Prophylactic Anticholinergic Medications to Prevent Drug-Induced Extrapyramidal Symptoms: A Systematic Review

THE UNIVERSITY OF ARIZONA College of Medicine Phoenix

Reese Dare, J. Stephan Stapcyznski MD, Paul Kang MPH, John Sarko MD

Introduction

Extrapyramidal symptoms (EPS) are a set of hyperkinetic movement disorders usually stemming from use of neuroleptic medications, such as haloperidol, or related medication, such as metoclopramide, an anti-emetic. This review focused on two common acute EPS; dystonia and akathisia. Medications with known extrapyramidal side effects are utilized in an emergency setting frequently. Haloperidol is commonly used for pharmacologic control of acutely psychotic patients, agitated patients and general sedation. Metoclopramide can be used to control severe nausea and vomiting, and is also used in the treatment of acute migraine headache. It is well understood that anticholinergic medications may be used in the treatment of EPS. However, their emergence is often distressing to patients and can have negative impact on patient throughput in an acute setting.

Research Question: Are prophylactically administered adjunctive anticholinergic medications effective in preventing extrapyramidal symptoms resulting from treatment with medications in an acute setting?

Methods

We electronically searched the following internet websites: Central, DARE, LILCS, PubMed, CINAHL, and OVID between January 2014 and February 2016. Search Terms: RCTs, Psychomotor Disorders, Anticholinergic, Antipsychotic Agents, Metoclopramide, Cholinergic Antagonists, Haloperidol Movement Disorders.

The inclusion criteria for the studies were:

- Randomized controlled trials
- An anticholinergic (benztropine, diphenhydramine) was given adjunctively or prior to treatment with medications with known extrapyramidal side effects.
- The patient was treated with a medication with known extrapyramidal side effects (metoclopramide, haloperidol, prochlorperazine etc.)

Results

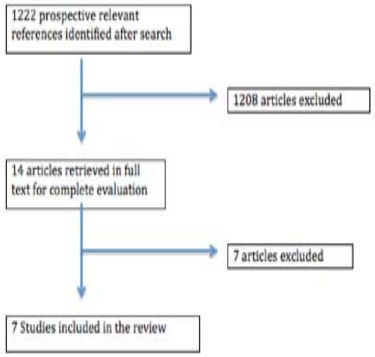

Figure 1: Search Strategy utilized in the review process.

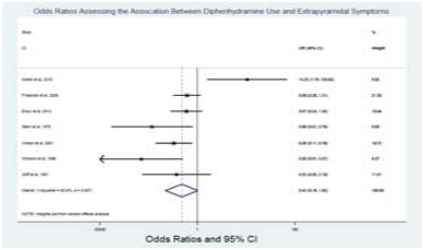

***Figure 4**:This figure demonstrates that utilization of diphenhydramine, as an adjunct medication in the prevention of EPS is significant. With an odds ratio of 0.43 there is a 57% overall reduction of risk by utilizing diphenhydramine adjunctively.*

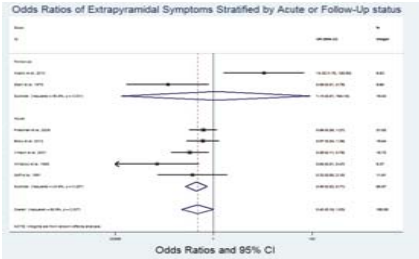

***Figure 2**: This figure demonstrates a significant effect of utilizing adjunct medications in the prevention of EPS in an acute setting. In studies where follow up was greater than 60 minutes, there is no significant benefit. The risk reduction in an acute setting is 60%.*

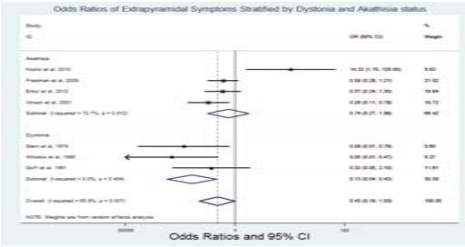

***Figure 3**:This figure demonstrates that utilization of adjunct medications to prevent dystonia is more significant that utilization to prevent akathisia. Utilization of adjunctive medication results in a decrease in risk of 87% and 26% for dystonia and akathisia respectively.*

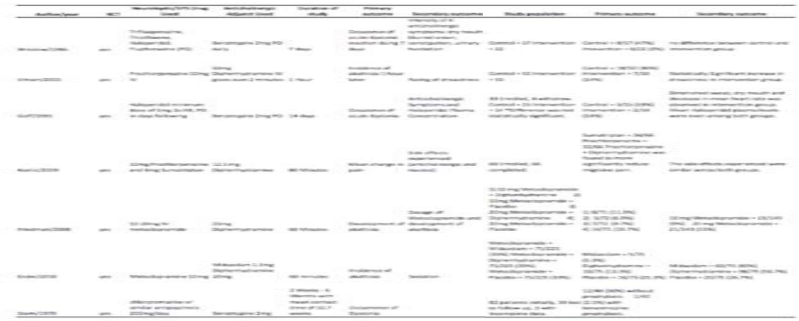

Table 1: Data Extraction Table after all inclusion criteria have been met.

Discussion and Conclusions

In this systematic review the authors found that anticholinergic adjuvant treatment prevented acute dystonia induced by antipsychotic medications for 60 minutes after administration. However, the two available studies that analyzed patients after 60 minutes had opposing results. Thus, there is no evidence of a long-term effect (defined as greater than 60 minutes from administration) in prevention of EPS with adjunctive medications. In the 4 studies and evaluated akathisia and the 3 studies that evaluated dystonia, adjuvant anticholinergic treatment was effective in preventing dystonia but not akathisia.

The prevention of EPS with adjuvant medications like benztropine or diphenhydramine has important clinical implications. Antipsychotics, prochlorperazine and metoclopramide are highly effective in treating acute psychotic episodes and nausea, vomiting respectively. However, the development of EPS may limit the utility of these medications in an acute setting. Diphenhydramine and benztropine are low-cost, benign medications and coadministration with any of the aforementioned medications may prevent dissatisfaction and disrupted patient care that can be associated with EPS.

Acknowledgements

I wish to thank my mentors Dr. Joseph Stapcyznski who has mentored me in many aspects throughout the duration of this project. I also wish to honor Dr. John Sarko, who dedicated his life to the teaching and care of others. He played an integral part in the inception of this project and is dearly missed.