

Patterns of use of medications used to treat urinary incontinence and potentially inappropriate prescriptions

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Abstract

Background: The pharmacological treatment of urinary incontinence (UI) may involve bladder antimuscarinics, which can generate risks in the elderly.

Objective: The aim was to determine the treatment patterns of a group of patients with UI and possible potentially inappropriate prescriptions.

Design and methods: This was a cross-sectional study that identified prescription patterns of medications for outpatient use in patients with UI between December 2020 and November 2021 based on a population database of members of the Colombian Health System. Patients were identified based on the codes of the international classification of diseases, version-10. Sociodemographic and pharmacological variables were considered.

Results: A total of 9855 patients with UI were identified, with a median age of 72 years, and 74.6% were women. Unspecified UI was the most frequent form (83.2%), followed by specified UI (7.9%), stress UI (6.7%), and UI associated with an overactive bladder (2.2%). A total of 37.2% received pharmacological treatment, mainly with bladder antimuscarinics (22.6%), mirabegron (15.6%), and topical estrogens (7.9%). Pharmacological management predominated in UI associated with overactive bladder, in women and in patients between 50 and 79 years of age. Of the patients who received bladder antimuscarinics, 54.5% were 65 years old or older, and 21.5% also had benign prostatic hyperplasia, sicca syndrome, glaucoma, constipation, or dementia. A total of 2.0% of women had been prescribed systemic estrogens and 1.7% had been prescribed peripheral α -adrenergic antagonists.

Conclusion: Differences in the prescriptions were found according to the type of UI, sex, and age group. Potentially inappropriate or risky prescriptions were common.

Keywords: adrenergic alpha-antagonists, elderly, estrogens, inappropriate prescribing, muscarinic antagonists, urinary incontinence

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Introduction

Urinary incontinence is defined by the International Continence Society (ICS) as the involuntary loss of urine.¹ This pathology may be a consequence of an imbalance between the mechanisms necessary for adequate urinary continence, such as an intraurethral pressure greater than the intravesical pressure, the ability to perceive the need to urinate or mechanical problems due to an external agent that controls urination.²

Urinary incontinence has typically been classified as urgency, stress, or mixed;³ stress urinary incontinence is the most common form in women, while urgency urinary incontinence is predominant in men.⁴ Its general prevalence has been estimated at 8.2%, but the prevalence increases with age and is higher in women, in patients residing in geriatric homes and in those with multiple comorbidities.⁴ Therefore, urinary incontinence is a common and distressing problem for patients that

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limits their social life and negatively impacts their physical activity, personal hygiene, and self-esteem.⁵

Treatment for urinary incontinence involves conservative management, which consists of bladder exercises, psychotherapy, fluid restriction, caffeine, weight reduction, constipation management, and avoiding precipitating drugs, among others approaches.^{3,6} The avoidance of precipitating medications is a potentially modifiable risk factor;⁷ however, few studies have evaluated the impact of drug exposure on urinary incontinence.⁷ According to the Beers criteria, the use of systemic estrogens and peripheral α -adrenergic antagonists can precipitate incontinence symptoms in women, which is why they are considered potentially inappropriate prescriptions (PIPs) and avoiding their use is recommended based on the results of clinical trials.⁸ Reports of observational studies have shown that medications with hypnotic properties may also be related to urinary incontinence.^{9,10}

Pharmacological treatment depends on the type of urinary incontinence and its severity and includes the use of bladder muscarinic antagonists and β 3-adrenergic receptor agonists, in addition to topical estrogens, duloxetine and botulinum toxin as well as invasive interventions in selected patients.^{3,6,11} Pharmacological management should also be individualized based on sociodemographic factors and comorbidities, since the use of antimuscarinic drugs is usually associated with greater adverse drug reactions in older adults than in younger patients and therefore can be considered a PIP in some cases.^{8,12}

The Colombian Health System offers universal coverage for the entire population through two regimes, one contributory (paid by the worker and employer) and the other subsidized (paid by the state). It has a benefit plan that includes some medications used for the treatment of urinary incontinence and others that worsen this condition. Therefore, the objective of this study was to determine the pattern of use of medications for the treatment of urinary incontinence and possible PIPs in a group of patients in Colombia.

Materials and methods

This was a cross-sectional study of the prescription patterns for drugs used in patients diagnosed with urinary incontinence based on a population

drug dispensing database that collects information from approximately 8.5 million people, distributed in all regions of Colombia and affiliated with the Colombian Health System in six health insurance companies, corresponding to approximately 30.0% of the population who are active members of the contributory, or paid, regime and 6.0% of the state-subsidized regime, which comprises 17.3% of the Colombian population.

Patients were identified using the international classification of diseases, version-10 (ICD-10) codes for stress urinary incontinence (N393), specified urinary incontinence (N394), and unspecified urinary incontinence (R32X) from 1 December 2020, to 30 November 2021. For the identified patients, those who presented a concomitant diagnosis of overactive bladder (ICD-10: N310, N311) were sought. The selected patients were of any age and sex and attended outpatient medical consultations. Patients who had more than one ICD-10 diagnostic code different related to some form of urinary incontinence and those who only had a diagnosis of urinary incontinence on a single occasion during the selection period were excluded to avoid introducing selection biases.

Based on drug consumption information for the affiliated population that was systematically obtained by the dispensing company (Audifarma SA), a database was designed that allowed the following groups of patient variables to be collected:

1. Sociodemographic: sex, age, health system affiliation (contributory or subsidized) and dispensing city. The place of residence was categorized by department according to the regions of Colombia and taking into account the classification of the National Administrative Department of Statistics (DANE) of Colombia, as follows: the Caribbean region, the Central region, the Bogotá-Cundinamarca region, the Pacific region, the Eastern region, and Amazonia-Orinoquía.
2. Comorbidities were identified based on the ICD-10 codes reported for the selected patients.
3. Medications for the management of urinary incontinence: bladder antimuscarinics (oxybutynin, tolterodine, flavoxate, solifenacin, trospium, and darifenacin), mirabegron, vaginal topical estrogens, duloxetine and botulinum toxin.

4. Possible potentially inappropriate or risky prescriptions:

- Bladder antimuscarinics in patients ≥ 65 years.^{8,12}
- Bladder antimuscarinics for concomitant comorbidities such as dementia, sicca syndrome, glaucoma, constipation and prostatic hyperplasia.^{8,12}
- In women, systemic estrogens or peripheral α -adrenergic antagonists (prazosin, terazosin, doxazosin).⁸

5. Comedications, grouped into the following categories: (a) antidiabetics (oral and subcutaneous), (b) antihypertensives and diuretics, (c) lipid-lowering drugs, (d) antiulcer drugs, (e) antidepressants, (f) anxiolytics and hypnotics (benzodiazepines and Z drugs), (g) thyroid hormone, (h) antipsychotics (typical and atypical), (i) antiepileptics, (j) antiarrhythmics, (k) antihistamines, (l) antidementia medications, (m) analgesics and anti-inflammatories, and (n) others. Antidepressants, antipsychotics, benzodiazepines, antiepileptics, opioids, antihistamines, and muscle relaxants were grouped in the anxiolytics and hypnotics category.

The data were analyzed using the statistical package SPSS Statistics, version 26.0 for Windows (IBM, USA). A descriptive analysis was performed using frequencies and proportions for the qualitative variables and measures of central tendency and dispersion for the quantitative variables depending on their parametric behavior, as established by the Kolmogorov–Smirnov test. Quantitative variables were compared using Student's *t*-test or the Mann–Whitney *U* test, and the χ^2 or Fisher's exact test was used for categorical variables. Multivariate binary logistic regression models were developed that included the associated variables in the bivariate analyses, as well as those with sufficient plausibility or reported association to identify those that could be associated with PIPs or risky prescriptions (yes/no). Statistical significance was determined at $p < 0.05$.

Results

A total of 9855 patients with a diagnosis of urinary incontinence distributed in 103 different cities

were identified. A total of 74.6% ($n=7347$) were women, and the median age was 72.0 years (interquartile range: 57.0–84.0 years; range: 19.0–103.0 years). The patients were distributed in the following age groups: <50 years ($n=1569$; 15.9%), 50–64 years ($n=2124$; 21.5%), 65–79 years ($n=2691$; 27.3%) and ≥ 80 years ($n=3471$; 35.2%). Most of the patients were in the Pacific Region ($n=4640$; 47.1%), followed by the Bogotá-Cundinamarca Region ($n=3027$; 30.7%), the Central Region ($n=1502$; 15.2%), the Caribbean Region ($n=558$; 5.7%), and the Eastern Amazon Region ($n=128$; 1.3%). A total of 92.5% ($n=9116$) were affiliated with the contributory regime, and 7.5% ($n=739$) were affiliated with the subsidized regime of the country's health system.

The majority had a diagnosis of unspecified urinary incontinence ($n=8195$; 83.2%), followed by specified urinary incontinence ($n=774$; 7.9%), stress urinary incontinence ($n=665$; 6.7%) and unspecified urinary incontinence associated with overactive bladder ($n=221$; 2.2%). Among the most frequent comorbidities in this group of patients were arterial hypertension ($n=5692$; 57.8%), diabetes mellitus ($n=2101$; 21.3%), dementia ($n=1120$; 11.4%), anxiety disorders ($n=1047$; 10.6%), hypothyroidism ($n=1039$; 10.5%), chronic kidney disease ($n=694$; 7.0%), osteoarthritis ($n=625$; 6.3%), chronic obstructive pulmonary disease ($n=554$; 5.6%), dyslipidemia ($n=541$; 5.5%), and sicca syndrome ($n=536$; 5.4%).

A total of 37.2% ($n=3662$) of the patients received pharmacological treatment for urinary incontinence, most commonly bladder antimuscarinics ($n=2231$; 22.6%), of which tolterodine predominated ($n=1348$; 13.7%). Among those who received antimuscarinics, prolonged-release pharmaceutical forms were the most frequently prescribed ($n=1727/2231$; 77.4%), and there were no significant differences according to age (<65 years *versus* 65 years: 77.3% and 77.5%; $p=0.881$) or sex (women *versus* men: 77.6% and 76.7%; $p=0.697$). Mirabegron was used in 15.6% ($n=1540$) of patients, and topical conjugated estrogens were used in 7.9% ($n=782$) of cases. Diapers were used by 36.6% ($n=3607$) of the patients. The main comedications were analgesics and anti-inflammatories ($n=6783$; 68.8%), antihypertensives and diuretics ($n=5365$; 54.4%), antiulcer medications ($n=4898$; 49.7%), lipid-lowering drugs ($n=4207$; 42.7%) and

antidepressants ($n=3390$; 34.4%). A total of 66.4% ($n=6544$) of the patients had been prescribed a medication with hypnotic or sedative properties. Of the patients with benign prostatic hyperplasia ($n=475$), 23.4% ($n=111$) received concomitant bladder antimuscarinics and α -adrenergic antagonists or 5 α -reductase inhibitors.

Comparison among types of urinary incontinence

The different types of urinary incontinence, especially stress urinary incontinence, predominately affected women. The highest median age was observed in patients with unspecified urinary incontinence, and comorbidities were less frequent in patients with stress urinary incontinence. Pharmacological management, especially with bladder antimuscarinics and mirabegron, predominated among those with urinary incontinence associated with overactive bladder and those with specified urinary incontinence. Diapers use was more frequent among those with unspecified urinary incontinence (see Table 1).

Comparison between women and men

Statistically significant differences were found in some variables according to sex. The men with urinary incontinence were older and had more comorbidities. Unspecified urinary incontinence predominated in men, while stress incontinence predominated in women. Pharmacological management predominated in women, who comprised the majority of patients who were prescribed bladder antimuscarinics and mirabegron; in contrast, diaper use was predominant in men (see Table 2).

Comparison among age groups

In each of the age groups, women represented the majority. The proportion of comorbidities increased with age. The frequency of patients with unspecified urinary incontinence increased with increasing age, while the rate of stress incontinence decreased with increasing age. Pharmacological treatment with both bladder antimuscarinics and mirabegron predominated in patients who were between 50 and 79 years of age, while the use of diapers was predominant in the group that was more than 80 years old (see Table 3).

Possible potentially inappropriate or risky prescriptions

Of the patients who received bladder antimuscarinics, 54.5% ($n=1215/2231$) were 65 years or older, and 21.5% ($n=480/2231$) had benign prostatic hyperplasia, sicca syndrome, glaucoma, constipation, or dementia as comorbidities (see Table 4). These pathologies predominate in those with urinary incontinence associated with overactive bladder (see Table 1) and in men (see Table 2). Among the women, 2.0% ($n=199/7347$) had been prescribed systemic estrogens, and 1.7% ($n=122/7347$) had been prescribed peripheral α -adrenergic antagonists (see Table 4). Systemic estrogens prescriptions were predominant in patients with stress urinary incontinence (see Table 1) and in women younger than 50 years (see Table 3), while peripheral α -adrenergic antagonist prescriptions were predominant among those older than 65 years (see Table 3).

Multivariate analysis

Binary logistic regression adjusted for sex, age, origin, pathologies, and taking other medications found that increasing age, having an overactive bladder, and comedications such as antihypertensive and antidiabetic drugs were associated with a higher probability of presenting PIPs. While neurological disorders and the use of diapers reduced this risk (see Table 5).

Discussion

This study identified the prescription patterns of medications used for patients with urinary incontinence as evidence of real-world medication use in a group affiliated to the Colombian Health System. These findings can assist healthcare, academic and scientific personnel in making decisions regarding patient risks and can contribute to strengthening the rational use of drugs among physicians as a way to reduce adverse drug reactions in the country.

An attempt was made to compare the results with the literature, but this was difficult, due to the different realities of the health systems of each country, the variability in the availability of medicines, the different ages of the population in each study, as well as the different years in which the studies were published. The median age of the patients was similar to that found in other studies (69.4–74.8 years)^{5,13–16} and there was a predominance

Table 1. Comparison of some sociodemographic, clinical, and pharmacological variables of 9855 patients with urinary incontinence, Colombia.

Variables	Unspecified urinary incontinence		Specified urinary incontinence		Stress urinary incontinence		Unspecified urinary incontinence associated with overactive bladder	
	<i>n</i> = 8195	%	<i>n</i> = 774	%	<i>n</i> = 665	%	<i>n</i> = 221	%
Women	5981	73.0	587	75.8	611	91.9	168	76.0
Age, median (IQR)	74.0 (59.0–85.0)		68.0 (56.0–79.0)		52.0 (40.0–64.0)		65.0 (55.5–77.5)	
Comorbidities	6994	85.3	649	83.9	423	63.6	196	88.7
Arterial hypertension	4900	59.8	413	53.4	252	37.9	127	57.5
Diabetes mellitus	1815	22.1	152	19.6	90	13.5	44	19.9
Dementia	1034	12.6	63	8.1	12	1.8	11	5.0
Anxiety disorders	876	10.7	101	13.0	39	5.9	31	14.0
Hypothyroidism	809	9.9	121	15.6	84	12.6	25	11.3
Use of diapers	3373	41.2	154	19.9	41	6.2	39	17.6
Pharmacotherapy	2742	33.5	496	64.1	238	35.8	186	84.2
Bladder antimuscarinics	1627	19.9	330	42.6	136	20.5	138	62.4
Tolterodine	948	11.6	240	31.0	91	13.7	69	31.2
Oxybutynin	355	4.3	36	4.7	24	3.6	21	9.5
Solifenacin	252	3.1	29	3.7	11	1.7	57	25.8
Darifenacin	179	2.2	43	5.6	11	1.7	16	7.2
Flavoxate	30	0.4	2	0.3	6	0.9	1	0.5
Mirabegron	1161	14.2	186	24.0	72	10.8	121	54.8
Conjugated estrogens vaginal cream	570	7.0	85	11.0	94	14.1	33	14.9
Duloxetine	80	1.0	14	1.8	10	1.5	8	3.6
Botulinum toxin	14	0.2	4	0.5	4	0.6	2	0.9
Comedications	7793	95.1	730	94.3	631	94.9	210	95.0
Analgesics and anti-inflammatories	5563	67.9	542	70.0	514	77.3	164	74.2
Antihypertensives and diuretics	4637	56.6	400	51.7	217	32.6	111	50.2
Anti-ulcer	4111	50.2	386	49.9	278	41.8	123	55.7
Lipid-lowering	3571	43.6	323	41.7	222	33.4	91	41.2
Antidepressants	2862	34.9	262	33.9	164	24.7	102	46.2
Potentially inappropriate or risky prescriptions	–	–	–	–	–	–	–	–
Bladder antimuscarinics in the elderly (<i>n</i> = 2231)	909	55.9	170	51.5	56	41.2	80	58.0
Bladder antimuscarinics in risk comorbidities (<i>n</i> = 2231)	355	21.8	62	18.8	17	12.5	46	33.3
Systemic estrogens (<i>n</i> = 7347)	107	1.8	10	1.7	78	12.8	4	2.4
Peripheral α -adrenergic antagonists (<i>n</i> = 7347)	100	1.7	15	2.6	4	0.7	3	1.8
IQR, interquartile range.								

Table 2. Comparison of some sociodemographic, clinical, and pharmacological variables between women and men with urinary incontinence, Colombia.

Variables	Women		Men		p
	n = 7347	%	n = 2508	%	
Age, median (IQR)	71.0 (56.0–84.0)		75.0 (60.0–85.0)		< 0.001 ^a
Comorbidities	6085	82.8	2177	86.8	< 0.001
Arterial hypertension	4137	56.3	1555	62.0	< 0.001
Diabetes mellitus	1523	20.7	578	23.0	0.014
Dementia	798	10.9	322	12.8	0.007
Anxiety disorders	762	10.4	285	11.4	0.164
Hypothyroidism	891	12.1	148	5.9	< 0.001
Type of urinary incontinence	–	–	–	–	–
Not specified	5981	81.4	2214	88.3	< 0.001
Specified	587	8.0	187	7.5	0.391
Stress	611	8.3	54	2.2	< 0.001
Unspecified with overactive bladder	168	2.3	53	2.1	0.613
Use of diapers	2284	31.1	1323	52.8	< 0.001
Pharmacotherapy	3060	41.6	602	24.0	< 0.001
Bladder antimuscarinics	1828	24.9	403	16.1	< 0.001
Tolterodine	1094	14.9	254	10.1	< 0.001
Oxybutynin	332	4.5	104	4.1	0.434
Solifenacin	292	4.0	57	2.3	< 0.001
Darifenacin	221	3.0	28	1.1	< 0.001
Flavoxate	35	0.5	4	0.2	0.027 ^b
Mirabegron	1257	17.1	283	11.3	< 0.001
Conjugated estrogens vaginal cream	782	10.6	0	0.0	< 0.001 ^b
Duloxetine	83	1.1	29	1.2	0.914
Botulinum toxin	19	0.3	5	0.2	0.603
Comedications	7000	95.3	2364	94.3	0.043
Analgesics and anti-inflammatories	5243	71.4	1540	61.4	< 0.001
Antihypertensives and diuretics	3938	53.6	1427	56.9	0.004
Anti-ulcer	3738	50.9	1160	46.3	< 0.001
Lipid-lowering	3142	42.8	1065	42.5	0.792

(Continued)

Table 2. (Continued)

Variables	Women		Men		p
	n = 7347	%	n = 2508	%	
Antidepressants	2557	34.8	833	33.2	0.148
Potentially inappropriate or risky prescriptions	-	-	-	-	-
Bladder antimuscarinics in the elderly (n=2231)	932	51.0	283	70.2	< 0.001
Bladder antimuscarinics in risk comorbidities (n=2231)	272	14.9	208	51.6	< 0.001
Systemic estrogens (n=7347)	199	2.7	-	-	-
Peripheral α -adrenergic antagonists (n=7347)	122	1.7	-	-	-

IQR, interquartile range.
^aMann-Whitney U test.
^bFisher's exact test.

Table 3. Comparison of some sociodemographic, clinical, and pharmacological variables between age groups in patients with urinary incontinence, Colombia.

Variables	<50 years		50–64 years		65–79 years		≥80 years	
	n = 1569	%	n = 2124	%	n = 2691	%	n = 3471	%
Women	1191	75.9	1722	81.1	1937	72.0	2497	71.9
Comorbidities	943	60.1	1681	79.1	2249	91.0	3189	91.9
Arterial hypertension	447	28.5	998	47.0	1761	65.4	2486	71.6
Diabetes mellitus	111	7.1	360	16.9	726	27.0	904	26.0
Dementia	10	0.6	47	2.2	212	7.9	851	24.5
Anxiety disorders	126	8.0	198	9.3	273	10.1	450	13.0
Hypothyroidism	139	8.9	285	13.4	351	13.0	254	7.6
Type of urinary incontinence	-	-	-	-	-	-	-	-
Not specified	1135	72.3	1618	76.2	2249	83.6	3193	92.0
Specified	105	6.7	231	10.9	250	9.3	188	5.4
Stress	298	19.0	203	9.6	121	4.5	43	1.2
Unspecified with overactive bladder	31	2.0	72	3.4	71	2.6	47	1.4
Use of diapers	358	22.8	294	13.8	756	28.1	2199	63.4
Pharmacotherapy	531	33.8	1159	54.6	1324	49.2	648	18.7
Bladder antimuscarinics	343	21.9	673	31.7	829	30.8	386	11.1
Tolterodine	216	13.8	420	19.8	494	18.4	218	6.3
Oxybutynin	64	4.1	104	4.9	184	6.8	84	2.4
Solifenacin	45	2.9	105	4.9	136	5.1	63	1.8

(Continued)

Table 3. (Continued)

Variables	<50 years		50–64 years		65–79 years		≥80 years	
	n = 1569	%	n = 2124	%	n = 2691	%	n = 3471	%
Darifenacin	38	2.4	80	3.8	87	3.2	44	1.3
Flavoxate	9	0.6	15	0.7	11	0.4	4	0.1
Mirabegron	215	13.7	431	20.3	570	21.2	324	9.3
Conjugated estrogens vaginal cream	51	3.3	357	16.8	295	11.0	79	2.3
Duloxetine	11	0.7	47	2.2	31	1.2	23	0.7
Botulinum toxin	5	0.3	12	0.6	3	0.1	4	0.1
Comedications	1395	88.9	2019	95.1	2608	96.9	3342	96.3
Analgesics and anti-inflammatories	999	63.7	1515	71.3	1856	69.0	2413	69.5
Antihypertensives and diuretics	240	15.3	842	39.6	1745	64.8	2538	73.1
Anti-ulcer	526	33.5	1029	48.4	1519	56.4	1824	52.5
Lipid-lowering	180	11.5	842	39.6	1481	55.0	1704	49.1
Antidepressants	362	23.1	712	33.5	991	36.8	1325	38.2
Potentially inappropriate or risky prescriptions	–	–	–	–	–	–	–	–
Bladder antimuscarinics in the elderly (n = 2231)	–	–	–	–	829	37.2	386	17.3
Bladder antimuscarinics in risk comorbidities (n = 2231)	31	9.0	110	16.3	187	22.6	152	39.4
Systemic estrogens (n = 7347)	118	9.9	69	4.0	10	0.5	2	0.1
Peripheral α-adrenergic antagonists (n = 7347)	6	0.5	12	0.7	50	2.6	54	2.2

Table 4. Potentially inappropriate or risky prescriptions in 9855 patients with urinary incontinence, Colombia.

Variables	n = 9855	%
Bladder antimuscarinics	2231	22.6
Age ≥65 years	1215	54.5
Comorbidities	480	21.5
Prostatic hyperplasia	163	7.3
Sicca syndrome	121	5.4
Glaucoma	113	5.1
Constipation	105	4.7
Dementia	71	3.2

(Continued)

Table 4. (Continued)

Variables	<i>n</i> = 9855	%
Women	7347	74.6
Systemic estrogens	199	2.7
Levonorgestrel + Ethinylestradiol (Tablet)	94	1.3
Conjugated Estrogens (Tablet)	71	1.0
Estradiol Hemihydrate (Transdermal Patch)	13	0.2
Estriol (Ovule)	12	0.2
Norethisterone + Estradiol valerate (Parenteral)	5	0.1
Estradiol valerate (Tablet)	4	0.1
Medroxyprogesterone + Estradiol (Parenteral)	4	0.1
Cyproterone + Ethinylestradiol (Tablet)	2	0.0
Dienogest + Ethinylestradiol (Tablet)	1	0.0
Drospirenone + Estradiol (Tablet)	1	0.0
Drospirenone + Ethinylestradiol (Tablet)	1	0.0
Peripheral alpha adrenergic antagonists	122	1.7
Prazosin	119	1.6
Doxazosin	3	0.0
Terazosin	0	0.0

Table 5. Multivariate analysis of the variables related to having potentially inappropriate prescriptions in patients with urinary incontinence.

Variables	Significance	OR	95% Confidence interval	
			Lower	Upper
Woman	0.001	0.808	0.710	0.919
Age: <65 years	< 0.001	Reference	Reference	Reference
65–79 years	< 0.001	4.992	4.318	5.771
≥80 years	< 0.001	2.425	2.052	2.864
Bogota-Cundinamarca Region	0.060	1.126	0.995	1.274
Overactive bladder	< 0.001	4.008	2.970	5.408
Neurological comorbidities	< 0.001	0.632	0.540	0.741
Psychiatric comorbidities	0.054	1.163	0.998	1.355
Comedication with antihypertensives	< 0.001	1.448	1.277	1.642
Comedication with antidiabetics	0.017	1.176	1.029	1.345
Use of diapers	< 0.001	0.248	0.212	0.290
OR, odds ratio.				

of women, as identified in the majority of studies (59.6–74.9%)^{5,14–18} probably due to the prolapse of the female genital organs due to weakening of the pelvic floor muscles.¹⁹ In addition, the characterization of the main comorbidities was consistent with that found in other publications from Europe and North America.^{7,9,18,20} Various pathologies, such as cardiovascular diseases, diabetes mellitus, constipation and obesity, have been shown to be predictors of urinary incontinence^{4,10} and pathologies such as anxiety and depression are more prevalent in this group of patients.²¹

In this study, the majority of the patients had unspecified urinary incontinence as a diagnosis; this differs from findings in Canada and the United States, where urgency urinary incontinence predominates (45.0–62.4%),^{7,13} and in China, where the mixed form predominates (38.1%).¹⁰ In addition, there was a lower proportion of stress urinary incontinence among the patients in this study than has been described in other studies (11.9–14.4%).^{10,13} These differences may be due to the methodologies used. For example, in this report, patients were identified by ICD-10 codes, which do not include a specific diagnosis for stress urinary incontinence or mixed urinary incontinence,²² hence the high frequency of the unspecified and specified forms. In addition, it is possible that the treating physicians would have had difficulties in establishing a more precise and specific diagnosis. In this way, primary care physicians can be recommended to use the Michigan Incontinence Symptom Index (M-ISI), which makes it possible to determine the type of urinary incontinence, the severity, and the related discomforts that patients present, allowing guidance in a best way treatment.^{23,24}

The proportion of patients who were prescribed bladder antimuscarinics was similar to that found by Odeyemi *et al.*²⁵ in England (21.0%) and by Ali *et al.*²⁶ in the United Kingdom (23.9%), but higher than that described by Zarowitz *et al.*¹⁴ in the United States (8.2%). In this report, tolterodine was the most commonly used antimuscarinic, consistent with findings in Sweden and the United States,^{17,18} but different from that described in Denmark and Spain, where the use of solifenacin predominated,^{18,27,28} and in the United Kingdom, where oxybutynin prevailed.^{18,25} A greater proportion of the patients in this report were prescribed mirabegron than was

previously reported for patients in the United Kingdom (2.1–5.5%)^{26,29} and the United States (<0.1%),²⁰ but in Spain, the proportion of prescriptions for this drug was higher, predominating over even bladder antimuscarinics.²⁸ These variations can be explained by the characteristics of health systems, the accessibility and availability of drugs in each country, local management guidelines, prescriber preferences, the marketing strategies of the pharmaceutical industry and patient tolerance of the treatment.^{30,31} These medications are indicated in patients with a diagnosis of urge urinary incontinence with or without overactive bladder who experience persistent symptoms despite conservative treatment.^{3,6,11} In this report, the patients who presented concomitant overactive bladder received the most bladder antimuscarinics and β 3-adrenergic agonists, as expected according to management guidelines.^{3,6,11} However, a significant proportion of patients with stress urinary incontinence received these medications without indication.^{3,6}

In addition, we found that the prescription of bladder antimuscarinics was not homogeneous with respect to sex and age. For example, in this report, the predominance prescriptions for this class of drugs in women was notable and is consistent with the findings of studies from the United States, Spain, and the United Kingdom.^{9,26,28,29} On the contrary, more than half of the patients who were prescribed bladder antimuscarinics were older adults, a finding that is consistent with findings in the United Kingdom for patients with overactive bladder (54.5%)²⁹ but lower than the situation described in Spain (62.6%).²⁸ In older adults, these drugs should be prescribed with caution because they can be associated with adverse reactions, mainly cognitive reactions.^{8,12,32} A meta-analysis of 20 clinical trials found that among older adults, the efficacy of antimuscarinics and mirabegron was similar, but the safety profile of the latter was much more favorable,³³ making it a valid option in this group of patients.

In addition to the above findings, one-fifth of the patients who were prescribed antimuscarinics presented with concomitant glaucoma, constipation, sicca syndrome, dementia or prostatic hyperplasia. This is in line with other pharmacoepidemiological studies that documented that the use of antimuscarinic drugs in patients with these pathologies ranged between 22.9% and

41.0%^{30,31,34–36} and for which drug–disease interactions could be associated with an increased risk of adverse drug reactions.^{8,12,33} Therefore, the anticholinergic burden at the time of comprehensive treatment of these patients should be taken into account,^{3,8,12,32} prolonged-release pharmaceutical forms should be preferentially used,³ and most importantly, other therapeutic options, such as mirabegron, vaginal estrogens, or nonpharmacological interventions, should be considered.³²

An important consideration is that of patients with benign prostatic hyperplasia who receive combined treatment with an α -adrenergic antagonist and a bladder antimuscarinic drug. This association is indicated for patients with lower urinary tract symptoms of moderate to severe intensity when the relief of storage symptoms has not improved with monotherapy.³⁷ Some authors recommend that these patients should initially receive an α -adrenergic antagonist and then antimuscarinic to reduce the risk of urinary retention.³⁸ In this report, it was found that almost one-quarter of patients with benign prostatic hyperplasia received this combined prescription, which was higher than previously documented in the United Kingdom (7.5%).²⁶ In addition, bladder antimuscarinics should not be prescribed for men who have a postvoiding residual volume greater than 150 ml.³⁷ However, in this study, urodynamic studies of patients were not available to identify PIPs.

According to the Beers criteria, the use of systemic estrogens and peripheral α -adrenergic antagonists for women with urinary incontinence are considered PIPs when symptoms worsen and should, therefore, be avoided.⁸ In several studies conducted in North America that involved patients with urinary incontinence, the authors found that between 11.8% and 22.2% of these patients received estrogens alone or with progestogens^{7,9,13} a proportion that was noticeably superior to what was found in this report. In contrast, the prescription of peripheral α -adrenergic antagonists was similar to that found in the United States (2.3%)⁷ and higher than that documented in Canada (0.3%).¹³ Several studies have documented that certain medications with sedative or hypnotic properties also seem to be related to an increased risk of urinary incontinence.^{9,10} However, at present, they are not considered PIPs in this clinical context according to the Beers criteria and the STOPP (Screening Tool of Older

Person's Prescriptions)/START (Screening Tool to Alert doctors to Right Treatment) criteria.^{8,12}

Variables were found that increased and reduced the probability of having possible PIPs. Several systematic reviews have shown that increasing age is related to a higher risk of presenting PIPs,^{39,40} which is consistent with this report. Likewise, the number of additional medications increases the risk, which is in line with what was found in this study in which receiving antihypertensive and antidiabetic drugs increased this probability,^{39,40} In addition, it was found that patients with overactive bladder had a higher risk of presenting possible PIPs. This is probably because they more frequently receive bladder antimuscarinics^{28,29} and therefore it would be more likely that these drugs can be used in inadequate conditions. On the contrary, those subjects with diagnoses of neurological diseases had a lower risk of receiving PIPs, which contrasts with other reports.^{39,40} It is possible that prescribers have considered the anticholinergic load of these patients, and therefore led them to reduce the use of bladder antimuscarinics, to avoid adverse drug reactions.³⁰

Some limitations in the interpretation of the results are recognized, since access to the patients' clinical histories was not obtained to verify the patients' clinical characteristics, the type of urinary incontinence they presented and its severity, or the paraclinical studies and nonpharmaceutical or surgical management the patients received. Similarly, medications that the patients may have received that were prescribed outside the health system or were not delivered by the dispensing company were not known. Finally, only the drugs' potential risk of triggering adverse reactions was considered; therefore, it is necessary to develop studies that clearly determine their safety. Nonetheless, this study has a significant number of patients distributed throughout most of the national territory and participating in both the contributory and subsidized health regimes of the country.

With these findings, we can conclude that there were differences in the prescription of medications according to the type of urinary incontinence, sex, and age group. Potentially inappropriate or risky prescriptions were frequent; therefore, continuing education strategies should be promoted as a crucial element to improve patients' safety and well-being when using medications.

Declarations

Ethics approval and consent to participate

The protocol was approved by the Bioethics Committee of the Technological University of Pereira in the category of ‘research without risk’ (approval number 0807-2019). In accordance with local legislation, informed consent for participation was not required. The principles established by the Declaration of Helsinki were respected.

Consent for publication

Not applicable.

Author contributions

Luis Fernando Valladales-Restrepo: Conceptualization; Data curation; Formal analysis; Methodology; Writing – original draft.

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Brayan Stiven Aristizábal-Carmona: Data curation; Formal analysis; Methodology; Writing – original draft.

Jorge Enrique Machado-Alba: Conceptualization; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing – review & editing.

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