

# Gender Stratification in Dopamine Antagonist induced Acute Dystonia

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## Introduction

The goal of this project was to determine whether there was a correlation between the gender of the patient and the medication which was thought to cause their acute dystonic reaction.

### Acute Dystonic Reaction

#### Definition:

Intermittent sporadic or sustained involuntary contraction of muscle, usually lasting between a couple of seconds and a few hours, located in the face, neck, trunk, pelvis, and upper and lower extremities caused by, but not limited to, antiemetic and antipsychotic medications.<sup>1</sup>

#### Pathophysiology:

Although the exact mechanism unclear, these reactions are typically induced by drugs antagonize dopamine D2 receptors, resulting in excess cholinergic tone.<sup>2</sup>

#### Treatments:

Administration of intramuscular 1-2 mg anticholinergic benztropine or intravenous diphenhydramine. Furthermore, anticholinergics have also been shown to be effective for prophylaxis.<sup>3</sup>

## Methodology

We used data from 277 patients across various hospitals, 202 female and 70 male. Data was stratified by sex. We selected 10 relevant medications known to cause dystonia. Of these, 4 were frequently prescribed to our patients and we were able to analyze them individually. All 10 medications were grouped into two classes, antipsychotic agents and anti-emetic agents, and analyzed the two groups. Antipsychotic agents given to our patients were quetiapine, chlorpromazine, droperidol, haloperidol, risperidone, and ziprasidone. Anti-emetic agents given to our patients were metoclopramide, prochlorperazine, promethazine, and trimethobenzamide.

In the statistical analysis, we analyzed the percentage of patients that were prescribed each medication as well as the percentage of each sex that was prescribed each medication and class of medication. We used a chi-square test to analyze the statistical differences between the male and female group in each of these.

In addition, we searched the entirety of the I2B2 database (773,438 total patients; 359,978 males and 413,460 females) in order to determine the total frequency of administration of specific medications (Haloperidol, Metoclopramide, and Prochlorperazine) that was then stratified by sex.

## Results

**Table 1.** Medication frequency stratified for gender (Patient sample).

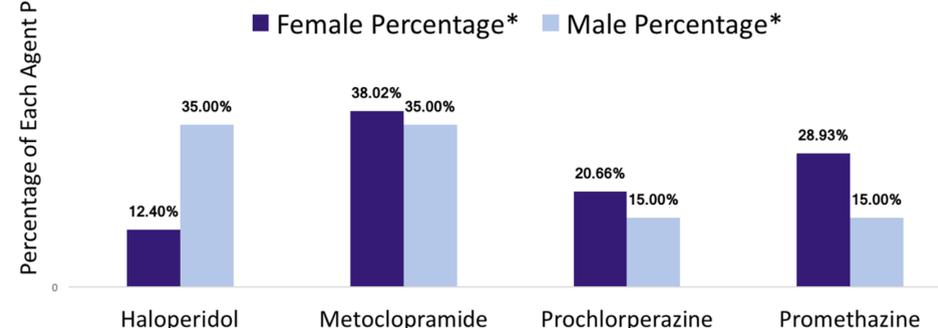
Drug Name	Female Frequency	Male Frequency	Total
Haloperidol	15	14	29
Metoclopramide	46	14	60
Prochlorperazine	25	6	31
Promethazine*	35	6	41
Total	121	40	161

**Table 2.** Medication frequency stratified for gender (Entirety of I2B2 database).

\*Promethazine did not return results in I2B2

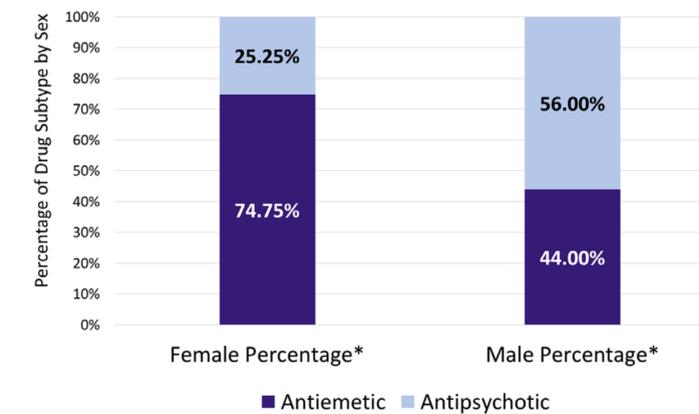
Drug Name	Male Frequency	Female Frequency	Total Frequency
Haloperidol	19239	20905	40144
Metoclopramide	204	483	687
Prochlorperazine	1219	2294	3513

### Individual Pharmacologic Agent Associated Percentage by Gender



**Summary:** The data showed that haloperidol was associated with acute dystonia at a significantly higher proportion in males ( $P < .0001$ ). Promethazine and prochlorperazine shared similar findings for that of females ( $P < .0001$ ). Stratifications based on sex proved not as significant for metoclopramide.

### Pharmacologic Agent Subtype with Associated Percentage by Gender



**Summary:** The suspected drug class thought to have caused the dystonia was stratified by sex and showed that antiemetics were the suspected cause of dystonia in a much higher proportion of women ( $P < .0001$ ). Antipsychotics shared similar findings for men, but not to the same degree.

## Summary/Conclusion

Female patients had a higher proportion of antiemetic prescription (Metoclopramide, Prochlorperazine, and promethazine), while male patients had a higher proportion of antipsychotic prescription (Haloperidol).

Patients who present with acute dystonic reaction have statistically different iatrogenic causes based on their sex. Further study is necessary to address the reasons for this difference.

Our analysis was correlational and retrospective, so further study must be conducted to look into these discrepancies. Limits to our study include the fact that the I2B2 database contained more total female patients compared to males.

It is possible that these results are due to antipsychotic and antiemetic medications being prescribed to males and females respectively at higher frequencies in other clinical settings, or that each sex reacts to the respective medications in a manner that predisposes them to acute dystonia.

## References

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  - <sup>2</sup>van Harten Peter N, Hoek Hans W, Kahn Rene S. Acute dystonia induced by drug treatment *BMJ*1999; 319 :623
  - <sup>3</sup>Campbell, Diane. "The Management of Acute Dystonic Reactions." *Australian Prescriber*, vol. 24, no. 1, Jan. 2001, pp. 19-20.
- We would like to thank Dr. Cheng for providing the statistical analysis as well as, Dr. Banderas and Dr. Bickel for their guidance and assistance.