Medication use and polypharmacy in patients referred to a tertiary gastroenterology practice

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Introduction. Commonly prescribed medications are associated with various gastrointestinal (GI) side effects but few data are available on prescription medication use and polypharmacy in a gastroenterology outpatient practice. We aimed to examine the prevalence of polypharmacy, defined as the simultaneous use of 5 or more medications.

Methods. A descriptive correlational study of consecutive outpatient consultations in 988 patients referred to a tertiary gastroenterology practice. Main outcome measurements were frequency of prescription medication use and polypharmacy.

Results. The most common GI symptoms were abdominal pain (72%), nausea (57%), and constipation (53%). The frequency of polypharmacy was 10%. Eighty percent of patients took at least one medication and 60% took two or more. The most frequently used medication classes were proton pump inhibitors (43%), followed by benzodiazepines (30%), selective serotonin-reuptake or norepinephrine-reuptake inhibitors (28%), non-steroidal anti-inflammatory drugs (27%), and opioids (21%).

Conclusion. There was a higher use of prescription medicine including antidepressants, and a lower frequency of polypharmacy in our study cohort compared to the general population. The use of medications may have contributed to the symptoms leading to our study's population GI consultation.

Key words: adverse effects, gastrointestinal, polypharmacy, prescription medicine.

INTRODUCTION

Polypharmacy and its risks have been extensively studied in the elderly population, but limited data are available on its prevalence in patients referred to tertiary centers and its association with disease clusters. Adverse drug reactions, drug-drug interactions, and drug-disease interactions are common undesirable consequences of polypharmacy that may confound clinical presentations [1, 2].

Despite the availability of evidence on the association between different classes of medication and GI disorders, there are limited data on polypharmacy in patients referred to tertiary centers and how the pattern of medication use affects presentation.

Aim of the study: To describe the prevalence of polypharmacy and the prevalence of certain medications in patients referred to a tertiary gastroenterology practice. Polypharmacy was defined as the simultaneous use of 5 or more medications – whether prescribed or obtained over-the-counter – at the time of gastroenterology consultation.

MATERIAL AND METHODS

Informed consent: Informed consent for this study was waived by the Institutional Review Board.

Ethical Approval: The research related to human use complied with all the relevant national regulations, institutional policies, and in accordance to the tenets of the Helsinki Declaration, has been approved by the authors' Institutional Review Board.

Study subjects: Data were collected retrospectively on 988 patients seen in consultation by gastroenterologists of different subspecialty interests from January 1, 2012 to December 31, 2016. Information regarding patient characteristics was collected for age, sex, race, body mass index (BMI), alcohol use, smoking, consulting gastroenterologist, and presenting GI symptoms (abdominal pain, nausea, vomiting, bloating/distention, diarrhea, and constipation). Prior diagnosis of gastroparesis was also recorded. We recorded whether patients were taking medications in various classes or groups. Classes of medications included PPIs (proton pump inhibitors), benzodiazepines,

SSRIs/SNRIs (serotonin-norepinephrine reuptake inhibitors), opioids, non-steroidal anti-inflammatory agents (NSAIDs), dopamine agonists, tricyclic antidepressants. Medication groups included anti-epileptic drugs (AEDs), central nervous system (CNS) stimulants, antihistamines, antihyperglycemic agents, antipsychotics, and supplements (iron and magnesium). If a patient was taking a medication in one of the aforementioned categories, the specific type(s) of medication and dose information were also collected.

The research was compliant with all relevant national regulations and institutional policies and has been approved by the Institutional Review Board.

STATISTICAL ANALYSIS

Continuous variables were summarized with the sample median and range. Categorical variables were summarized with number and percentage of patients. Age and BMI were the only continuous variables while the rest were categorical variables. For medication, in addition to estimating the percentage of patients who were taking each type

of medication, we also estimated 95% confidence intervals for these percentages. Statistical analyses were performed using SAS (version 9.4; SAS Institute, Inc., Cary, North Carolina).

RESULTS

A summary of patient demographic and clinical information is provided in Table 1. The median age was 53 years (range: 15–95 years), and the majority of patients were female (74%), and white (90%). The median BMI was 26 kg/m² (Range: 13–58). The most common presenting GI symptoms were abdominal pain (72%), nausea (57%), and constipation (52%); 82% of patients presented with two or more GI symptoms. The median number of allergies reported was 1 (Range: 0–30). Overall, 806 patients (82%, 95% CI: 79%–84%) were taking at least one medication at the time of their GI consultation. More specifically, 231 patients (23%) were taking one medication, 218 (24%) were taking two, 148 (16%) were taking three, 106 (11%) were taking four, and the remaining 103 patients (10%) were taking five or more medications.

Table 1
Patient demographics and clinical information

	Summary (N = 988)
Age	53 (15, 95)
Female	730 (73.9%)
Race	
Caucasian	873 (89.8%)
African American	73 (7.5%)
American Indian/Alaskan Native	5 (0.5%)
Asian/Hawaiian/Pacific Islander	11 (1.1%)
Other	10 (1.0%)
BMI	26.1 (12.9, 58.4)
Current alcohol use	392 (45.4%)
Current smoker	93 (9.8%)
Presenting symptom(s)	
Abdominal Pain	715 (72.4%)
Nausea	565 (57.2%)
Constipation	519 (52.5%)
Diarrhea	383 (38.7%)
Bloating/Distension	349 (35.3%)
Vomiting	300 (30.3%)
Total number of presenting symptoms	
1	177 (17.9%)
2	241 (24.4%)
3	273 (27.6%)
4	165 (16.7%)
≥ 5	203 (20.5%)
Total number of different medications currently taking	
0	182 (18.4%)
1	231 (23.4%)
2	218 (22.1%)
3	148 (15.0%)
4	106 (10.7%)
≥ 5	103 (10.4%)

The sample median (minimum, maximum) is given for continuous variables. Information was unavailable regarding race (N = 16), current alcohol use (N = 124), current smoker (N = 37), and BMI (N = 13).

Table 2 displays the frequencies of patient medication use for different categories of medications and specific medication types within the given category. The most frequently used category of medications was PPIs (43%), followed by benzodiazepines (30%),

SSRIs/SNRIs (28%), NSAIDs (27%), opioids (21%), AEDs (10%), antihyperglycemic agents (9%), and magnesium (6%). TCAs, CNS stimulants, iron, antihistamines, antipsychotics, and dopamine agonists were used by less than 5% of the patients.

Table 2

Frequency of selected medication use.

Medication	Number (%) of patients	95% confidence interval
Proton pump inhibitors	427 (43.2%)	40.1%–46.3%
Benzodiazepines	292 (29.6%)	26.8%–32.5%
SSRIs and SNRIs	275 (27.8%)	25.0%–30.6%
Nonsteroidal anti-inflammatory drugs	264 (26.7%)	23.9%–29.5%
Opioids	205 (20.7%)	18.2%–23.3%
Tricyclic Antidepressants	49 (5.0%)	3.6%–6.3%

DISCUSSION

Although universally recognized as having a major impact on a patient's health, polypharmacy has been defined in multiple different ways. Variables that lead to the diagnosis of polypharmacy include not only the number of medications, but also the duration of therapy, appropriateness of the treatment, and comorbidities among others [17]. In our study, we used a numerical definition of polypharmacy (the use of 5 or more medications) that included drugs dispensed by prescriptions as well as over the-counter products.

An analysis of a nationally representative survey showed an increase use of prescription drugs among United States adults after adjusting for age distribution [3]. The same study also revealed an increase in the use of proton pump inhibitors (PPI), antidepressants (tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs), narcotic analgesics, anticonvulsants, and antidiabetics. These commonly prescribed medications have been associated with a variety of GI side effects.

Of special significance, PPIs are the most commonly prescribed medications for digestive diseases [4]. PPI use has been linked to alterations of the small intestinal microbiome, by theoretically eliminating the protective acidic environment in the stomach [5]. It is also conceived that excess gas production from bacteria in the small intestine promotes the development of irritable bowel syndrome (IBS) [6]. Opioids inhibit normal bowel function leading to constipation, abdominal pain, bloating, nausea and vomiting, narcotic bowel syndrome, and esophageal motility disorders [7–9]. In the same fashion, opioids and antidepressants may alter intestinal transit time via mechanisms that include cholinergic antagonism and excess gut serotonin levels [9–11].

The results of this analysis showed a high frequency of prescription medication use amongst patients referred to a tertiary GI practice. The prevalence of prescription medication use was higher in our study population (80%) compared to the American population (68%) as estimated from the Rochester Epidemiology Project. However, the prevalence of polypharmacy was lower in our study group (10% versus 21%) [12]. The prevalence of antidepressant use (33%) [SSRI-28%, TCA-5%] was higher than the national average of 10% from the same study.

The negative consequence of polypharmacy in the elderly population has been the subject of research, but few studies have examined the subject within specific disease clusters [13–15]. To our knowledge, this is the first study evaluating prescription medication use, polypharmacy, and GI complaints in patients referred to a tertiary gastroenterology practice. In a similar study done in an outpatient endocrinology practice amongst 95 diabetic patients with nonalcoholic fatty liver disease, the authors found a high prevalence of polypharmacy (59% taking 5–9 medications and 31% more than 10 medications) [15]. After excluding cardiovascular and hypoglycemic medications, the most commonly prescribed medication was PPIs (43%) as it was in our study. However, the prevalence of NSAIDs (3%), SSRIs (15%), benzodiazepines (6%), and opioids (12%) were lower compared to our findings. Their smaller sample size, narrower range of GI disorder, predominantly male population, higher rate of obesity, and older population could explain the differences between the two studies. We also realize that psychiatric disease may be associated with gastrointestinal complaints, but establishing a correlation between the reported symptoms and the psychological profile of the population was beyond the scope of our analysis.

A more holistic approach to assessing polypharmacy within specific disease clusters and exploring how drug-drug interactions and drug-disease interactions affect disease presentation is the future of polypharmacy research [1]. The only published research in this area was a population study aimed at determining the specific interactions and synergistic effects between combinations of medications [16]. This primary care pharmacy database analysis identified disease clusters and examined the common medications used in each cluster, frequency of polypharmacy, and attempted to hypothesize causal relations. Finally, as some of the symptoms of gastrointestinal disorders may also be caused by medications commonly used to treat GI disease, primary care providers should consider making a numerical and/or non-numerical assessment of polypharmacy and requesting the assistance of a pharmacist prior to subspecialty medical consultation [18].

LIMITATIONS

Our study has several limitations. There was lack of data on the chronicity and frequency of

medication use. As a result, it was difficult to establish the temporal relationship between medication use and the onset of GI symptoms, and therefore causality. Also, the presenting GI symptoms were reported by the patients, and not standardized. Furthermore, due to the retrospective design and the corresponding lack of systematic data entry, it is possible that the use of certain medications was not recorded for some patients, which means that the frequencies of medication use reported herein could be biased slightly too low. We did not report data on the volume or frequency of alcohol consumed by the study subjects. The findings in our study are only applicable to the patient population in an outpatient tertiary GI clinic and may not apply to the general population.

CONCLUSION

In conclusion, we found a high frequency of prescription medication use, but lower prevalence of polypharmacy amongst patients referred to a tertiary gastroenterology practice. Further studies are needed to explore possible associations between polypharmacy and disease-clusters in patients with GI symptoms.

Introducere. Majoritatea medicamentelor prescrise în mod uzual se asociază cu efecte adverse de natură gastrointestinală (GI) și există puține date în literatură despre aceste aspecte.

Metode. A fost realizat un studiu descriptiv pe 988 de pacienți care se prezintă la un centru terțiar de îngrijire gastrointestinală. Efectele urmărite au fost frecvența prescripțiilor medicale și polimedicatia.

Rezultate. Cele mai frecvente simptome GI au fost durerea abdominală (72%), urmată de greață (57%) și constipație (53%). Frecvența polimedicatiei a fost de 10%. 8% dintre pacienți au luat cel puțin un medicament și 60% au luat două sau mai multe medicamente. Cea mai frecventă clasă de medicamente prescrisă ce a dus la consultația GI au fost inhibitorii de pompă de protoni (43%) urmată de benzodiazepine (30%), antidepresive (28%), AINS (27%), opioide (21%).

Concluzii. Se administrează frecvent antidepresive, cu o frecvență mai mare față de populația generală. Polimedicatia ar putea contribui la simptomele care se asociază cu prezentarea la medic din cauza simptomatologiei GI.

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