# Factors Predicting Adverse Effects to Subcutaneous Apomorphine

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## ABSTRACT

**Objective:** To determine clinical factors associated with adverse effects (AE) to apomorphine (APO).

**Background:** Poor drug tolerance limits APO use in nearly one fifth of patients. While AE associated with APO are known, clinical features that predict the appearance of AE are not well-defined.

**Methods:** We prospectively recorded AE in consecutive patients treated with APO and correlated AE with pre-injecion clinical features.

**Results:** Patients already taking an oral dopamine agonist had less orthostatic hypotension (OH). Frequency of nausea was similar in patients who completed 3 days of premedication with trimethobenzamide (TMB) to those treated with 1 dose.

**Conclusions:** Concomitant oral dopamine agonist use may reduce the risk of APO-related OH. Additional studies are warranted to assess whether a shorter course of TMB adequately prevents nausea.

## INTRODUCTION

Many patients with advanced Parkinson's disease (PD) develop motor fluctuation that are refractory to adjustments in oral dopaminergic therapies. Intermittent subcutaneous injection of APO, a nonergot dopamine agonist, has a rapid onset of action and is an effective rescue medication for unpredictable "off" periods in this population. However, despite proven efficacy, APO use is limited by potential AE, and approximately 20% of patients discontinue APO because of an AE.[1] The spectrum and frequency of AE from APO is known, the most common being nausea, dyskinesias, hallucinations, drowsiness and orthostatic hypotension (OH), yet predictors of AE are less studied.

## METHODS

We evaluated 26 consecutive patients (mean age 60.8±10.3, mean disease duration 13.2±5.0 yrs.) who were administered subcutaneous APO 0.2 mg.

## METHODS

22 patients had idiopathic PD, 2 had other forms of parkinsonism, and 2 had restless legs syndrome.

Blood pressure (recumbent and standing) and AE were recorded before APO injection and at 10, 20, 40 and 60 minutes thereafter. AE were assessed via examination and visual analog scales. OH was defined as a drop in blood pressure >20/10 mmHg. AE were correlated with pre-injection demographic features, PD duration, weight, UPDRS, total dopamine replacement therapy (DRT) dosage, dopamine agonist use, antihypertensive use, history of DRT-related AE (gathered by patient report and chart review), and duration of TMB premedication (300 mg TID x 3 days or 300 mg x 0-1 dose).

Differences between patients who experienced AE vs. those without AE were analyzed using parametric (t test) or nonparametric (Mann-Whitney test, Chi-Square, and Fisher exact) tests and logistic regression was used to determine predictors of AE. Statistical analysis was done with the SPSS, version 14.0 (SPSS Inc, Chicago, Ill). P-values of 0.05 or less were considered significant.

## RESULTS

| APO-related Adverse Events | |
|---|---|
| **Adverse Event** | **N (%)** |
| Yawning | 14 (54) |
| Drowsiness | 6 (23) |
| Nausea/emesis | 5/1 (19/4) |
| Dyskinesias | 5 (19) |
| Orthostatic hypotension | 4 (15) |
| Flushing | 3 (12) |
| Headache | 3 (12) |
| Tachycardia | 2 (8) |
| Tachypnea | 1 (4) |
| Rhinorrhea | 1 (4) |
| Hallucinations | 1 (4) |

## RESULTS

Patients taking an oral dopamine agonist had less OH ($P < 0.005$), but OH was not associated with prior DRT-related orthostasis, total DRT dosage, antihypertensive use, age or disease duration.

APO-related drowsiness and nausea co-occurred ($P < 0.03$), but were not predicted by other factors, including prior DRT-related drowsiness or nausea.

Nausea frequency was similar in patients (N=13) who completed 3 days of TMB premedication to those treated with only 1 dose (N=11) or no drug.

## DISCUSSION

In our cohort, the spectrum and frequency of APO-related AE was similar to prior studies.

Patients who were taking oral dopamine agonists experienced less APO-related OH independent of other factors. Previous work shows that patients taking levodopa tolerate APO better than those not on dopamine replacement therapy.[2,3] Our data suggest oral dopamine agonists in particular may mitigate against APO-related OH.

We could not demonstrate that three days of TMB premedication is superior to a single dose in preventing APO-associated nausea. A larger cohort is needed to confirm whether 1 TMB dose is sufficient, as this would simplify test-dose procedures.

## REFERENCES

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