

Evaluating Adverse Event Risk with Propoxyphene: Are There Differences between Elderly versus Younger Patients?

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Objectives

- Propoxyphene is among the most commonly prescribed opioid analgesic in the elderly.
- Many guidelines, including the American Geriatric Society and Beer's List of Potentially Inappropriate Medications, recommend restricting propoxyphene use among the elderly.
- These guidelines are based on expert opinions with limited empirical evidence.
- The objective of this study was to evaluate whether there were differences in adverse event reporting for propoxyphene, by age group, using a large post-marketing safety surveillance database.

Methods

- The analysis was conducted using the 2005-2008 Adverse Event Reporting System (AERS) data in the US, which was developed to support the FDA's post-marketing safety surveillance program for all approved products.
- Adverse events reported with propoxyphene as primary, secondary or interacting drug were categorized into central nervous system (CNS) and gastrointestinal (GI) adverse events (AEs) using the MedDRA Version 7.0.
- Logistic regressions were used to assess the risk of CNS and GI adverse events (AEs) among the elderly (age \geq 65) and younger patients (age $<$ 65) controlling for gender and those reporting the AEs.
- Proportional reporting ratios (PRR) for the propoxyphene-AE combination were also computed for the elderly and younger patients.

Results

- Table 1 describes the patient and reporting characteristics by the type of propoxyphene-AE experienced.
- In the period 2005-2008, a total of 2679 propoxyphene-AE combinations were reported; 309 were CNS-related and 153 were GI-related.
- Over 60% of the reported propoxyphene-CNS and propoxyphene-GI AEs were among patients less than 65 years old, and among females. Physicians reported approximately 35% of these AEs.
- In multivariate analysis, controlling for gender and those reporting the AEs, no significant differences were observed in the odds of reporting CNS-related AEs (Odds Ratio (OR): 0.827; $p=0.199$) or GI-related AEs (OR: 1.216; $p=0.313$) among elderly versus young patients using propoxyphene (Table 2).
- Figure 1 describes the PRR by age group and type of AE experienced. The PRR were similar by age group both for propoxyphene-CNS AEs (Elderly patients: 0.795; Young patients; 0.700) and for propoxyphene-GI AEs (Elderly patients: 0.596; Young patients: 0.439).

Study Limitations

- The study uses the FDA AERS dataset, which is based on voluntary reporting of AEs and is known to have multiple limitations such as:
 - Substantial under-reporting of AEs
 - Patients or other AE reporters may have recall bias with poor case documentation
 - Missing data on patient and other characteristics.
 - Data does not provide a denominator indicating population at risk for a particular drug-AE interaction.
- As a result, accumulated reports from sources such as FDA AERS data cannot be used to calculate incidence rates (occurrence rates) or drug risk. However, using methods employed in this study, they can provide 'signals' of drug-AE interactions that may benefit from further investigation.

Conclusions

- Using a voluntary post-marketing surveillance database, the study found no differences in the extent of CNS AEs and GI AEs reported with propoxyphene among elderly patients versus younger patients.

Table 1. Patient & Reporting Characteristics

| Characteristics | Propoxyphene -CNS AEs N (%) | Propoxyphene -GI AEs N (%) |
|--------------------------------|--------------------------------|-------------------------------|
| N | 309 | 153 |
| Age Group | | |
| <65 years old | 186 (71.3%) | 82 (64.6%) |
| \geq 65 years old | 75 (28.8%) | 45 (35.4%) |
| Gender | | |
| Female | 190 (61.5%) | 96 (62.8%) |
| Male | 109 (35.3%) | 55 (36.0%) |
| Occupation of AE Reporter | | |
| Consumer | 36 (11.7%) | 17 (16.2%) |
| Lawyer | 43 (13.9%) | 0 |
| Physician | 105 (34.0%) | 40 (38.1%) |
| Other Health Care Professional | 28 (9.1%) | 44 (41.9%) |
| Pharmacist | 97 (31.4%) | 4 (3.8%) |

Table 2. Odds Ratios (OR) by Propoxyphene-AE Type

| Characteristics | Propoxyphene-CNS AEs OR (95% CI) | Propoxyphene-GI AEs OR (95% CI) |
|---|-------------------------------------|------------------------------------|
| Elderly Patients (vs. Younger Patients) | 0.83 (0.62 - 1.11) | 1.22 (0.83 - 1.78) |
| Female (vs. Male) | 1.12 (0.85 - 1.47) | 0.96 (0.66 - 1.39) |
| Occupation (vs. Consumer) | | |
| Lawyer | 0.35 (0.20 - 0.61) | 0.85 (0.42 - 1.69) |
| Physician | 0.99 (0.61 - 1.59) | 1.14 (0.58 - 2.23) |
| Other Health Care Professional | 1.09 (0.60 - 1.92) | 0.33 (0.10 - 1.03) |
| Pharmacist | 0.92 (0.57 - 1.47) | 0.89 (0.46 - 1.72) |

Figure 1. Proportional Reporting Ratios for AEs by Age Group

