

Année 2021/2022

N°

Thèse

Pour le

DOCTORAT EN MEDECINE

Diplôme d'État

par

Hélène BASSAC

Née le 28 avril 1992 à Briey (54)

TITRE

Facteurs influençant la charge anticholinergique de l'ordonnance des patients âgés hospitalisés pour confusion

Présentée et soutenue publiquement le **26 avril 2022** devant un jury composé de :

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* PS : attention, stimulant lacrymal.

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En présence des Maîtres de cette Faculté,
de mes chers condisciples
et selon la tradition d'Hippocrate,
je promets et je jure d'être fidèle aux lois de l'honneur
et de la probité dans l'exercice de la Médecine.

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et n'exigerai jamais un salaire au-dessus de mon travail.

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ne verront pas ce qui s'y passe, ma langue taira
les secrets qui me seront confiés et mon état ne servira pas
à corrompre les mœurs ni à favoriser le crime.

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l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime
si je suis fidèle à mes promesses.
Que je sois couvert d'opprobre
et méprisé de mes confrères
si j'y manque.

Facteurs influençant la charge anticholinergique de l'ordonnance des patients âgés hospitalisés pour confusion

RÉSUMÉ

Contexte : La confusion est un motif fréquent d'admission aux urgences chez les patients âgés. Parmi les étiologies, une iatrogénie peut exister, due à la poly-médication et notamment aux effets anticholinergiques parfois cachés de nombreux médicaments. Une réduction de la charge anticholinergique (CAC) de l'ordonnance, serait bénéfique pour les patients.

Objectifs : identifier les facteurs influençant la diminution de la CAC de l'ordonnance de patients ≥ 75 ans, hospitalisés pour confusion. Analyser l'impact de la CAC sur les réhospitalisations précoces (dans les 30 jours) pour le même motif.

Conception : étude observationnelle descriptive mono-centrique, réalisée au CHRU de Tours.

Participants : 160 patients âgés de 75 ans ou plus, hospitalisés entre le 1/01/2019 et le 31/12/2019 via le service des urgences pour syndrome confusionnel ont été inclus. Les patients ont été répartis en deux groupes : CAC diminuée, ou CAC stable et augmentée à la sortie d'hospitalisation.

Résultats : 51 (31.9%) patients avaient une CAC diminuée à la sortie d'hospitalisation. L'analyse multivariée montrait que ces patients bénéficiaient significativement plus souvent d'une conciliation médicamenteuse (CM) à l'entrée (OR [IC 95%] = 7.57 [2.81-20.43]) et avaient une charge anticholinergique à l'entrée plus élevée (OR [IC 95%] = 1.77 [1.29-2.42]) que les patients présentant une CAC stable ou augmentée à la sortie d'hospitalisation. Les patients avec une CAC diminuée étaient significativement moins réhospitalisés dans les 30 jours (OR [IC 95%] = 0.22 [0.02 ; 0.99]).

Conclusion : La diminution de la charge anticholinergique de l'ordonnance de patients âgés confus est favorisée par la présence d'une CM et d'un plus grand nombre de traitement à l'entrée d'hospitalisation. Cette optimisation de l'ordonnance permet également de réduire les réhospitalisations précoces.

MOTS CLÉS

Charge anticholinergique, effets indésirables, patients âgés, confusion, service des urgences, conciliation médicamenteuse, échelles anticholinergiques.

Factors influencing the anticholinergic burden of the prescription of older patients hospitalized for delirium

ABSTRACT

Background: Delirium is a frequent cause for admission to the emergency department (ED) for older patients. Among the etiologies, there is a part of iatrogeny due to the polymedication, in particular to the sometimes hidden anticholinergic effects of many treatments. A reduction of the anticholinergic burden (AB) of the prescription, and its adverse effects would be beneficial for patients.

Objectives: this study aims to identify factors that influence a decrease in the AB of the prescription of older patients, hospitalized for delirium. Moreover, we also investigated whether this variation in AB can make a real impact in early rehospitalization (less than 30 days) for the same cause of ED admission.

Design: observational descriptive study conducted at the University Hospital of Tours.

Participants: 160 patients ≥ 75 years old, hospitalized via the ED for delirium were included. The patients were divided into 2 groups according the AB variation at discharge: decreased AB, or stable and increased AB.

Results: 51 (31.9%) patients had a decreased AB at hospital discharge. Multivariate analysis shows significant results for the medication reconciliation (OR [95% CI] = 7.57 [2.81-20.43]), and the highest AB at admission (OR [95% CI] = 1.77 [1.29-2.42]) on the anticholinergic burden decrease. Patients with decreased AB were significantly less re-admitted within 30 days (OR [95% CI] = 0.22 [0.02; 0.99]).

Conclusion: the reduction of the AB of the prescription of confused older patients is facilitated by the presence of medication reconciliation and higher anticholinergic burden at admission. This optimization of the prescription also reduces the early re-admission of patients.

KEYWORDS

Anticholinergic burden, adverse effects, older patients, confusion/delirium, emergency department, medication reconciliation, anticholinergic scale.

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INTRODUCTION

Delirium is a frequent cause for admission to the emergency department (ED) representing about 10% of older patients over 70 years old (1). The diagnosis is missed in 2/3 of the patients, in part due to the heterogeneous clinical presentation of the delirium: hyperactive, hypoactive, or mixed type (2). In addition, patients who leave the ED confused are at higher risk of mortality within 30 days than those who are not confused. This association remained significant for up to 1 year, regardless of the patient's home environment (3,4).

Drugs with anticholinergic activity are potentially inappropriate in older people because of their many adverse effects, peripheral (urinary retention, constipation, tachycardia, hyperthermia, xerostomia) and central (delirium, agitation and behavioural disorders, hallucinations, memory impairment). They constitute nearly 50% of the commonly prescribed medications to people over 60 years old (5). These medications can lead to delirium and the development of cascading comorbidities, resulting in a hospitalization (6). The anticholinergic burden (AB) of the prescription represents the cumulative effect of drugs with acetylcholine inhibition potential. There are multiple contradictory studies on the association between AB and health-related quality of life (HRQoL) (7). In contrast, a high AB is associated with delirium (OR [90%IC] 1,65 [1,09-2,51]) (8), lower functional performance and cognitive decline in the long term (9).

Confusion detection and complete review of the patient's prescription have recently been defined as quality geriatric emergency care indicators (10). The AB increases progressively with age in the general population, and the prevalence of a high Anticholinergic Cognitive Burden (ACB) score (> 3) is more important in women (31.8%, > 90 years old) than in men (25.7%, > 90 years old) (11). Hsu W-H et al. evaluated the association between anticholinergic burden and adverse clinical events over a 10-year follow-up and showed that high AB leads to an increased risk of ED admission and hospitalization (for fracture, and all-cause hospitalization) (12).

Identification of frailty with a comprehensive geriatric assessment, including systematic review of the prescription is necessary in the ED and allows for a reduction in mortality (13). However, the AB of the prescription is not included in the iatrogenic evaluation of delirium. Medication reconciliation (MR) is a helpful instrument for collecting an exact list of the patient's actual medications. It helps to reduce unintentional medication mistakes in older hospitalized patients (14). Pharmacist's Comprehensive Geriatric Assessment (pCGA) is a geriatric evaluation including the intervention of a pharmacist in the care process of older patients. This scale allowed for optimized prescriptions during hospitalization, such as dosage adjustment, the adding of a forgotten drug on admission, and ending inappropriate medications (15).

The overall AB is measured from scales that give a score to each medication. In practice, there are three scales frequently used: the Anticholinergic Drug Scale (ADS) (16), the Anticholinergic Cognitive Burden (ACB) (17), and the Anticholinergic Risk Scale (ARS) (18). The Anticholinergic Impregnation Coefficient (AIC) scale is another method for measuring anticholinergic burden based on the three previous scales and presents a more exhaustive list of treatments and specific anticholinergic potential for each drug (19).

In this context, a reduction in the AB and the consequences of its adverse effects should be beneficial for patients. This would require an understanding of the factors that influence the AB. The main objective of this study is to identify factors influencing the reduction of AB of the prescription of older hospitalized delirium. We hypothesized that medication reconciliation (MR) was one of these factors. The secondary objective is to assess the impact of changes in AB on early rehospitalization - defined as less than 30 days- for the same cause of ED admission.

METHODS

Study design

This study is an observational descriptive study conducted at the University Hospital of Tours. The data was collected from January 1, 2019 to December 31, 2019.

Participants

The study population screened on the medical records at admission to the ED. Medical records extracted from software using the following French keywords: [*confusion, syndrome confusionnel, état confusionnel, démence, agitation/agressivité, désorientation, déambulation, troubles du comportement, errance sur la voie publique, maintien à domicile difficile*] corresponding in English to [delirium, confusional syndrom, confusional state, dementia, agitation/aggressiveness, disorientation, wandering behaviour, behaviour disorders, wandering on the public highway] defined from the literature.

The study inclusion criteria were: age ≥ 75 years old, presence of confusional syndrom screened with the Confusion Assessment Method (CAM scale)(20), and hospitalization via the ED from January 1, 2019 to December 31, 2019.

Exclusion criteria were: no data on input or output treatments, zero anticholinergic burden at admission, in-hospital death.

Sociodemographic and clinical variables

Sociodemographic variables included: age, sex, living accommodation (medicalized in a follow-up care and rehabilitation service or nursing home, or non-medical living space, at home).

Clinical variables were: previous history of delirium and cognitive impairment, presence of comorbidities or a fragile state (measured with the Charlson Comorbidity Index (21) and the Hospital Frailty Risk Scale (HFRS) (22)). We also collected the total number of treatments at admission, intervention of a geriatrician and the presence of MR at admission or discharge. The variation of the AB was calculated to separate the population into two groups: decreased AB group and stable or increased AB group.

Anticholinergic burden scale

After conducting a pre-protocol analysis, the AIC scale (19) was chosen as the most accurate in assessing AB in our study compared to Anticholinergic Drug Scale (ADS). The AIC scale showed a better sensitivity to assess the anticholinergic potential of each drug. Comparison data between ADS and AIC scales are available in [Appendix 1](#).

Statistical analysis

We analysed the characteristics of older patients using descriptive statistics. The qualitative variables are described by their number and the respective percentages; quantitative variables are expressed as medians with interquartile ranges (IQR).

We assessed the associations between patient characteristics and a reduction of the AB using bivariate (Chi2 or Fischer test for categorical variables, Student or Mann-Whitney test for continuous variables) and multiple logistic regression analyses. Multivariate analyses included variables potentially influenced the primary outcome and which had $p < 0.2$ on bivariate analyses. A value of $p < 0.05$ was considered significant.

Ethics and patient information

No nominative, sensitive or personal data of patients have been collected. Our study involved the reuse of already recorded and anonymized data. The study falls within the scope of the French Reference Methodology MR-004 (declaration 2205437 v 0, August 22nd, 2018, subscribed by the Teaching Hospital of Tours), which require neither information nor consent of the included individuals. This study was consequently registered with the French Data Protection Board (n° 2021_141).

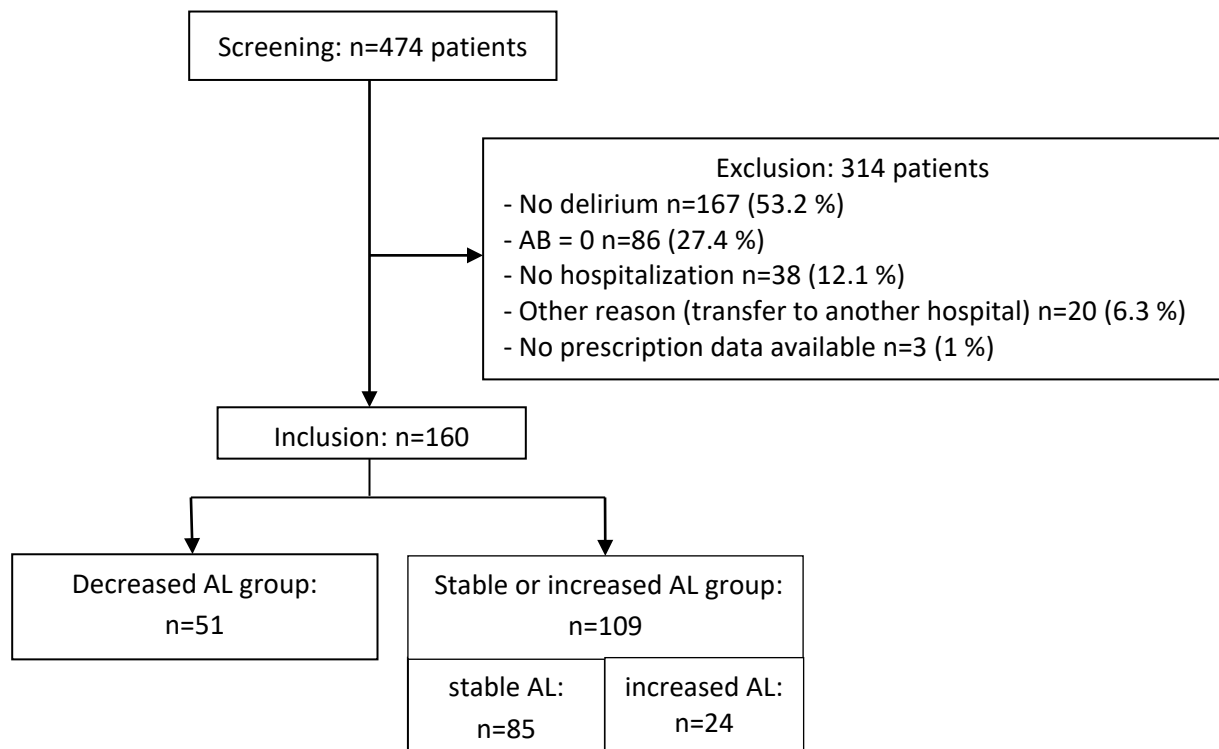
RESULTS

Participants

A total of 474 patients with a cause hospitalization that could correspond to delirium were selected. Of these, 314 (66.2%) patients were excluded based on predefined exclusion criteria: 167 (53.2%) patients were not confused, 86 (27.4%) had no AB at admission.

This resulted in 160 older patients eligible for the study of which 51 (31.9%) had a decreased AB at hospital discharge and 109 (68.1%) patients which had a stable AB ($n=85$) or an increased AB ($n=24$). [Figure 1](#) provides more details on the participants inclusion process.

Figure 1. Flowchart of participants



AB=anticholinergic burden

Descriptive data

Overall, in descriptive analyses, patients were more often female (n=100, 62.5%), had a median [IQR] age of 86 [81.8-90] years, 140 (87.5%) are living in a non-medical living place (at home). 96 (60%) patients had cognitive impairment, less than a third had a history of delirium (n=36, 22.5%). The median [IQR] Charlson Comorbidity Index was 2 [1-3], and 5.6 [2.2-14.3] according to HFRS. 48 (30%) patients had missing data, regarding the HFRS. The median [IQR] number of treatments on the admission prescription was 8 [6-10], and a majority of patients (n=100, 62.5%) received medication reconciliation at admission. The median [IQR] AB score of the overall population, calculated with the AIC scale, is 2 [1-3] at admission, with the decreased AB group scored at 3 [2-4] and the stable or increased AB group at 2 [1-2]. 19 (11.9%) patients were readmitted early to the ED after discharge. Characteristics of the population are provided in [table 1](#).

Factors associated with decreased AB

[Table 2](#) shows the results of bivariate logistic regression analysis of the factors associated with a decrease in AB.

There were no differences between the groups regarding medical history and comorbidity scores. The intervention of a geriatrician during hospitalization did not significantly promote a decrease in the AB of the prescription in this study (Odd ratio (OR) [95% Confidence Interval (95% CI)] OR=0.74 [0.37-1.48].

Table 1. Patient characteristics

	Group decreased AB	Group stable or increased AB	Total
	n = 51 (31.9%)	n = 109 (68.1%)	n = 160
Age (years)	86 [83-90.5]	86 [81-90]	86 [81.8-90]
Sex:			
- Female	33 (64.7%)	67 (61.5%)	100 (62.5%)
- Male	18 (35.3%)	42 (38.5%)	60 (37.5%)
Living accommodation:			
- Medical	7 (13.7%)	13 (11.9%)	20 (12.5%)
- Non-medical	44 (86.3%)	96 (88.1%)	140 (87.5%)
History of delirium	8 (15.7%)	28 (25.7%)	36 (22.5%)
History of cognitive impairment	28 (54.9%)	68 (62.4%)	96 (60%)
Charlson	2 [1-3]	2 [1-3]	2 [1-3]
Frailty (HFRS)	4.7 [1.5-7.6]	6.2 [2.3-15.7]	5.6 [2.2-14.3]
Hospitalization department:			
- Medical	49 (96.1%)	105 (96.3%)	154 (96.3%)
- Surgical	2 (3.9%)	3 (2.8%)	5 (3.1%)
- Other	0	1 (0.9%)	1 (0.6%)
Intervention of a geriatrician	18 (35.3%)	44 (40.4%)	62 (38.8%)
Total number of treatments	9 [7-11.5]	8 [6-9]	8 [6-10]
Medication reconciliation (MR):			
- MR at admission	43 (84.3%)	57 (52.3%)	100 (62.5%)
Of witch CM at admission and discharge	13 (30.2%)	13 (22.8%)	26 (26%)
- No MR	8 (15.7%)	52 (47.7%)	60 (37.5%)
Anticholinergic burden (med[IQR])			
- Entry	3 [2-4]	2 [1-2]	2 [1-3]
- Exit	1 [0.5-2]	2 [1-3]	2 [1-2.3]
- Variation	-2 [-2 - -1]	0 [0-0]	0 [-1-0]
Length of hospitalization (days)	9 [5-15]	7 [2-13]	7 [3-13]
Exit orientation:			
- Medical	25 (49%)	52 (47.7%)	77 (48.1%)
- Non-medical	26 (51%)	57 (52.3%)	83 (51.9%)
Early re-hospitalization	2 (3.9%)	17 (15.6%)	19 (11.9%)

AB=anticholinergic burden

HFRS=Hospital Frailty Risk Factor

MR=medication reconciliation

AIC=Anticholinergic Impregnation Coefficient

However, a significant association was found between the presence of MR at admission and a decrease in the AB of the prescription at discharge from the hospital (OR [95%CI] 4.9 [2.11-11.39]. In

addition, patients with a higher AB at discharge were at risk for early rehospitalization (OR [95%CI] 0.22 [0.05-0.99]). A higher AB at admission and a larger number of treatments was also associated with a decreased anticholinergic burden at discharge (respective OR [95%CI] 1.58 [1.23-2.02] and 1.15 [1.03-1.28]).

Multivariate analysis (Table 3) included adjustment for history of delirium, the total number of treatments, the presence of medication reconciliation at admission, AB at admission and the length of hospitalization. We observed more significantly patients with a MR in the decreased AB group than in the AB stable or increased group (OR [95% CI] = 7.57 [2.81-20.43]). Similarly, patients in the decreased AB group had a higher AB significantly at the time of hospitalization than patients in the stable or increased AB group (OR [95%CI] = 1.77 [1.29-2.42]).

Table 2. Bivariate analyses between the AB decrease group and the AB stable or increased group

	OR [95% IC]	p value
Age (years)	1.01 [0.95 ; 1.07]	0.75
Sex:	1.15 [0.58 ; 2.3]	0.69
- Female		
- Male		
Living accommodation:	1.17 [0.44 ; 3.14]	0.75
- Medical		
- Non-medical		
History of delirium	0.54 [0.23 ; 1.28]	0.16
History of cognitive impairment	0.72 [0.36 ; 1.41]	0.33
Charlson	1.03 [0.88 ; 1.21]	0.70
Frailty (HFRS)	1.03 [0.93 ; 1.14]	0.58
Hospitalization department:	0.88 [0.20 ; 3.86]	0.87
- Medical		
- Surgical		
- Other		
Intervention of a geriatrician	0.74 [0.37 ; 1.48]	0.39
Total number of treatments	1.15 [1.03 ; 1.28]	0.009*
Medication reconciliation:		
- MR at admission	4.9 [2.11 ; 11.39]	<0.001*
Of witch MR at admission and discharge	6.5 [2.23 ; 18.95]	0.40
- No MR		
Anticholinergic burden (AIC):		
- Entry	1.58 [1.23 ; 2.02]	<0.001*
Length of hospitalization (days)	1.03 [0.99 ; 1.06]	0.11
Early re-hospitalization	0.22 [0.05 ; 0.99]	0.049*

AB=Anticholinergic Burden

HFRS=Hospital Frailty Risk Factor

MR=Medication Reconciliation

AIC=Anticholinergic Impregnation Coefficient

* Significant results

Ancillary statistical analysis allowed us to identify factors that contributed to an increase in AB. We found that the more length of hospitalization was significantly associated with an increase of AB (median [IQR] 12.5 [6.8-21.5] compared to stable AB (median [IQR] 6 [2-11]) ($p < 0.01$) ([Appendix 2](#)).

Using the ADS scale to calculate the AB of prescription, we found similar results for medication reconciliation (OR [95% IC] 9.78 [2.65-35.97]) and a highest number of treatments at admission (OR [95% IC] 1.19 [1.04-1.37]) ([Appendix 3](#)). In contrast, a larger AB at admission was not associated with an anticholinergic load decrease. No patients of the decreased group were early rehospitalized. In this analysis, the intervention of a geriatrician was a factor associated with an increased AB (OR [95%CI] 0.27 [0.09-0.82]).

Table 3. Multivariate logistic regression model for associated factor with decreased anticholinergic burden

	Odds-Ratio	p value
History of delirium	0.54 [0.20 ; 1.50]	0.24
Number of treatments	1.01 [0.88 ; 1.16]	0.85
Medication reconciliation at admission	7.57 [2.81 ; 20.43]	<0.001*
AB at admission	1.77 [1.29 ; 2.42]	<0.001*
Length of hospitalization	1.03 [0.98-1.07]	0.25

* Significant results

DISCUSSION

This study shows that MR and higher anticholinergic load at admission are factors that allow a reduction in AB of the prescription of older people hospitalized for delirium. Also, the reduced burden could prevent early readmissions to the hospital.

The CAM scale we used to screen for delirium is the 4-item adaptation, more efficient in practice than the 1990 CAM scale and validated in the ED (23,24). One of the difficulties in including patients on record was that the description of the delirium was not always explicit, and the CAM items were not even clearly identified. However, identifying keywords that could correspond to delirium to extract data from patients for our study allowed us to select a larger population at the baseline. The sudden beginning with the break in the anterior status was the CAM item the most written in the medical records of ED patients.

We saw that diagnosis of delirium can be difficult to establish. In the ED, the most common complaint in the older population is altered mental status, without being specific (25). Han et al. examined the relationship between the complaint of an altered mental status and the presence of

delirium: 50 (12.3%) patients were confused and 23 (5.7%) complained of having an altered mental state. The presence of this complaint was 98.9% (95% CI = 97.2% to 99.6%) specific and the positive likelihood ratio was 33.82 (95% CI = 11.99 to 95.38) for the confusion diagnosis. In contrast, the absence of this complaint did not decrease the likelihood of being confused (26). It is essential to correctly identify confusion in the ED and establish an etiological diagnosis to adjust the medical management and limit the negative consequences (27). Other rapid delirium detection scales have been developed and validated in practice in older patients, including those with visual and hearing impairments, such as the 4 'A's Test (28). This scale is more commonly used than the CAM in the UK (29) and the implementation of specific delirium detection scales shows the ongoing efforts to progress in the management of this syndrome.

Potentially inappropriate medications are described in the Beers criteria (30) for older. Park et al. investigated the concordance between anticholinergic drugs among those present in the Beers criteria (2003, 2012 and 2015) and those scored by different AB scales (including Anticholinergic Drug Scale (ADS), Anticholinergic Cognitive Burden (ACB), Anticholinergic Risk Scale (ARS)). The more recent versions of the Beers criteria showed a better correlation with the AB scales and the 2015 criteria had the highest concordance for the ADS scale (κ [95%CI] 0.530 [0.406-0.654]) (31).

The AIC scale we used in our study was more sensitive in evaluating the anticholinergic potential of each treatment. [Appendix 1](#) shows the comparison between ADS and CIA scale. The variation in AB is higher when calculated with the AIC scale than the ADS scale, for the same prescription ($p < 0.001$). The AB variation with the CIA scale ranged from -4 to +3 with a median [IQR] of 0 [-1; 0] (versus -2 to +3 with the ADS scale, median [IQR] of 0 [0; 0]). Using the AIC scale, we limited the selection bias of missing medications with anticholinergic potential that was not included in the other scales.

Group stable or increased AB contains more patients who received the expertise of a geriatrician, some of whom have an increased AB due to the addition of necessary treatments for the medical management of the patients. Using the ADS scale in the ancillary analysis, the intervention of a geriatrician was significantly disadvantageous for a decrease in AB ([Appendix 3](#)). In the literature, we find that most treatments prescribed to older people are medications with low anticholinergic potential (11). Among these drugs, there were: opioids, antidepressants antipsychotics and benzodiazepines, cardiovascular medications including diuretics, antibiotics, and medications for urinary incontinence or overactive bladder (AIC scale score = 3). The consumption of opioids, gastrointestinal medication and medication for respiratory diseases increased with age and was higher in patients over 90 years old.

In our study the high overall burden is mainly due to the cumulative effect of these treatments. This was shown in a study describing the prescription treatments of patients living in nursing homes. The high AB was principally related to the cumulative load of cardiovascular and antidepressant drugs. Medications for urinary incontinence or overactive were not in the majority of the prescription (32).

Deschodt et al. aimed to evaluate the characteristics of elderly patients admitted to the ED and the risks of their rehospitalization. Hospitalized patients had higher dependence on Activities of Daily Living (ADL), a higher comorbidity index (determined with the Modified Cumulative Illness Rating Scale (CIRS) (33)), and were more undernourished. Risk factors for ED readmission were: an alteration in the score of Instrumental Activities of Daily Living, the presence of home care aides, a fall in the last year, and a recent hospitalization under 3 months (34). Bradshaw et al. described outcomes in older people with mental comorbidities (confusion, dementia, depression) 6 months after an ED admission resulting in hospitalization: 78 (30%) patients were dead, 104 (41%) were readmitted to the hospital, and 76 (29%) survived in their living environment without recovering the loss of autonomy associated with the hospitalization. Furthermore, 78/110 (71%) of the patients who survived developed new behavioural symptoms. Factors predicting poor outcomes were: cognitive impairment, behavioural problems, depression, medical and nutritional comorbidities, and altered ADL on admission (35).

Lu W-H et al. showed that multi-medication and the number of inappropriate medications contributed to hospital admissions (36). Nevertheless, the AB of the prescription was not considered in the research of factors promoting hospital readmission in these studies. Recently a study revealed that a high AB is associated with a dose-dependent risk of ED admissions (OR [95% IC] 1.65 [1.56-1.75]), for causes corresponding to anticholinergic adverse effects (constipation, urinary retention, dizziness, confusion) (37). In this study, AB was quantified according to the Korean Anticholinergic Burden Scale (KABS) (38), specifically developed to apply to the Korean population and based on the 3 scales ADS, ACB and ARS. This scale revealed a stronger association with the risk of ED admission for anticholinergic adverse events than previously used scales, even if ADS showed the same results.

The importance of a comprehensive geriatric assessment with screening for frailty and the review of the prescription in the ED has already been demonstrated (13). Rhalimi et al. aimed to evaluate the impact of a clinical pharmacist's intervention on the identification of drug-related problems in hospitalized patients over 65 years old. They have therefore developed the Pharmacist's Comprehensive Geriatric Assessment (pCGA) (15). This pharmaceutical assessment includes: evaluation of the medication adherence of the patients, realization of medication reconciliation and implementation of a Pharmacist Intervention (PI) if required. Out of a total of 539 older people (median age 84 years), 462 (86%) patients were consuming between 4 and 12 medications, half of the patients had an adherence problem, and 260 (48%) patients presented at least one unintentional discrepancy in their prescription. The review of medications during hospitalization resulted in the proposition of 828 PI, of which 2/3 were accepted by the physician. The main interventions were about dose adjustment, addition or discontinuation of a treatment and drug switches.

This study confirms that the achievement of a MR or the intervention of a pharmacist among comprehensive geriatric assessment allows for reducing the risk of inappropriate prescribing and supports our results.

Several studies investigated the effects of interventions in promoting medication deprescribing. Interventional Medication Therapy Management (MTM) trials are promising to prevent

inappropriate medication use. Physician-pharmacist collaboration has improved the relevance of prescribed anticholinergic drugs and limited the use of inappropriate medications. AB (using ADS scale) was decreased after MTM but not significantly compared to the no intervention group (39). A randomized controlled trial wanted to study the effect on the long-term of a MTM intervention to support deprescribing. At 1 year, 50% of treatment modifications (especially antihistamines, bladder agents and antidepressants) in the prescription were maintained (40).

Another study evaluated pharmacists' intervention on potentially inappropriate prescribing (PIP), the omission of appropriate prescribing and the reduction of adverse drug events. The STOPP and START tools (41) were used to analyse the medications of 1262 patients (for a total of 16,542 prescriptions). Intervention through conferences and publications on STOPP and START criteria has resulted in a significant decrease in PIP and serious drug interaction. In addition, the risk of developing confusion and readmission to the ED was also reduced (42).

All these studies demonstrate the importance of not forgetting iatrogeny and its consequences in geriatrics. The confusional syndrome is an often multifactorial medical emergency requiring global management. The investigation of the etiological diagnosis of delirium requires a revision of the prescription to limit the development of potentially serious adverse effects in the long term. Implementing medication reconciliation in ED is challenging to do in practice. AB calculator software would be a tool that might help emergency physicians to evaluate this burden when registering the patient's prescription in the medical record in the ED. Indeed, the software would quickly identify drugs with high anticholinergic potential. It could also compensate for the observed differences in the many current assessment scales by incorporating those that are most appropriate in practice. A list of treatments could be associated, mentioning the most prescribed anticholinergic drugs with potential risk in the older population. The research of inappropriate treatments and the evaluation of the global AB in geriatrics must not exempt the use of indicated treatments according to the patient's pathologies. Finally, the collaboration between geriatricians and emergency physicians (already in existence via the Mobile Geriatric Services) in detecting and managing delirium remains the best way to provide appropriate care to older patients.

CONCLUSION

Detection of inappropriate prescriptions, especially drugs with anticholinergic side effects in older people, is necessary to reduce their adverse effects. Our study showed that MR is a helpful tool for reducing the AB of the prescription and complements pre-existing research on optimizing prescriptions for older patients. The ED receives many older people for medical reasons that may be correlated with anticholinergic side effects, such as urinary retention or delirium. The beneficial effect of reduced AB on the risk of early rehospitalization suggests that medication reconciliation would have a place in delirium assessment in the ED.

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APPENDIX

Appendix 1. Anticholinergic burden (AB) of the prescription according to the ADS scale and the AIC scale

	ADS scale Median [IQR]	CIA scale Median [IQR]	p value
Group decreased AB	n=31 (22.3%)	n=46 (33.1%)	
- Entry AB	1 [1 ; 2]	2 [1 ; 3]	<0.001*
- Exit AB	1 [1 ; 2]	2 [1 ; 3]	<0.001*
- AB variation	0 [0 ; 0]	0 [-1; 0]	<0.001*

AB=anticholinergic burden

IQR=interquartile ranges

ADS=Anticholinergic Drug Scale

AIC=Anticholinergic Impregnation Coefficient

* Significant results

Appendix 2. Patient characteristics with stable or increased AB, and bivariate analysis

	Group stable AB n = 85 (78%)	Group increased AB n = 24 (22%)	p value
Age (years)	86 [81-89]	86.5 [80.8-90]	0.1
Sex:			0.55
- Female	51 (60%)	16 (66.7%)	
- Male	34 (40%)	8 (33.3%)	
Living accommodation:			1
- Medical	10 (11.8%)	3 (12.5%)	
- Non-medical	75 (88.2%)	21 (87.5%)	
History of delirium	23 (27.1%)	5 (20.8%)	0.54
History of cognitive impairment	54 (63.5%)	14 (58.3%)	0.81
Charlson	2 [1-3]	1.5 [1-3]	0.14
Frailty (HFRS)	5.9 [1.9-15.2]	8 [5.3-15.9]	0.69
Hospitalization department:			0.64
- Medical	82 (96.4%)	23 (95.8%)	
- Surgical	2 (2.4%)	1 (4.2%)	
- Other	1 (1.2%)	0	
Intervention of a geriatrician	31 (36.5%)	13 (54.2%)	0.12
Total number of treatments	8 [6-10]	8 [5-9]	0.30
Medication reconciliation:			
- MR at admission	41 (48.3%)	16 (66.3%)	0.11
Of which MR at admission and discharge	10 (24.4%)	3 (18.8%)	0.74
- No MR	44 (51.7%)	8 (33.3%)	
Length of hospitalization (days)	6 [2-11]	12.5 [6.8-21.5]	<0.01*
Exit orientation:			—
- Medical	36 (42.4%)	16 (66.7%)	
- Non-medical	49 (57.6%)	8 (33.3%)	
Early re-hospitalization	14 (16.5%)	3 (12.5%)	0.76

AB=Anticholinergic Burden

HFRS=Hospital Frailty Risk Factor

MR=Medication Reconciliation

* Significant results

Appendix 3. Multivariate analyses between the AB decrease group and the AB stable or increased group when AB variation is calculated with ADS scale

	OR [95% IC]	P value
History of delirium	0.68 [0.18 ; 2.58]	0.57
History of cognitiv impairment	0.96 [0.35 ; 2.59]	0.93
Intervention of a geriatrician	0.27 [0.09 ; 0.82]	0.022*
Number of treatments	1.19 [1.04; 1.37]	0.016*
Medication reconciliation on admission	9.78 [2.65 ; 35.97]	<0.001*
Length of hospitalization	1.05 [0.99; 1.10]	0.057

* Significant results

Vu, les Directeurs de Thèse

Dr COULONCEAT Matthieu



Dr BLANC Pascal



Vu, le Doyen
De la Faculté de Médecine de Tours
Tours, le

BASSAC Hélène

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RESUME

Contexte : La confusion est un motif fréquent d'admission aux urgences chez les patients âgés. Parmi les étiologies, une iatrogénie peut exister, due à la poly-médication et notamment aux effets anticholinergiques parfois cachés de nombreux médicaments. Une réduction de la charge anticholinergique (CAC) de l'ordonnance, serait bénéfique pour les patients.

Objectifs : identifier les facteurs influençant la diminution de la CAC de l'ordonnance de patients ≥ 75 ans, hospitalisés pour confusion. Analyser l'impact de la CAC sur les réhospitalisations précoces (dans les 30 jours) pour le même motif.

Conception : étude observationnelle descriptive mono-centrique, réalisée au CHRU de Tours.

Participants : 160 patients âgés de 75 ans ou plus, hospitalisés entre le 1/01/2019 et le 31/12/2019 via le service des urgences pour syndrome confusionnel ont été inclus. Les patients ont été répartis en deux groupes : CAC diminuée, ou CAC stable et augmentée à la sortie d'hospitalisation.

Résultats : 51 (31.9%) patients avaient une CAC diminuée à la sortie d'hospitalisation. L'analyse multivariée montrait que ces patients bénéficiaient significativement plus souvent d'une conciliation médicamenteuse (CM) à l'entrée (OR [IC 95%] = 7.57 [2.81-20.43]) et avaient une charge anticholinergique à l'entrée plus élevée (OR [IC 95%] = 1.77 [1.29-2.42]) que les patients présentant une CAC stable ou augmentée à la sortie d'hospitalisation. Les patients avec une CAC diminuée étaient significativement moins réhospitalisés dans les 30 jours (OR [IC 95%] = 0.22 [0.02 ; 0.99]).

Conclusion : La diminution de la charge anticholinergique de l'ordonnance de patients âgés confus est favorisée par la présence d'une CM et d'un plus grand nombre de traitement à l'entrée d'hospitalisation. Cette optimisation de l'ordonnance permet également de réduire les réhospitalisations précoces.

Keywords: Charge anticholinergique, effets indésirables, patients âgés, confusion, service des urgences, conciliation médicamenteuse, échelles anticholinergiques.

Jury :

Président du Jury : Professeur Bertrand FOUGÈRE
 Directeur de thèse : Docteur Pascal BLANC,
 Docteur Matthieu COULONGEAT
 Membres du Jury : Professeur François MAILLOT
 Docteur Julie BOURGUEIL
 Docteur Vincent GARROUSTE

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