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Original Investigation

Consistency between anticholinergic burden scales in patients with Sjögren's syndrome

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ABSTRACT

Introduction: Sjögren's syndrome is the second most frequent autoimmune rheumatic disease and is characterized by exocrine gland involvement manifesting as sicca symptoms. The objective of this study was to estimate the degree of agreement between three anticholinergic burden scales related to the prescriptions of patients diagnosed with Sjögren's syndrome in Colombia.

Materials and methods: An analytical concordance study was conducted. The weighted kappa coefficient with quadratic weights was used to identify consistency between the Anticholinergic Drug Scale (ADS), Anticholinergic Cognitive Burden Scale (ACB) and Anticholinergic Risk Scale (ARS), which address the prescriptions used for 3 months by patients with Sjögren's syndrome, in a population database.

Results: A total of 15,696 patients with Sjögren's syndrome were identified, with a mean age of 65.4 ± 13.9 years, and 74.2% were women. A total of 94.1% of the patients received at least one topical lubricant, with carboxymethyl cellulose being the most commonly prescribed (22.9%), while oral pilocarpine was prescribed to 3.5% of patients. The ACB was the tool identified more antimuscarinic prescriptions (37.5%), followed by the ADS (35.3%) and ARS (25.2%). The greatest degree of agreement was found between the ADS and ACB (kappa 0.6520; confidence interval (CI): 0.6393–0.6648).

Conclusions: Except for the ADS and ACB, little agreement was found between the three scales gauging the anticholinergic burden. Additional studies are needed to determine how these differences can impact the clinical outcomes of patients.

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Consistencia entre escalas de carga anticolinérgica en pacientes con síndrome de Sjögren

Palabras clave:
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Pilocarpina
Antagonistas colinérgicos
Interacciones medicamentosas
Farmacovigilancia

RESUMEN

Introducción: El síndrome de Sjögren es la segunda enfermedad reumática autoinmune más frecuente, caracterizada especialmente por el compromiso de glándulas exocrinas manifestándose con síntomas sicca. El objetivo fue estimar el grado de acuerdo de 3 escalas de carga anticolinérgica en las prescripciones de pacientes con diagnóstico de síndrome de Sjögren en Colombia.

Materiales y métodos: Estudio analítico de concordancia. Se empleó el coeficiente Kappa con ponderación cuadrática para identificar la consistencia entre los instrumentos Anticholinergic Drug Scale (ADS), Anticholinergic Cognitive Burden Scale (ACB) y Anticholinergic Risk Scale (ARS) de las prescripciones utilizadas durante 3 meses por pacientes con síndrome de Sjögren, a partir de una base de datos poblacional.

Resultados: Se identificaron 15.696 pacientes con síndrome de Sjögren, con una edad media de 65,4 ± 13,9 años y el 74,2% de mujeres. El 94,1% recibieron por lo menos un lubricante tópico siendo el más prescrito la carboximetilcelulosa (22,9%), mientras que la pilocarpina oral se formuló en el 3,5% de ellos. La escala ACB fue la herramienta que más prescripciones anti-muscarínicas identificó (37,5%) seguida de la ADS (35,3%) y ARS (25,2%). El mayor grado de acuerdo se presentó entre las escalas ADS-ACB (Kappa: 0,6520; IC: 0,6393-0,6648).

Conclusiones: Con excepción de las escalas ADS-ACB, hubo poco acuerdo al comparar las 3 escalas de carga anticolinérgica. Se requieren estudios adicionales para determinar cómo estas diferencias pueden impactar en la validez de los desenlaces clínicos de los pacientes.

Introduction

Sjögren's syndrome is the second most common autoimmune rheumatic disease and is characterized by lymphocytic infiltration of the exocrine glands, causing their dysfunction and destruction, especially the salivary and tear glands, thus leading to dry mouth and dry eyes, which are known as sicca symptoms.[1–3] Sjögren's syndrome is a systemic disease that can compromise the musculoskeletal, peripheral and/or central nervous, cardiovascular, circulatory, respiratory, renal and gastrointestinal systems, among others, in 50–60% of patients.[1,2,4]

The general prevalence of Sjögren's syndrome is estimated to range from 0.3 to 1 per 1000 people,[5] females are more often affected, with a female:male ratio of 9 to 1, and the maximum incidence is observed among individuals aged from 40 to 55 years.[3,5,6] In Colombia, the prevalence is 0.12% among patients over 18 years old, with a female:male ratio of 4.6:1, and the age group with the highest prevalence is that to 65–69 years (0.5%).[7] In another study, in 6 cities in the country, the prevalence was 0.08% (95%CI: 0.02–0.27).[8]

Treatments for sicca symptoms include moisturizers, eye lubricants, ophthalmic cyclosporine, artificial saliva and muscarinic agonists such as pilocarpine, as well as nonpharmacological measures.[9–11] Inadequate management of dry eye can lead to complications such as surface wear, corneal perforation, conjunctivitis, keratitis and vision loss, while dry mouth can produce dysphagia, speech difficulties, an atrophic or fissured tongue, ulcers, stomatitis, oral candida and dental caries, resulting in quality of life deterioration and disability.[1–3]

Sicca symptoms can be exacerbated by numerous medications, especially diuretics, antidepressants, neuroleptics, muscle relaxants, hypnotics, opioids, benzodiazepines, antihistamines and antispasmodics, among others,[1,3,4,6] and many of these medications have antimuscarinic properties that contribute to the anticholinergic burden of patients. The anticholinergic burden is defined as the cumulative effect of taking one or more drugs capable of producing adverse antimuscarinic reactions,[12,13] which can include dryness of the skin and mucous membranes, constipation, urinary retention, mydriasis, delirium, cognitive deterioration and sedation, among others.[12,14,15] Scales developed to quantify the anticholinergic burden use equations and medication lists to classify and assign points according to the medications' antimuscarinic activity.[12,13,16]

These tools present variations due to the different methodologies used for their preparation and validation, which may influence patient outcomes.[12,13,17] In a systematic review in 2015, the ACB (Anticholinergic Cognitive Burden Scale), ARS (Anticholinergic Risk Scale) and ADS (Anticholinergic Drug Scale) were identified as the most validated instruments[13]; however, no standardized quantification scale is available.[13,16]

Concordance studies use different designs to evaluate the degree of agreement between two or more observers or between different methods, techniques or instruments on the same observed phenomenon. If one technique or instrument is considered the "gold standard", then the resulting concordance will be considered a measure of conformity. However, if

no techniques or instruments are considered "gold standards" or references, then any concordance identified will serve as a measure of consistency.[18,19] Because no "gold standard" is available to quantify the anticholinergic burden or for comparison with other tools, this is a study of consistency. Some studies have shown that the anticholinergic burden increases the risk of mucosal dryness[20,21]; therefore, the objectives of the study were to use the three most validated anticholinergic burden scales to assess the prescriptions of patients with Sjögren's syndrome and to determine the degree of agreement between these scales, in addition, to characterize some of their sociodemographic, clinical, and pharmacological variables.

Materials and methods

An analytical study of consistency was performed with three anticholinergic burden scales and the drugs currently used by patients diagnosed with Sjögren's syndrome according to a population database. This database collects information from approximately 8.5 million people affiliated with Colombia's Health System, including six health insurance companies, corresponding to approximately 30.0% of the active affiliate population of the contributing regime and 6.0% of patients registered with the state-subsidized health insurance regime in the country, representing 16.3% of the Colombian population.

The identification of the patients was made through the diagnosis of Sjögren's syndrome from the 1st of July to the 30th of September 2019. The diagnosis was identified using the International Statistical Classification of Diseases and Related Health Problems (ICD-10), where M35.0 is the code for sicca (Sjögren) syndrome. Male and female patients older than 14 years of age who attended outpatient consultations were included. We analyzed the prescriptions of patients diagnosed with Sjögren's syndrome who were receiving drugs with anticholinergic properties using the ADS, ACB and ARS.

Based on information regarding medication consumption among the affiliated population, which was systematically collected by the dispensing company (Audifarma S.A.), a database was designed to allow collection of the following groups of patient variables:

1. Sociodemographic variables: sex, age and city of care.
2. Chronic comorbidities, which were identified from primary and secondary diagnoses coded according to the ICD-10 during the same study period, were grouped into four categories: none, 1–2, 3–4 and 5 or more pathologies; the following groups of diseases were considered.
   - Cardiovascular diseases: hypertension, ischemic cardiomyopathy, arrhythmias, heart failure and valvulopathies.
   - Endocrine diseases: diabetes mellitus, hypothyroidism, dyslipidemia, obesity and hyperthyroidism.
   - Rheumatologic diseases: osteoarthrosis, rheumatoid arthritis, osteoporosis, fibromyalgia, systemic lupus erythematosus, vasculitis, systemic sclerosis, ankylosing spondylitis, polymyalgia rheumatica, amyloidosis, scleroderma and inflammatory myopathy.
   - Renal diseases: chronic kidney disease.
   - Psychiatric diseases: depression, anxiety, bipolar affective disorder, sleep disorders and schizophrenia.
   - Neurologic diseases: peripheral neuropathies, dementia, migraine, epilepsy, Parkinson's disease, stroke and mental retardation.
   - Digestive diseases: gastritis, gastroesophageal reflux, constipation, fecal incontinence, cirrhosis, peptic ulcer and ulcerative colitis.
   - Respiratory: chronic obstructive pulmonary disease and asthma.
3. Pharmacological management variables:
   - Medications used for symptomatic management of xerostomia/xerophthalmia:
   - Local: artificial tears (carboxymethyl cellulose, hyaluronate, hydroxypropyl methyl cellulose, chondroitin, polyethylene glycol, propylene glycol, glycerin and polyacrylic acid), ophthalmic cyclosporine and artificial saliva.
   - Systemic: oral pilocarpine.
   - Synthetic disease-modifying antirheumatic drugs: methotrexate, sulfasalazine, chloroquine, hydroxychloroquine, azathioprine and leflunomide.
   - Biological disease-modifying antirheumatic drugs: rituximab, abatacept, etanercept, infliximab, tocilizumab, certolizumab, golimumab and adalimumab.
4. Anticholinergic drugs: A search was conducted for 88 of the 117 drugs included in the ADS, 64 of the 88 drugs included in the ACB and 43 of the 49 included in the ARS that are marketed in Colombia according to the Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA, Colombia's National Food and Drug Surveillance Institute). The total anticholinergic burden was determined by the sum of the risk of each of the prescribed medications. Accordingly, the patients were classified into four groups: 1. Patients with a score of 0 (no anticholinergic activity); 2. Patients with a score of 1 (mild anticholinergic activity); 3. Patients with a score of 2 (moderate anticholinergic activity); and 4. Patients with a score ≥ 3 (high anticholinergic activity).

The protocol was approved by the Bioethics Committee of the Universidad Tecnológica de Pereira in the risk-free research category. The ethical principles established by the Declaration of Helsinki were respected. Patients' personal data were not considered.

The data were analyzed with the statistical package SPSS Statistics, version 24.0 for Windows (IBM, USA). A descriptive analysis was performed in which frequencies and proportions were used to describe qualitative variables, while measures of central tendency and dispersion were used for quantitative variables. Quantitative variables were compared using Student's t test or ANOVA, and the X^2 test was used for categorical variables. Binary logistic regression models were established using the consumption of drugs with an anticholinergic burden (1 or more points, according to the ADS, ACB and ARS) as the dependent variable, and variables that were significantly associated with these drugs in bivariate analyses as covariables. $p < 0.05$ was set as the level of statistical significance.

Using the Epidat software version 4.2 of 2016, the concordance analysis was performed between the ADS, ARS and ACB using the weighted kappa coefficient with quadratic weights

and a confidence interval (CI) of 95%. To classify the results, the scale described by Landis and Koch was used as follows: weak agreement, 0–0.2; mild agreement, 0.2–0.4; moderate agreement, 0.4–0.6; substantial or high agreement, 0.6–0.8; and almost perfect agreement, 0.8–1.[22]

Results

A total of 15,696 patients diagnosed with Sjögren's syndrome and distributed among 99 different cities were identified. The mean age was 65.4 ± 13.9 years (range: 14.08–104.83 years), and 74.2% (n = 11,641) of the patients were women. The female:male ratio in the study population was 2.9:1. A total of 94.1% (n = 14,765) of the patients were receiving pharmacological treatment for Sjögren's syndrome, with carboxymethylcellulose (n = 3594, 22.9%) being the most prescribed eye lubricant, while oral pilocarpine was prescribed to 3.5% (n = 544) of patients. The use of synthetic disease-modifying antirheumatic drugs was identified in 8.3% (n = 1299) of the patients, while the use of biological drugs was identified in 0.3% (n = 46) of the patients (Table 1).

Anticholinergic burden

The scale that identified the highest proportion of patients with antimuscarinic prescriptions was the ACB (n = 5886, 37.5%; 46 different medications), followed by the ADS (n = 5546, 35.3%; 59 different medications) and the ARS (n = 3959, 25.2%; 29 different medications). The drug most frequently identified by the ACB was metoprolol (n = 1436, 9.1%), the ADS most frequently identified furosemide (n = 1061, 6.8%), and the ARS most frequently identified methocarbamol (n = 965, 6.1%) (Table 2).

Comorbidities

The most frequently identified comorbidities were hypertension (n = 6243, 39.8%), diabetes mellitus (n = 1965, 12.5%), glaucoma (n = 1774, 11.3%), hypothyroidism (n = 1206, 7.7%), chronic kidney disease (n = 1028, 6.5%), dyslipidemia (n = 682, 4.3%), osteoarthritis (n = 602, 3.8%), rheumatoid arthritis (n = 579, 3.7%), benign prostatic hyperplasia (n = 442, 2.8%) and depression (n = 403, 2.6%). Among the patients, 71.5% (n = 11,225) had chronic comorbidities, with cardiovascular

Table 1 – Pharmacological management of patients diagnosed with Sjögren's syndrome, Colombia.

Pharmacotherapy	Frequency n = 15,696	%
Symptomatic	14,765	94.1
Lubricants and ocular humectants	14,509	92.4
Carboxymethylcellulose	3594	22.9
Hyaluronate	3575	22.8
Chondroitin + hyaluronate	2915	18.6
Polyacrylic acid	2104	13.4
Polyethylene glycol + propylene glycol	1560	9.9
Carboxymethylcellulose + glycerin + hyaluronate	1315	8.4
Carboxymethylcellulose + glycerin	895	5.7
Hydroxypropylmethylcellulose	402	2.6
Polyethylene glycol + propylene glycol + hyaluronate	101	0.6
Hydroxypropylmethylcellulose + dextran	12	0.1
Carboxymethylcellulose + glycerin + polysorbate	9	0.1
Oral pilocarpine	544	3.5
Cyclosporine ophthalmic	229	1.5
Artificial saliva	31	0.2
Synthetic disease-modifying antirheumatic drugs	1299	8.3
Methotrexate	589	3.8
Chloroquine	458	2.9
Leflunomide	251	1.6
Sulfasalazine	187	1.2
Azathioprine	169	1.1
Hydroxychloroquine	101	0.6
Biologic disease-modifying antirheumatic drugs	46	0.3
Abatacept	11	0.1
Etanercept	11	0.1
Adalimumab	9	0.1
Certolizumab	9	0.1
Tocilizumab	5	0.0
Golimimab	1	0.0
Oral corticosteroid	865	5.5
Prednisolone	723	4.6
Deflazacort	71	0.5
Prednisone	70	0.4
Methylprednisolone	21	0.1

Table 2 – Principal antimuscarinic drugs identified with the ADS, ACB and ARS scales in patients diagnosed with Sjögren's syndrome, Colombia.

Drugs	Anticholinergic load	Frequency $n = 15,696$	%
ACB ($n = 46$)	–	5886	37.5
Metoprolol	1	1436	9.1
Furosemide	1	1061	6.8
Prednisolone	1	723	4.6
Codeine	1	676	4.3
Trazodone	1	629	4.0
Chlorpheniramine	3	513	3.3
Ranitidine	1	465	3.0
Nifedipine	1	395	2.5
Dimenhydrinate	3	307	2.0
Imipramine	3	306	1.9
ADS ($n = 59$)	–	5546	35.3
Furosemide	1	1061	6.8
Prednisolone	1	723	4.6
Codeine	1	676	4.3
Chlorpheniramine	3	513	3.3
Sertraline	1	469	3.0
Ranitidine	2	465	3.0
Dexamethasone	1	458	2.9
Nifedipine	1	395	2.5
Dimenhydrinate	3	307	2.0
Imipramine	3	306	1.9
ARS ($n = 29$)	–	3959	25.2
Methocarbamol	1	965	6.1
Loratadine	2	673	4.3
Trazodone	1	629	4.0
Chlorpheniramine	3	513	3.3
Ranitidine	1	465	3.0
Imipramine	3	306	1.9
Amitriptyline	3	243	1.5
Metoclopramide	1	214	1.4
Quetiapine	1	200	1.3
Loperamide	2	120	0.8

ACB: Anticholinergic Cognitive Burden Scale; ADS: Anticholinergic Drug Scale; ARS: Anticholinergic Risk Scale.

($n = 6445$, 41.1%), endocrine ($n = 3701$, 23.6%) and rheumatologic ($n = 1841$, 11, 7%) diseases being the most frequent pathologies. A total of 57.6% ($n = 9036$) of the patients had 1–2 comorbidities, 12.5% ($n = 1958$) had 3–4 comorbidities, and 1.5% ($n = 231$) had 5 or more comorbidities.

Comparison between age groups

The use of topical lubricants or moisturizers by patients with Sjögren's syndrome did not show significant variations across the different age groups, while oral pilocarpine was predominately prescribed to patients between 40 and 64 years of age. Chronic comorbidities increased with increasing age. The ARS identified the lowest proportions of patients using antimuscarinic drugs in all age groups; the proportions identified using the ACB among patients aged 65 years and older were higher than those identified using the ADS, while the opposite results were found for patients younger than 65 years (Table 3).

Consistency analysis

The ADS and ACB showed the best degree of agreement (kappa 0.6520; 95%CI: 0.6393–0.6648), while comparisons involving the ARS yielded low consistencies (Table 4).

Multivariate analysis

The multivariate analysis revealed that female sex increased the probability of receiving anticholinergic medications (ADS: odds ratio (OR):1.26, 95%CI:1.16–1.37; ACB: OR:1.24, 95%CI:1.14–1.35; ARS: OR:1.31, 95%CI:1.19–1.44), as well as having 1–2 chronic comorbidities (ADS: OR:1.71, 95%CI:1.50–1.94; ACB: OR:1.88, 95%CI:1.65–2.15; ARS: OR:1.40, 95%CI:1.23–1.60) and 3–4 chronic comorbidities (ADS: OR:2.11, 95%CI:1.70–2.63; ACB: OR:2.35, 95%CI:1.89–2.93; ARS: OR:1.45, 95%CI:1.16–1.81). Among the comorbidities, psychiatric disorders were most associated with the risk of having antimuscarinic prescriptions on the three scales (ADS: OR:3.56, 95%CI:2.97–4.27;

Table 3 – Comparison of some sociodemographic, clinical and pharmacological variables by age group in patients diagnosed with Sjögren's syndrome, Colombia.

Variable	Total		<40 years		40–64 years		65–74 years		75–84 years		≥85 years	
	n = 15,696	%	n = 832	%	n = 6319	%	n = 4708	%	n = 2795	%	n = 1042	%
Woman	11,641	74.2	575	69.1	4955	78.4	3475	73.8	1925	68.9	711	68.2
Symptomatic treatment	14,765	94.1	785	94.4	5966	94.4	4433	94.2	2600	93.0	981	94.1
Lubricants/humectants	14,509	92.4	768	92.3	5830	92.3	4367	92.8	2571	92.0	973	93.4
Oral pilocarpine	544	3.5	23	2.8	314	5.0	146	3.1	53	1.9	8	0.8
Cyclosporine ophthalmic	229	1.5	35	4.2	109	1.7	53	1.1	21	0.8	11	1.1
Chronic comorbidities	11,225	71.5	268	32.2	3974	62.9	3691	78.4	2360	84.4	932	89.4
Cardiovascular	6445	41.1	63	7.6	1903	30.1	2224	47.2	1611	57.6	644	61.8
Endocrine	3701	23.6	64	7.7	1349	21.3	1378	29.3	695	24.9	215	20.6
Rheumatologic	1841	11.7	69	8.3	857	13.6	542	11.5	283	10.1	90	8.6
Renal	1028	6.5	13	1.6	164	2.6	339	7.2	359	12.8	153	14.7
Psychiatric	766	4.9	33	4.0	337	5.3	203	4.3	127	4.5	66	6.3
Anticholinergic load	–	–	–	–	–	–	–	–	–	–	–	–
ACB ≥ 1 point	5886	37.5	173	20.8	2005	31.7	1805	38.3	1335	47.8	568	54.5
ACB ≥ 1–2 points	3797	24.2	101	12.1	1257	19.9	1167	24.8	889	31.8	383	36.8
ACB ≥ 3 points	2089	13.3	72	8.7	748	11.8	638	13.6	446	16.0	185	17.8
ADS ≥ 1 point	5546	35.3	198	23.8	2059	32.6	1637	34.8	1151	41.2	501	48.1
ADS ≥ 1–2 points	3534	22.5	133	16.0	1295	20.5	1020	21.7	750	26.8	336	32.2
ADS ≥ 3 points	2012	12.8	65	7.8	764	12.1	617	13.1	401	14.3	165	15.8
ARS ≥ 1 point	3959	25.2	144	17.3	1538	24.3	1195	25.4	758	27.1	324	31.1
ARS ≥ 1–2 points	2491	15.9	85	10.2	937	14.8	744	15.8	491	17.6	234	22.5
ARS ≥ 3 points	1468	9.4	59	7.1	601	9.5	451	9.6	267	9.6	90	8.6

ACB: Anticholinergic Cognitive Burden Scale; ADS: Anticholinergic Drug Scale; ARS: Anticholinergic Risk Scale.

Table 4 – Analysis of the consistency between the ADS, ACB and ARS scales in patients diagnosed with Sjögren's syndrome, Colombia.

Scales	Kappa coefficient	Standard error	CI:95%		p
			Lower	Upper	
ADS-ACB	0.6520	0.0065	0.6393	0.6648	<0.001
ACB-ARS	0.3063	0.0080	0.2907	0.3219	<0.001
ARS-ADS	0.2746	0.0083	0.2583	0.2909	<0.001

ACB: Anticholinergic Cognitive Burden Scale; ADS: Anticholinergic Drug Scale; ARS: Anticholinergic Risk Scale.

ACB: OR:3.84, 95%CI:3.19–4.62; ARS: OR:5.20, 95%CI:4.37–6.17). The OR was adjusted for sex, age, city and comorbidities (supplementary Tables 1–3).

Discussion

This study identified potentially inappropriate prescriptions of antimuscarinic drugs among patients diagnosed with Sjögren's syndrome using three different anticholinergic burden scales and determined the degree of agreement between the scales. The findings may be useful for caregivers, scholars and scientists with respect to clinical decision-making regarding potential harmful interactions and adverse drug reactions experienced by patients. In Colombia, the ADS has historically identified an anticholinergic burden of 39.1% among patients with Sjögren's syndrome.[23]

The ACB identified the highest amount of drugs with antimuscarinic properties (37.5%), followed by the ADS (35.3%) and the ARS (25.2%). These findings are similar to those reported in Finland by Tiisanoja et al. in patients with xerostomia, where antimuscarinic prescriptions were mostly identified by the ACB (33.7%), followed by the ADS (29.6%) and ARS (28.9%).[17] Identifying these drugs is important because the number of adverse antimuscarinic reactions increases with a higher anticholinergic burden; however, no evidence indicates that the association is linear, and ultimately, a plateau most likely occurs when burden values become very high.[12]

In another study conducted in Finland, Tiisanoja et al. found that a score of 3 or higher on the ADS was a risk factor for developing xerostomia (risk ratio (RR): 3.17: 95%CI:1.44–6.96).[20] Based on a list of drugs with anticholinergic properties, Rudolph et al. found that patients with a high anticholinergic burden had an increased risk (OR:1.9; 95% CI:1.50–2.50) of experiencing adverse peripheral effects (xerostomia, xerophthalmia and constipation).[21] No studies relating ACB scores with an increased risk of mucosal dryness are available.

When comparing the three tools, the ADS and ACB showed the best agreement (0.65). In contrast, the degree of agreement between the ACB and ARS and between the ADS and ARS was low. Discrepancies between these scales may be related

to how they were developed, the associated methodologies and validation measures, the number of drugs listed in each instrument, differences in the classification of the antimuscarinic potency of each drug and the inclusion of routes of administration other than oral or parenteral.[21,24,25]

No consistency studies comparing anticholinergic burden scales specifically among patients with Sjögren's syndrome have been identified. However, some studies have been conducted in different populations and clinical contexts.[26–29] Naples et al. found the best agreement between the ADS and ACB (0.70) for seniors living at home in the USA.[26] Pont et al. found the highest degree of agreement between the ADS and ACB (0.62) for nonhospitalized men in Australia,[27] and Turró-Garriga et al. identified high concordance between the ADS and ACB (0.62) for patients with dementia in Spain.[29] However, in other research conducted in Spain, Lertxundi et al. found the best agreement between the ACB and ARS (0.25) in patients hospitalized for psychiatric disorders.[28] Possible explanations for this discrepancy may include differences in the characteristics of the population (community, hospitalized and specific population groups) and the inclusion of medications in the instruments that are not available in all countries.

Related to the above, the multivariate models used to find the variables that were related to anticholinergic load, calculated with the ADS, ACB and ARS scales, showed risk or protective associations that varied according to the tool used (see supplementary tables). These discrepancies were also evidenced in a study that compared the three anticholinergic burden scales, but in patients with vertebral and non-vertebral fractures.[30]

Anticholinergic drugs are necessary in the treatment of various pathologies, such as overactive bladder, urinary incontinence, chronic obstructive pulmonary disease, asthma, Parkinson's disease, psychotic disorders, mood disorders and allergic reactions.[14] Anticholinergic burden scales are tools that help guide clinical decision-making, allowing clinicians to stop or change a drug with potent antimuscarinic activity in favor of another drug with little or no burden and thus guaranteeing greater safety and a lower probability of adverse reactions.[14] In recent years, problems related to prescribing practices have attracted increasing interest, which has promoted the development of tools for more appropriate drug prescription practices, such as the Beers criteria[31] and the STOPP (Screening Tool of Older Person's Prescriptions),[32] which include anticholinergic medications.[31,32]

In this study, most patients received useful topical prescriptions for the management of sicca symptoms, which is consistent with the recommendations of different clinical practice guidelines.[9–11] The use of oral pilocarpine (3.5%) differed from that found in other studies (20–31.7%).[33,34] These differences are probably due to the prescribing habits of physicians, the availability or lack of such drugs in the health systems of various countries or the degree of xerostomia and xerophthalmia severity among patients included in the studies.

Some limitations related to the interpretation of the results should be noted. Clinical histories were not obtained to identify nonpharmacological management measures used by patients, the evolution of the disease was not considered, the classification of the disease as a primary or secondary diagnosis was not determined, and possible complications experienced by patients were not evaluated. Furthermore, whether some of the possible adverse effects actually occurred was not investigated. In addition, the diagnosis of sicca (Sjögren) syndrome found in the ICD-10 can be used in patients with symptoms secondary to adverse drug reactions as well as to chemotherapy or radiotherapy. On the other hand, as a specific limitation of cross-sectional studies, it was found that the different variables were collected at a certain point in time, therefore the anticholinergic load and the pharmacological treatment of patients with Sjogren's syndrome are distributed in a 3-month period and not throughout the course of the disease.

Conclusions

Based on the above findings, we found little agreement between the three scales gauging the anticholinergic burden, although greater consistency was found between the ADS and ACB. Therefore, additional studies are needed to determine how these differences may impact clinically relevant outcomes such as mucosal or skin dryness, among others. Most patients received topical treatments for Sjögren's syndrome according to clinical practice recommendations. These results should be useful to promote and strengthen educational and pharmacovigilance strategies that improve the prescription habits of physicians involved in the care of these patients.

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Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.rcreu.2020.04.008.

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