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Original Research

Assessing appropriateness of drug therapy in older persons: Development and application of a medication assessment tool for long-term management of atrial fibrillation

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Abstract

Background: Atrial fibrillation (AF) is highly prevalent in older persons and is associated with considerable morbidity and mortality. Assessing appropriateness of drug therapy in AF may be facilitated by application of medication assessment tools (MATs).

Objective: To develop, psychometrically evaluate and apply an innovative MAT for the long-term management of AF with particular relevance to older persons.

Methods: Key recommendations from clinical practice guidelines for the long-term management of AF were selected and review criteria defining appropriate drug therapy were constructed as a 'qualifying statement' followed by a 'standard'. The developed MAT was given the designation MAT-AF. An application guide was compiled where justifications for non-adherence were specified. Content validity was tested by an expert group using a three-round Delphi process. Inter- and intra-observer reliability testing was conducted with agreement expressed by Cohen's kappa and application time measured to assess feasibility. MAT-AF was applied to 150 patients with a diagnosis of AF admitted to a rehabilitation hospital.

Results: MAT-AF consists of 15 criteria sectioned into antithrombotic, rate control and rhythm control therapy. Content validity was demonstrated for all criteria. Reliability was confirmed with kappa values of 0.84 and 0.91 for inter- and intra-observer agreements. Mean application time for the two observers was 3.9 and 2.4 minutes, which decreased significantly in the second application conducted after a four-week interval ($p<0.001$). Overall adherence to applicable criteria was 59.8%. Non-adherence was evident for prescription of anticoagulation in patients with a CHA_2DS_2VASc score ≥1 (29.5%). Monitoring of laboratory parameters for digoxin was suboptimal. Ophthalmic and pulmonary monitoring and patient counselling regarding amiodarone therapy could not be assessed since relevant records were not readily available.

Conclusion: MAT-AF application highlighted key aspects which need to be addressed to improve patient care.

Keywords

Atrial Fibrillation; Inappropriate Prescribing; Clinical Audit; Aged; Drug Therapy; Validation Studies as Topic

INTRODUCTION

Atrial fibrillation (AF) is considered to be one of the major causes of stroke and heart failure.[1] In a systematic review, Chugh *et al*. reported a progressive increase in global prevalence of AF with higher rates observed in the older age groups.[2] Management recommendations focus on reducing thromboembolic risk and on rate and rhythm control.[1,3-5] Although recent data shows good progress in the management of patients with AF, there is still substantial evidence of suboptimal therapy.[6-9]

A number of drug utilisation review tools have been developed for the purpose of identifying potentially inappropriate drug therapy, predominantly targeting the older population from a generic perspective rather than for specific disease states.[10,11] Only some aspects of AF management have been incorporated in these tools, the most commonly cited being the Beers' Criteria[12], the Screening Tool of Older Persons' Prescriptions (STOPP) and the Screening Tool to Alert Doctors to Right Treatment (START).[13] Medication assessment tools (MATs) are disease-specific, evidence-based instruments designed to assess appropriateness of drug therapy and have been developed and applied in various diseases including heart failure, diabetes mellitus, coronary heart disease, cancer pain, asthma, pneumonia and rheumatoid arthritis.[14-21] A MAT that is specific for AF, taking into consideration different management strategies, concurrent multiple

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morbidities and monitoring for safe use of therapeutic agents, provides an assessment of appropriateness of drug therapy for this disease state.

The aim of the study was to design, psychometrically evaluate and apply an innovative MAT for the long-term management of AF, with particular relevance to older persons, so as to assess adherence to guideline recommendations.

METHODS

MAT design and validation

The MAT was designed by the researcher (MG) according to the most recent evidence-based guidelines for the long-term management of AF.[1,3-5] Additional information relating to therapeutic agents was obtained from drug monographs. Review criteria defining appropriate drug therapy were constructed as a 'qualifying statement' followed by a 'standard', based on the format of previously published MATs.[14-21] For example, 'patient with atrial fibrillation who has a CHA_2DS_2VASc score of ≥1 (≥2 if female)' is the qualifying statement and 'is prescribed warfarin (INR 2.0-3.0) or other oral anticoagulant' is the standard. Response options include 'not applicable' when the criterion is not applicable, 'yes' for adherence, 'no' for non-adherence and 'justified no' when there is a justified reason for non-adherence to the standard. When data is insufficient to apply the criterion or to assess if the standard is achieved, the response options are 'insufficient data relating to qualifying statement' or 'insufficient data relating to standard'. The developed MAT was given the designation MAT-AF. An application guide incorporating instructions for response options for each criterion was compiled.

Content validation of MAT-AF was undertaken by an expert group composed of three consultant cardiologists, three consultant geriatricians and three clinical pharmacists practising in geriatrics using a three-round Delphi technique. Consensus threshold was set to ≥75%.[16,19,20] The application guide was reviewed based on recommendations by the expert group. The final version of MAT-AF consisted of a one-page paper-based tool.

Reliability and feasibility testing

Reliability and feasibility testing was conducted during a pilot study in which MAT-AF was applied by the researcher (MG) to a sample of 30 patients admitted to a rehabilitation hospital. Inclusion criteria were a diagnosis of AF (reason for admission or past history) and age ≥60 years. Patients who were discharged to acute care or deceased during the study period were excluded. Information for MAT application was obtained from patient profiles compiled by clinical pharmacists in daily practice for each patient admitted to the hospital for the purpose of pharmaceutical care issue documentation.

MAT-AF was tested by two pharmacists (observers) who each applied the review criteria to the 30 patient profiles. The observers were selected on the basis that they were familiar with the study setting and had a comparable level of experience in clinical pharmacy. The application guide was given to the observers to ensure consistency in application and interpretation of MAT-AF. Application of MAT-AF was repeated by the same observers for the same 30 patient profiles after a period of four weeks. Reliability testing in terms of inter- and intra-observer agreement to the response option selected was calculated using Cohen's kappa. Feasibility testing was performed using paired-samples t-test to identify inter- and intra-observer differences in application time and correlation between the observers' application time.

Adherence to the compiled MAT

Adherence to MAT-AF was assessed in a sample of 150 patients admitted to the rehabilitation hospital with a diagnosis of AF. MAT-AF was applied by the researcher to patients identified consecutively at discharge during the period March to September 2016. Selection of patients and data extraction was according to the methodology adopted for reliability and feasibility testing. Clinical notes, laboratory results and discharge case summaries were used as necessary. Adherence to MAT criteria was calculated by the sum of the 'yes' responses expressed as a percentage of the applicable criteria. Criterion responses which were not applicable or which had insufficient data relating to the qualifying statement were not considered in the adherence calculation.

RESULTS

In the first round of the Delphi validation process, consensus was achieved for eight of the fifteen criteria in MAT-AF. Adjustments were made to five criteria, two criteria were removed and three new criteria were created. In the second validation round, consensus was obtained for

Table 1. Patient characteristics for study population (n=150)

Gender (n, %)*		
male	54	36.0%
female	96	64.0%
Age (years)		
mean (SD)	81.7	(7.6)
min, max	60	97
≥75 years (n, %)	127	84.7%
Atrial fibrillation (n, %)		
paroxysmal	54	36.0%
persistent	12	8.0%
permanent	84	56.0%
Comorbidities (current or past history) (n, %)		
heart failure	93	62.0%
hypertension	108	72.0%
diabetes	48	32.0%
stroke/TIA/systemic thromboembolism	51	34.0%
vascular disease**	52	34.7%
anaemia	68	45.3%
chronic kidney disease (CrCl <60ml/min)	103	68.7%
CHA_2DS_2VASc score (0-9)		
mean (SD)	5.0	(1.6)
min, max	0	9
HAS-BLED score (0-9)		
mean (SD)	2.0	(0.8)
min, max	1	4

*male to female ratio of study population reflects gender ratio of rehabilitation hospital
**acute coronary syndrome or peripheral arterial disease (including revascularisation)

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Table 2. Adherence to applicable criteria of MAT-AF in 150 patients (n=458)

		Applicable cases		Adherence			Justified non-adherence		Non-adherence		Insufficient data for standard	
Antithrombotic therapy		n	%	n	%	95%CI	n	%	n	%	n	%
1	No antithrombotic therapy if CHA_2DS_2VASc score 0	1	0.7	1	100	-	0	0	0	0	0	0
2	Oral anticoagulant if CHA_2DS_2VASc score ≥1	149	99.3	91	61.1	53.3:68.9	14	9.4	44	**29.5**	0	0
3	Recommended dose of direct anticoagulant if CrCl ≥50 mL/min	5	3.3	4	80.0	44.9:100	0	0	1	20.0	0	0
4	Direct oral anticoagulant at lower dose or warfarin if CrCl between 15 – 49 mL/min	47	31.3	47	100	-	0	0	0	0	0	0
5	Warfarin if CrCl <15 mL/min	1	0.7	1	100	-	0	0	0	0	0	0
Rate control therapy												
6	Beta-blocker, non-dihydropyridine calcium channel blocker or digoxin	97	64.7	51	52.6	42.6:62.6	31	32.0	15	15.5	0	0
7	Cardiology referral/follow-up if non-dihydropyridine calcium channel blocker and contraindicated/not tolerated	1	0.7	0	0	-	0	0	1	**100.0**	0	0
8	Beta-blocker or digoxin if heart failure with left ventricular ejection fraction <40%	12	8.0	8	66.7	40.0:93.4	4	33.3	0	0	0	0
9	Monitoring of renal and thyroid function, serum electrolytes with digoxin and within range	53	35.3	27	50.9	37.4:64.4	0	0	26	**49.1**	0	0
10	Monitoring of serum digoxin level if at risk of high serum concentration and within range	23	15.3	17	73.9	55.9:91.9	0	0	6	**26.1**	0	0
11	Amiodarone for additional rate control or contraindication/intolerance to other agents	1	0.7	0	0	-	0	0	1	100	0	0
12a	Monitoring of liver and thyroid function with amiodarone and within range	21	14.0	17	81.0	64.1:97.9	0	0	4	19.0	0	0
12b	Monitoring of ophthalmic and pulmonary function, and counselling with amiodarone	21	14.0	0	0	-	0	0	0	0	21	**100.0**
Rhythm control therapy												
13	Continuation at prescribed dose if maintained in sinus rhythm with antiarrhythmic agent and well tolerated	10	6.7	7	70.0	41.6:98.4	0	0	3	30.0	0	0
14	Cardiology referral/follow-up if maintained in sinus rhythm with antiarrhythmic agent and contraindicated/not well tolerated	3	2.0	0	0	-	0	0	3	**100.0**	0	0
15	Cardiology referral/follow-up if prescribed antiarrhythmic agent and not maintained in sinus rhythm	13	8.7	3	23.1	0.2:46.0	2	15.4	8	**61.5**	0	0
Total criteria		458	19.1	274	59.8	55.3:64.3	51	11.1	112	24.5	21	4.6

'applicable criteria' exclude 'not applicable' and 'insufficient data relating to qualifying statement' response options. CrCl: Creatinine clearance.

all sixteen criteria. A third round was necessary to review three criteria which were adjusted to reflect guideline updates regarding digoxin use following which consensus was achieved for two criteria and one criterion was removed. MAT-AF after validation was composed of fifteen review criteria sectioned into antithrombotic, rate control and rhythm control therapy. Details on criteria validation may be viewed in Table 1 of the supplementary material.

Reliability testing resulted in kappa values of 0.84 ($p<0.001$) and 0.91 ($p<0.001$) for inter- and intra-observer agreements. Mean application time was 3.90 (SD=1.18) minutes for observer 1 and 2.38 (SD=0.95) minutes for observer 2. Following the four-week period, mean application time for observer 1 was 2.12 (SD=0.92) minutes and 1.56 (SD=0.41) minutes for observer 2, both significantly lower than the time for the first application ($p<0.001$). Correlations were significant for both inter-observer ($r=0.5$, $p=0.005$) and intra-observer tests ($r=0.7$, $p<0.001$ and $r=0.5$, $p=0.008$).

Patient characteristics and MAT-adherence results of the 150 patients assessed during MAT-AF application are shown in Table 1 and Table 2, respectively. Adherence to the applicable criteria was 59.8% and justified non-adherence was 11.1%. Non-adherence was evident for prescription of anticoagulation in patients with a CHA_2DS_2VASc score ≥1 (29.5%). Monitoring of laboratory parameters relating to digoxin therapy was deficient in 49.1% of patients, predominantly due to absence of magnesium levels, and in 26.1% of patients at risk of high serum digoxin concentrations. Ophthalmic and pulmonary monitoring and patient counselling regarding amiodarone therapy could not be assessed as relevant records were not readily available. Cardiology referral was not performed in most of the patients for whom it was recommendable.

DISCUSSION

Reliability of MAT-AF was confirmed and was similar to other MATs.[16,19,20] There was a significant correlation for the two observers in the time spent on MAT-AF application for the same patient case. Following the four-week interval, the application time for both observers was significantly lower compared to the first application, possibly indicating that repeated use of the MAT facilitates application. The

short application time supports application of MAT-AF in a clinical setting.

Specific aspects that are applicable to a few patients were also included in the MAT resulting in a low applicability for these criteria when considering the entire patient cohort. The incorporation of such criteria is clinically relevant as otherwise important aspects may be overlooked.

Application of MAT-AF indicated the need for increased prescribing of anticoagulation in the study population. Underutilisation of anticoagulation, particularly in the older population, has been reported in several studies.[7-9] Appropriate anticoagulation is particularly important among older persons since this patient group is at greater risk of stroke attributable to AF.[22] Recurrent falls or a high risk for falls was a common reason for withholding anticoagulation therapy in the study population as has been reported in other studies.[8,23,24] Although AF guidelines caution the use of anticoagulation therapy in patients at risk for falls, recommendations specify that these agents should only be withheld in patients with severe uncontrolled falls such as epilepsy or advanced multisystem atrophy with backward falls.[1]

Monitoring of laboratory and other parameters is recommended to reduce complications of AF therapy.[1] Chronic kidney disease, other comorbidities and multiple medication increase the risk of adverse drug reactions in this patient group. MAT-AF application highlighted deficiencies in the monitoring required with digoxin therapy, predominantly regarding serum magnesium and digoxin levels in patients at risk of toxicity. Shortcomings were also evident in assessing whether the required monitoring with amiodarone was conducted.

Guidelines for the management of AF emphasize that patients on antiarrhythmic agents should be periodically evaluated to confirm appropriateness of treatment.[1] Drug therapy which was favourable when initially prescribed may not remain effective in maintaining sinus rhythm or may become inappropriate once the patient develops additional comorbidities. During MAT-AF development, cardiology referral was considered recommendable in these patients. In this study there was a tendency for treatment decisions to be taken without cardiology referral, predominantly resulting in patients being retained on antiarrhythmic agents despite sinus rhythm not being maintained.

The application of MAT-AF has led to identification of areas for improvement in terms of prescribing of anti-thrombotics, monitoring parameters to ensure drug safety and identification of patients warranting referral. MAT-AF additionally provides a means for individual patient assessment by the clinical team to identify patient-specific therapy needs. In a follow-up study, MAT-AF is being implemented by clinical pharmacists at the rehabilitation hospital to assess whether application of the tool in daily practice enhances optimisation of treatment.

CONCLUSIONS

MAT-AF application highlighted key aspects which need to be addressed. The application of such tools in clinical practice can support the challenging task of optimising drug therapy in older persons.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest to disclose.

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