**Background:** Dexmedetomidine (DXM), is a selective $\alpha_2$-adrenoreceptor agonist agent that used because of its sedative, anxiolytic and analgesic effect. Dexketoprofen (DXT), which used for analgesic properties, is a non-selective nonsteroidal anti-inflammatory drug. In this study, we aimed to investigate and compare DXM and DXT effects on the peripheral nerve transmission.
**Material and Methods:** Isolated rat sciatic nerves which were transferred to the nerve chamber includes Krebs solution, were stimulated by standard square wave pulse protocols. The compound action potentials (CAPs) were recorded from stimulated nerves with electrophysiological methods. DXM (n = 8) and DXT (n = 8) were administered in the nerve chamber with cumulative concentrations (10-9 to 10-5 M) and CAPs were recorded for 5th and 10th minutes. The area under a CAP waveform, maximum depolarization values, maximum derivatives, latency periods and conduction velocity of the CAPs were calculated.
**Results:** In this in vitro study, both of DXM and DXT, significantly depressed all CAPs parameters in a dose dependent and reversible manner ($P < 0.05$). The significantly differences were found between DXM and DXT in terms of the nerves transmission inhibition ($P > 0.05$).
**Conclusions:** Higher doses of DXM were found to suppress the transmission of fast conducting fibers, but DXT was found to suppress the time-dependent effects on the slow conducting fibers, the dose-dependent effect on medium and fast conducting fibers.

## GENERIC OLANZAPINE SUBSTITUTION IN PATIENTS WITH SCHIZOPHRENIA: ASSESSMENT OF SERUM CONCENTRATIONS AND THERAPEUTIC RESPONSE AFTER SWITCHING

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**Introduction:** Several reports of loss of efficacy or adverse effects have been described after generic substitution of antipsychotics. To date, studies comparing serum drug levels in patients switched to generic antipsychotics in a standard clinical setting are lacking. The aim of this study was to investigate if switching to generic olanzapine in patients affected by schizophrenia is associated with differences in its serum concentrations and therapeutic response.
**Methods:** Pre- and post-switching serum olanzapine concentrations were compared in schizophrenic outpatients who were switched from a chronic treatment with branded olanzapine to the same dose of its generic alternative. The Positive and Negative Syndrome Scale (PANSS) was concurrently administered to assess modifications in schizophrenia symptom control.
**Results:** A total of 25 patients (13 females and 12 males, mean age 41.2 ± 12.8 years) concluded the study. Mean olanzapine dose was 12.2 ± 5.4 mg/day. The mean olanzapine serum concentrations decreased from 27.7 ± 14.4 ng/mL during treatment with the branded formulation, to 22.6 ± 12.3 ng/mL after the switching to the generic formulation ($P < 0.01$). The log-transformed ratio of generic/brand-name olanzapine serum concentration at steady-state was 0.81 (90% CI: 0.72–0.91). Total PANSS scores did not significantly change after switching from branded to generic formulation (49.6 ± 8.3 vs 48.6 ± 9.5, $P = 0.777$). No patient exhibited disease relapse or required dose adjustment after switching.
**Conclusions:** Significantly lower serum olanzapine concentrations were found after switching from branded to generic olanzapine. Although these modifications did not significantly impair schizophrenia symptoms control, it cannot be excluded that a longer exposure to lower olanzapine serum concentrations may result in relapse of schizophrenic symptoms. Generic substitution should be considered as an indication for therapeutic drug monitoring in psychiatry.

## THE CYP 2C19*2 AND CYP2C19*17 POLYMORPHISMS PLAY A VITAL ROLE IN PLATELET RESPONSIVENESS TO CLOPIDOGREL AFTER PERCUTANEOUS CORONARY INTERVENTION: A PHARMACOGENOMIC STUDY

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**Background:** Clopidogrel inhibits platelet activation and aggregation by blocking the P2Y12 receptor. Dual antiplatelet therapy with clopidogrel and aspirin is recommended treatment by current guidelines for patients undergoing percutaneous interventions. Recurrent ischemic cardiac events after this treatment showed the lack of platelet responsiveness to clopidogrel and defined as clopidogrel resistance. Several mechanisms have been implicated in the development of clopidogrel resistance, but genetic variations have a most pronounced effect. Therefore, we aimed to investigate the most noticeable variations in the genes involved in clopidogrel pharmacokinetics and pharmacodynamics.
**Material and Methods:** Three hundred forty-seven Turkish patients underwent elective or emergency percutaneous coronary interventions with stent implantation are included in our study. Platelet reactivity (PRU) and % inhibition were measured with VerifyNow P2Y12 assay in blood samples collected from patients that took a standard dose of clopidogrel (75 mg/day) for at least 7 days. The variations in the CYP2C19, CYP3A4, CYP2B6, ABCB1, ITGB3 and PON1 genes are genotyped using the Sequenom MassARRAY system.
**Results:** When grouped the patients with PRU values >208 as resistant to clopidogrel, it was determined that 104 (30%) patients were resistant and 243 (70%) patients were nonresistant. A significant association was found between CYP2C19*2 (G636A) polymorphism and clopidogrel resistance ($\chi^2 = 25.09$, $P < 0.001$). A allele frequency of this polymorphism was high in patients with resistance, its odds ratio was 2.92 compared to G allele ($P < 0.001$, 95% CI, 1.91-4.46). PRU values of CT genotypes were lower ($P = 0.029$) and % inhibition values of CT genotypes were higher ($P = 0.008$) compared to CC genotypes for CYP2C19*17 (C806T) polymorphism. None of the other genetic variations was found to be statistically associated with clopidogrel resistance and antiplatelet response.
**Conclusions:** Our findings suggest that CYP2C19*2 polymorphism is associated with clopidogrel resistance and CYP2C19*17 polymorphism enhances antiplatelet activity of clopidogrel. According to genotype status of these two polymorphisms, clopidogrel-treated patients can be protected from stent thrombosis.

## TOXIC TOBRAMYCIN LEVELS AFTER TOBRAMYCIN INTAKE VIA SELECTIVE DECONTAMINATION OF THE DIGESTIVE TRACT (SDD)

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**Background:** Intensive Care Unit (ICU) patients in our hospital are treated for selective decontamination of the digestive tract (SDD). In SDD tobramycin is given as mouth paste and oral suspension, dosing 4–8 times a day 80 mg. High trough blood levels of tobramycin can