**Title**: Oral Versus Intravenous Diphenhydramine for the Prevention of Prochlorperazine-induced Extrapyramidal Symptoms

**Authors**: Aaron Effoe, PharmD; Kelsey Billups, PharmD, BCPS; Erin Weeda, PharmD, BCPS; Lindsey Jennings, MD, MPH

**Practice Site**: Medical University of South Carolina; Charleston, SC

**Background**: Prochlorperazine is an effective and commonly used agent for headache, nausea, and vomiting in the emergency department (ED). Prochlorperazine is a first-generation antipsychotic with dopaminergic blocking properties. One of the most common adverse effects seen with dopamine antagonists are extrapyramidal symptoms (EPS) such as akathisia, tardive dyskinesia, and dystonic reactions. These symptoms can occur with multiple or single doses. To prevent these adverse events, diphenhydramine is often given concurrently with prochlorperazine.

**Purpose**: Previous studies have only evaluated intravenous (IV) diphenhydramine in the prevention of prochlorperazine-induced akathisia. However, IV diphenhydramine may not always be preferred given its sedating properties and potential for abuse. Therefore, in practice, either IV or oral diphenhydramine is used at the discretion of the provider. The purpose of this study is to compare the incidence of EPS in patients that receive IV push versus oral diphenhydramine.

**Methods**: The electronic medical record (EMR) system will identify the following patients for study inclusion: those who received IV push prochlorperazine 10 mg, received either IV or oral diphenhydramine 25 mg, were seen and discharged from the main hospital ED, those 18 years old and older, and those given an ICD code for nausea/vomiting or headache. Patients will be excluded based on the following: pre-existing motor disorders (e.g. Parkinson’s Disease, restless leg syndrome) or administration of a dopamine antagonist prior to prochlorperazine administration. The primary outcome is to evaluate the incidence of EPS in patients receiving IV push versus oral diphenhydramine. EPS episodes will be identified by documentation in the patient EMR or additional doses of diphenhydramine or benzodiazepines. Secondary outcomes include time from treatment to ED discharge, and treatment failure defined by additional medications given for headache, nausea, or vomiting. The following data will be collected: gender, date of birth, indication for prochlorperazine, time of prochlorperazine administration, route and time of diphenhydramine administration, other medications given during the ED visit such as additional anticholinergic agents, time of arrival and discharge from the ED.

**Results**: Of the 150 patients that received IV diphenhydramine, four (3%) experienced an EPS event, compared to seven (5%) of the 150 patients that received oral diphenhydramine (p = 0.357). However, patients that received oral diphenhydramine had a shorter ED visit compared to those that received the IV formulation (117 minutes vs 122 minutes; p = 0.009). There was a higher incidence of treatment failure in the patients that were administered the oral formulation compared to the IV formulation (65 (43%) vs 47 (31%); p = 0.032).

**Conclusion**: There is no difference in efficacy between oral or intravenous diphenhydramine for preventing prochlorperazine-induced EPS events. The oral formulation can be considered equally effective for the prevention of prochlorperazine-induced EPS as the IV formulation based on the results of this study. Though the ED visit time was shorter in patients that received the oral formulation, there was not a clinical difference between the two groups. However, there was an increase in treatment failure in patients receiving oral diphenhydramine.