimen<sup>1,\*</sup>, M. Ozcan<sup>2</sup>, H. Karatas<sup>2</sup>, A. Sakiz<sup>2</sup>, F. Kacar<sup>2</sup>, F. Korkmaz<sup>2</sup>, L.S. Demir<sup>3</sup>

<sup>1</sup> Konya state hospital, Konya, Turkey

<sup>2</sup> Konya training and research hospital, Konya, Turkey

<sup>3</sup> Konya Public Health, Konya, Turkey

**Background:** The impairment in function of the cellular and humoral immune cells and deterioration in physiological defense mechanism in elderly makes them prone to infectious diseases. The urinary tract infections in elderly constitute 25% of the community-acquired bacterial infections.

**Methods & Materials:** The records of patients over 65 years-old diagnosed as urinary tract infection (UTI) according to Centers for Disease Control and Prevention criteria were retrospectively evaluated.

**Results:** Fifty-six patients diagnosed as UTI were included in the study. Of the 56 patients recruited, 27 were male (48.2%) and 29 were female (51.8%) and the mean age of the females was 75.5±7.1 years, and the mean age of males was 76.8±7.5. Of the total number of UTI, 75% were community-acquired and 25% were nosocomial. The urine cultures of the female patients yielded Extended Spectrum Beta Lactamase (ESBL) positive E. coli in 7 cases, ESBL negative E. coli in 9 cases, pseudomonas aeruginosa in 1 case and no pathogen in 12 cases. The urine cultures of the male patients yielded ESBL positive E. coli in 8 cases, ESBL negative E. coli in 4 cases, ESBL positive Klebsiella pneumonia in 3 cases, pseudomonas aeruginosa in 1 case, Enterococcus avium in 1 case, Meticilline resistant coagulase negative stafilococcus in 1 case and no pathogen 9 cases. Culture was negative in patients who has received antimicrobial treatment before. The UTI was treated in 51 patients.

**Conclusion:** Bacteriuria is frequent in geriatric population. The most encountered pathogen was E. Coli in this age group. There are many risk factors predisposing to infections in elderly patients: deterioration in immune functions, diabetes mellitus, prostatism and long hospitalization. The most significant predisposing factor was diabetes mellitus in elderly patients diagnosed as UTI.

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