



Original Research

Awareness of physicians and pharmacists of aldosterone antagonists in heart failure and myocardial infarction in Jordan

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Received (first version): 6-Apr-2017

Accepted: 22-Aug-2017

Published online: 3-Sep-2017

Abstract

Objective: to evaluate physicians and clinical pharmacists' awareness and practices regarding use of aldosterone antagonists in heart failure (HF) and post-myocardial infarction (MI).

Methods: First, we reviewed the prescription of aldosterone antagonists among 408 patients presenting to the cardiology clinic at a major hospital in Jordan. Second, physicians and pharmacists working in cardiovascular departments completed a questionnaire related to use of aldosterone antagonists in HF and post-MI.

Results: Thirty patients (7.59%) were eligible for aldosterone antagonist; only 4 received them at discharge (13.3%). The survey was completed by 153 professionals (response rate 76.12%). About 72.1% of participants were aware of studies regarding use of aldosterone antagonists post-MI and in HF. Moreover, 10.45%/53.6% of participants strongly agreed/agreed that these agents are useful in normotensive post-MI and HF patients. Spironolactone was the most prescribed drug by 92.1% of participants. About 41.8% of participants reported use of spironolactone in post-MI and HF. With respect to guidelines, only 39.2% of participants agreed that adding spironolactone to standard therapy in HF is recommended, and 48.3% agreed on adding it directly post-MI. Clinical pharmacists and cardiologists were generally more aware of guidelines than pharmacists, cardiac surgeons and residents/fellows.

Conclusions: there is an under-use of aldosterone antagonists in HF and post-MI patients, and a lack of detailed awareness of current guidelines among health care providers. Dissemination of evidence-based guidelines and usage protocols may improve management of post-MI and HF.

Keywords

Health Knowledge, Attitudes, Practice; Pharmacists; Physicians; Mineralocorticoid Receptor Antagonists; Heart Failure; Myocardial Infarction; Clinical Audit; Surveys and Questionnaires; Jordan

INTRODUCTION

Aldosterone antagonists are commonly prescribed medications to reduce blood pressure while optimizing potassium level.¹ Numerous studies have demonstrated the cardio-protective effects of aldosterone antagonists on cardiac patients²⁻⁴, this therapy may have a significant clinical impact on patients' health outcomes independent of its effects on blood pressure.¹

Current guidelines support the use of aldosterone antagonists in patients with moderate to severe HF and reduced left ventricular ejection fraction (LVEF).⁵ Aldosterone antagonists are considered as class IA, "useful and recommended" within the American Heart Association and the American College of Cardiology (AHA/ACC)⁵⁻⁷, and the European Society of Cardiology.⁸ While spironolactone is the most commonly used drug in this class, eplerenone is increasingly used in patients with HF following acute MI. Despite their recommendations by international guidelines, the use of aldosterone antagonists remains suboptimal in eligible patients. Previous studies revealed modest use in

patients with HF.⁹ A large study from 219 hospitals in the USA suggested widespread under-use of aldosterone antagonists post MI, with only 9% of eligible patients receiving them.¹⁰ Recently, a national large cohort study revealed that aldosterone antagonists prescription decreased over time in patients with HF.¹¹ Factors contributing to the discrepancy between current practice and evidence-based guidelines are unclear. The assessment of physicians and pharmacists' knowledge of guidelines is important to narrow the treatment gap for use of aldosterone antagonists. In Jordan, awareness of evidence based guidelines among health care providers and practice of aldosterone antagonists in HF and post MI patients has not yet been explored.

The primary aims were to evaluate prescription of aldosterone antagonists in HF and MI patients, and to determine and compare physicians and pharmacists' practices, and awareness of current guidelines pertaining to use of aldosterone antagonists in post-MI and HF patients.

METHODS

Ethical Approval

The study was approved by the institutional review board of King Abdullah University Hospital (KAUH) and Jordan University of Science and Technology (JUST). Individual approvals from included hospitals were obtained following approval from Ministry of Health and Royal Medical Services. The procedures followed were in accordance with the ethical standards of the Helsinki Declaration.

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Eligibility and use of aldosterone antagonists in HF and MI patients

In an evaluation of current clinical practice, 408 patients who presented to the cardiology clinic at KAUH with history of HF, coronary artery disease (CAD), diabetes (DM), and hypertension (HT) were prospectively reviewed for eligibility and prescription of aldosterone antagonists. Use of all medications was evaluated at both admission and discharge after optimization of medical therapy.

Study Participants

Physicians and pharmacists working in major Jordanian hospitals were voluntarily invited to complete a cross sectional survey investigating their practices and awareness of guidelines related to use of aldosterone antagonists post MI and in HF. The study was performed between June 2013 and June 2014. A self-completed questionnaire specifically designed for this study was used. The questionnaire was assessed for content and face validity by academic experts and piloted by 10 participants at our institution (KAUH). A reliability test was carried out and produced a Cronbach's alpha coefficient of >0.7.

Invited participants included all physicians (consultants, fellows and residents) and pharmacists/clinical pharmacists (pharmacists with BSc degree and PharmDs) working in cardiology and cardiac surgery departments who are involved in the care of cardiovascular disease patients. Cardiologists/internal medicine residents and cardiac surgeons/surgery residents were surveyed, as they guide the follow up care of post MI and HF patients and are responsible for medication prescriptions. Among residents, only those in the last 2 years of their residency in the surgery or internal medicine program, and who had finished their rotations or were rotating at the cardiology or cardiac surgery departments were included in this study. A written consent was obtained from all participants.

The questionnaire (Online Appendix) is comprised of 30 questions in four sections, regarding 1) demographics, 2) awareness and perceptions, 3) practice, and 4) awareness of current guidelines. Physicians and clinical pharmacists completed all sections; pharmacists working in pharmacies of cardiovascular departments who were less actively involved in practice omitted items 17-25 (practice).

The hospitals included in the survey were the main tertiary hospitals (public and private) in the north and middle of Jordan that provide cardiac care (# 8 hospitals). The same research assistant invited participants in all hospitals to avoid participant duplication. Survey non-responders were sent reminders by email, phone call or personal interaction.

Statistical Analysis

Data are presented as mean and standard error of the

All patients	n= 408	
Demographics		
Age, y	56.46 [0.56]	
Male sex, n (%)	289 (70.8)	
Body Mass Index, n (%)	29.06 [0.29]	
Smoking	171 (41.9)	
CAD ≥50% stenosis, n (%)	231 (56.6)	
Myocardial infarction (MI)	97 (23.7)	
Hypertension, n (%)	270 (66.2)	
Heart Failure (NYHA class III/IV), n (%)	53 (12.9)	
Diabetes mellitus, DM (%)	156 (38.2)	
Ejection Fraction (%)	51.8 [0.6]	
Aldosterone antagonist eligible		
	n=30	
Age, y	60.4 [2.04]	
Male sex, n (%)	27 (90)	
HF with LVEF ≤35%	8 (26.6)	
MI with LVEF≤40% and DM or HF	22 (73.3)	
Potassium level (mmol/L)	4.32 [0.08]	
Creatinine level (mmol/L)	82.1 [1.7]	
Contraindication to aldosterone		
	1 (3.2)	
Medication use in eligible patients (%)		
	Admission	Discharge
Aspirin	18 (60%)	29 (96.6)
ACEIs/ARBs	10 (33.3)	21 (70)
Beta-adrenergic receptor blockers	13 (43.3)	22 (73.3)
Aldosterone antagonists	0 (0)	4 (12.9)
Diuretics	11 (36.6)	9 (30)
Statins	9 (30)	27 (90)
Calcium channel blockers	2 (6.6)	2 (6.6)
Oral hypoglycemic drugs	8 (26.6)	8 (26.6)

Values are expressed as mean [SEM], unless otherwise indicated. MI; myocardial infarction, CAD: coronary artery disease, HF: heart failure, DM: diabetes mellitus, ACEIs: angiotensin converting enzyme inhibitors, ARBs: angiotensin receptor blockers.

mean for continuous variables and percentages for categorical variables. Responses were entered into JMP 11 software (USA). Descriptive statistics were used to analyze proportions and frequencies. Statistical differences among groups were evaluated using Pearson's chi-squared test. Graph Pad prism 5 was used to prepare figures. A p-value <0.05 was considered statistically significant.

RESULTS

We prospectively reviewed data for 408 patients who presented with HF, DM, HT, and CAD (Table 1). Among these, 97 patients (23.7%) presented with MI, 156 patients with DM (38.2%), 53 patients (12.9%) with moderate to severe HF (Stage C / D, or NYHA classes III / IV), and 270 (68%) presented with HT. Of the 408 reviewed patients, 30 patients (7.5%) were eligible for aldosterone antagonist treatment; among these, 22 patients were post-MI with HF or DM and reduced LVEF (≤40%), and 8 were non-MI patients presenting with moderate to severe HF and reduced LVEF (EF≤35%). Of the eligible patients, only 4 patients received spironolactone at discharge (13.3%); 2

Groups	Number (%)	Age range (Years)	Males (%)	Experience (Years)
1. Consultants, cardiac surgeons	7 (4.6)	40-60	7 (100)	13.6 [1.7]
2. Consultants, cardiologists	7 (4.6)	40-60	6 (85.7)	10.3 [4.2]
3. Residents/fellows, internal medicine	77 (50.4)	<30-39	58 (75.3)	3.1 [0.18]
4. Residents/fellows, general surgery	29 (18.9)	<30-39	22 (75.8)	4.6 [0.57]
5. Pharmacists	12 (7.8)	<30-50	1 (8.3)	7.2 [1.2]
6. Clinical Pharmacists	21 (13.7)	<30-50	1 (4.7)	5.9 [1.0]

Experience is presented as mean [standard error of the mean]

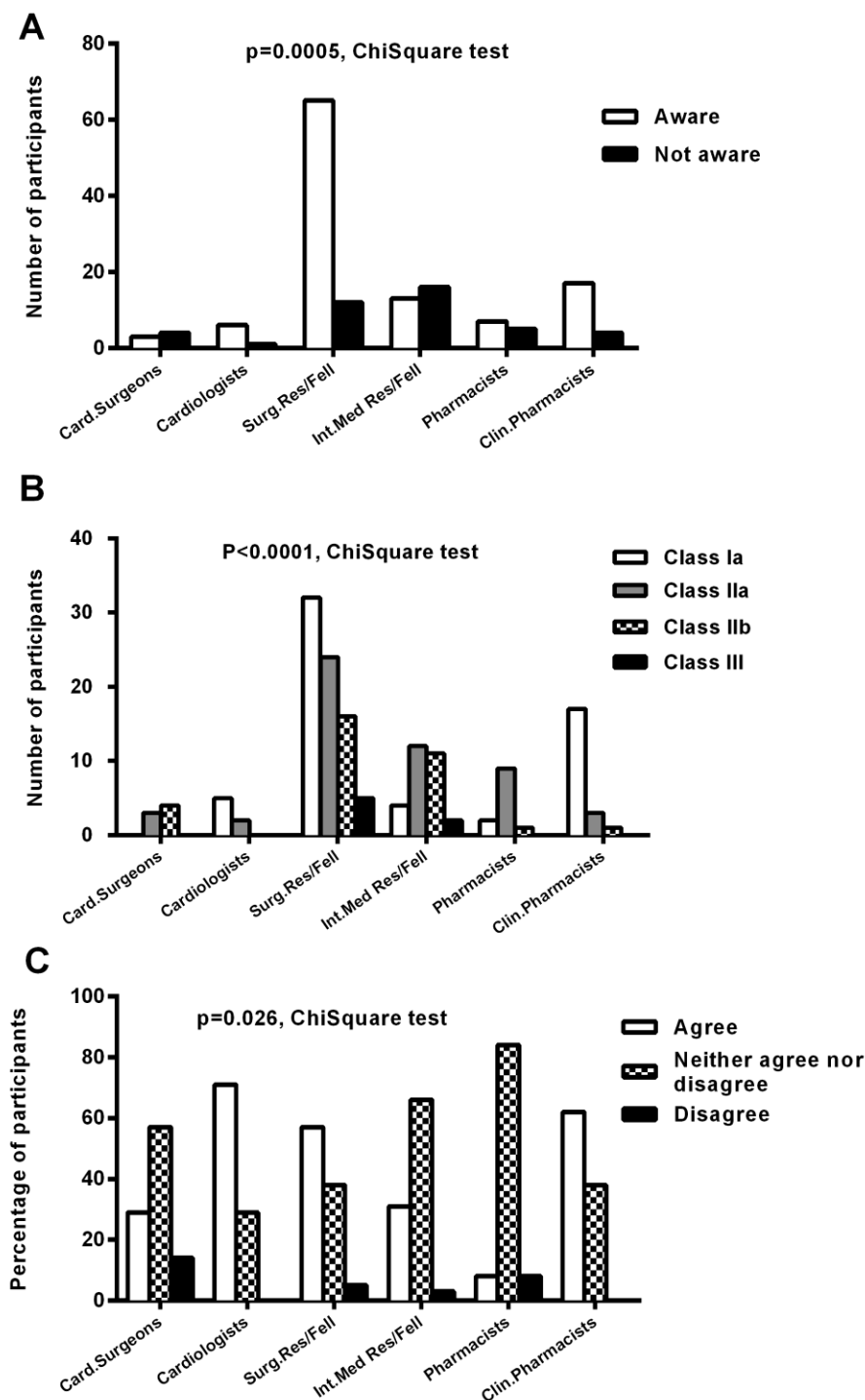


Figure 1. Awareness and knowledge of current guidelines

Figure 1-A summarizes responses to the question “Are you aware of studies in the literature regarding cardio-protective use of aldosterone antagonists in patients with post-myocardial infarction (MI) or heart failure (HF)?” among study groups (Gps).

Figure 1-B summarizes responses to the question “The American College of Cardiology and the American Heart Association (ACC/AHA) consider adding spironolactone to standard therapy in moderately severe to severe HF patients (stage C or D) with reduced LVEF ($EF \leq 35\%$) as?”

Figure 1-C summarizes responses to the guideline “The AHA/ACC recommends adding eplerenone to standard therapy **directly** (within 2 weeks) post-MI in patients with reduced LVEF ($EF \leq 40\%$) who also have HF or diabetes mellitus?” Card: Cardiac, Surg.Res/Fell: General surgery residents/fellows, Int.Med.Res/Fell: Internal medicine residents/fellows, Clin: clinical.

post-MI patients, and 2 non-MI patients with HF. One patient was on spironolactone at admission and remained on it at discharge. Most eligible patients were on and/or received at discharge guideline-based therapies for

management of HF or MI (ACEIs/ARBs, aspirin, statins, and beta-blockers, Table 1).

We designed a questionnaire to evaluate factors related to use of aldosterone antagonists in HF and post-MI patients.

Table 3. Knowledge and beliefs regarding use of aldosterone antagonists (%)					
	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
In your opinion, is the use of aldosterone antagonists in post-MI patients with left ventricular dysfunction who also have HF or diabetes mellitus useful?	22.8	54.2	21.5	0.65	0.65
In your opinion, is the use of aldosterone antagonist in patients with moderately severe to severe HF (NYHA class III & IV) and reduced left ventricular ejection fraction (LVEF) useful?	25.5	54.9	16.9	1.3	1.3
In your opinion, is the use of aldosterone antagonists in HF or post-MI (patients of the above Qs) useful when patients are normotensive?	10.5	53.6	24.2	9.8	1.9
Are you aware of studies in the literature regarding cardio-protective use of aldosterone antagonists in patients with post - myocardial infarction (MI) or heart failure (HF)?	Yes		No		Others
	72.5		27.5		
Are you aware of studies which showed that use of aldosterone antagonists improves cardiac remodeling/oxidative stress, ventricular dysfunction and mortality?	55.5		39.2		5.2
Are you aware of studies in the literature regarding use of aldosterone antagonists to prevent or treat cardiac arrhythmia?	12.4		87.6		

A total of 201 participants were eligible to complete the survey; 153 participants completed the survey and 48 did not (76.1% response rate). Respondents to the survey included 14 consultants: 7 cardiac surgeons and 7 cardiologists (groups 1, 2), 106 residents and fellows: 77 in the internal medicine program, 29 in the general surgery program, (groups 3, 4), 12 pharmacists (group 5) and 21 clinical pharmacists (group 6) (Table 2).

We evaluated participants' awareness and perceptions regarding use of aldosterone antagonists (Table 3). A total of 111 participants (72.5%) were aware of studies regarding the cardio-protective use of aldosterone antagonist in HF and MI. Cardiologists, internal medicine residents/fellows, and clinical pharmacists were more aware than other groups ($p=0.0005$, Figure 1 (A)).

About 22.8% and 54.2% of participants either strongly agreed/agreed with the usefulness of aldosterone antagonist post-MI in patients with HF and/or DM (Table 3), without significant differences across the groups ($p=0.1487$). Similar responses were reported on the utility of aldosterone antagonists in treating moderate-severe HF (Table 3). Consultants and pharmacists/clinical pharmacists were more aware than residents/fellows ($p=0.0493$). Only 10.4% strongly agreed that these agents are useful in HF and MI patients when they are normotensive ($p=0.1155$, Table 3).

In treating moderate to severe HF patients or post-MI patients with HF or DM, 75.2% reported that ACEIs/ARBs are usually prescribed as part of standard therapy, 70.6% reported routine use of beta-blockers, and 41.8% reported use of aldosterone antagonists. Interestingly, 35.9% were not aware if their institutions had a protocol for use of aldosterone antagonists in patients, and only 11.7% reported that they do have a protocol. Spironolactone was reported by 92.1% to be the most commonly prescribed drug. With respect to clinical indication, 54.5% consider prescribing aldosterone antagonists in HT patients with hypokalemia, 67.1% for cardio-protection in HF, and 47.7% post-MI (Table 4).

With respect to the frequency of prescription, most participants (67.3%) reported that they sometimes

prescribe aldosterone antagonists in practice (regardless of the indication, Table 4). Specifically, 34.2% reported that they consider aldosterone antagonists as diuretics once or twice per week, whereas 42% prescribe them 3-10x/week (Table 4). In contrast, aldosterone antagonist' use as a cardio-protective medication in HF or post-MI is less frequent (Table 4); 44% reported prescribing it 1-2x/week and 29.4% prescribe it 3-10x/week. With respect to dosing, 25.9% reported that they consider the same dose of aldosterone antagonist regardless of the indication, Table 4.

Aldosterone antagonists are recommended directly (within 2 weeks) post MI.⁵ Only 30.7% ($p<0.0001$) consider adding aldosterone antagonist directly post MI (Table 4).

With respect to side effects, 13.3% and 62.2% strongly agreed / agreed that spironolactone is associated with gynecomastia more than eplerenone ($p=0.1028$, Table 4). In addition, 67.8% of participants reported that they monitor both [K+] and creatinine level when using aldosterone antagonists.

Current guidelines recommend adding aldosterone antagonists to standard therapy, including ACEIs or ARBs and recommend against adding them to combination of ACEIs and ARBs.⁵⁻⁸ Interestingly, 64.3% of participants reported that patient use of ACEIs/ARBs influenced their decision about whether or not to use aldosterone antagonists. Only 58% of participants consider adding aldosterone antagonists when their patients are on ACEIs/ARBs, whereas 17.5% do not consider aldosterone antagonist if their patients are already on ACEIs/ARBs (Table 4).

We evaluated the awareness of physicians and clinical pharmacists of recent guidelines⁵ regarding appropriate use of aldosterone antagonists in post-MI and in HF patients, Table 5. Only 39.2% of participants consider adding spironolactone to standard therapy in moderately severe to severe HF patients with reduced LVEF ($\leq 35\%$) as class Ia (useful and recommended). On the other hand, 34.6% consider this practice as class IIa (most of the time useful), 21.6% as class IIb (not sure if useful), and 4.5% as class III (not useful and not recommended). Cardiologists

Table 4. Practice regarding use of aldosterone antagonists in HF and MI. (%)					
When do you consider using aldosterone antagonists?					
	In hypertensive patients with hypokalemia				54.5
	In hypertensive patients in which diuretics are not sufficient or intolerant				29.8
	In moderately severe to severe HF patients with low LVEF				67.1
	For cardio-protection in post-MI patients with HF or diabetes				47.7
	In patients with hyper-aldosteronism				42.5
	I do not use these agents				5.9
If you are planning to use aldosterone antagonist in post-MI patients with HF and left ventricular dysfunction, when do you generally consider it?					
	Directly (within 2 weeks) following MI				30.8
	A month after MI				20.3
	Whenever use of standard therapy is insufficient to control LV dysfunction				25.9
	Whenever blood pressure is not controlled by standard therapy				4.2
	Others				4.9
	I do not use it				13.9
If you plan to use aldosterone antagonist for cardio-protection in HF or post-MI, and the patient is taking ACEI or ARB, how would you use it?					
	Replace it with ACEI/ARBs				5.6
	Add it to ACEI/ARB				58.0
	Replace it with diuretic if the patient is taking diuretic				11.9
	I do not consider patient drug therapy				7.0
	I do not consider use of aldosterone antagonist				17.5
How often are aldosterone antagonists used as a routine care in your patients (regardless of the purpose, diuretic or non-diuretic indications)?					
	Always	Usually	Sometimes	Seldom	Never
	2	17.6	67.3	7.8	5.3
Approximately, how many times do you consider aldosterone antagonist per week as a diuretic to lower blood pressure or optimize K ⁺ levels?					
	0 time	1-2 times	3-5 times	5-10 times	>10 times
	16.1	34.2	22.4	19.6	7.7
How many times do you consider using aldosterone antagonist per week as a cardio-protective drug but not diuretic in patients with HF or post MI?					
	0 time	1-2 times	3-5 times	5-10 times	>10 times
	18.9	44.0	13.3	16.1	7.7
When you use aldosterone antagonist, do you use the same dose regardless of the indication (diuretic or cardio-protective indication)?					
	Yes		No	Others	
	25.9		68.5	5.6	
Spironolactone is associated with increased risk of gynecomastia and hyperkalemia more than eplerenone?					
	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
	13.3	62.2	21.7	2.1	0.70

and clinical pharmacists were most aware of this guideline ($p < 0.0001$, Figure 1 (B)). On the other hand, 48.3% agree that eplerenone should be added to standard therapy directly (within 2 weeks) post-MI in patients with reduced LVEF ($EF \leq 40\%$) who also have HF or DM, Table 5. Cardiologists, internal medicine residents and clinical pharmacists were most aware of this guideline ($p = 0.0266$, Figure 1 C). With respect to dose, 55.6% agreed that the recommended daily dose of spironolactone in congestive HF or post MI is 25-50 mg, but higher doses are typically used in HT, Table 5.

Most of participants were aware of contraindications of aldosterone antagonists in significant renal dysfunction, Table 5.

DISCUSSION

In this study, we sought to evaluate prescription of aldosterone antagonists in HF and post-MI patients, and compare awareness and practices regarding the cardio-protective use of aldosterone antagonists among physicians and pharmacists working in cardiovascular departments of major hospitals in Jordan. This study revealed a general lack

of awareness of current guidelines, which might affect the use of aldosterone antagonists and the primary care of cardiac patients.

Recent ACC/AHA guidelines recommend use of spironolactone in stage C and D HF (NYHA class III and IV) and eplerenone directly post MI in patients with HF or DM and low LVEF.⁵⁻⁸. At a major hospital in Jordan, we found that spironolactone is under prescribed in eligible patients, with only 13.3% of those eligible receiving it. This usage rate is similar to the rate previously reported in the USA.¹⁰ Most of health care providers reported use of aldosterone antagonist sometimes in practice; their use as diuretics to optimize [K⁺] was more frequent than their use as cardio-protective medications post MI and in HF. We observed a lack of awareness regarding their usefulness in normotensive MI or HF patients, with only 10.5% / 53.6% strongly agreeing / agreeing on their usefulness in this subpopulation. This suggests that appropriate aldosterone antagonist use is perceived to require the presence of HT. In addition, 25.9% of participants reported the use of the same dose, regardless of the indication, suggesting a lack of knowledge regarding dosing of these medications. This was also confirmed by their responses to current dosing

Table 5. Knowledge of guidelines regarding use of aldosterone antagonists. (%)			
	Agree	Neither agree nor disagree	Disagree
Aldosterone antagonists should not be used in patients with significant renal dysfunction (e.g. creatinine >2.5 in men or >2.0 mg/dl in women) or hyperkalemia (K ⁺ level >5.0 mEq/L)?	80.4	16.3	3.3
Risk of hyperkalemia increases with concomitant use of aldosterone antagonists with ACE inhibitors/ARB or Non-Steroidal Anti Inflammatory Drugs (NSAID)	77.8	19.6	2.6
The recommended cardio-protective <i>daily</i> dose of spironolactone in congestive HF or post-MI is 25-50 mg, but the dose used in hypertension is usually 50-100 mg?	55.6	37.9	6.5
The AHA/ACC recommends adding eplerenone to standard therapy <i>directly</i> (within 2 weeks) post-MI in patients with reduced LVEF (EF≤40%) who also have HF or diabetes mellitus?	48.3	47.1	4.6

guidelines. Additional important aspects of dosing include the timing and possibility of drug-drug interaction. Around 52% of participants were unaware that these agents should be added to standard therapy within 2 weeks post-MI, even when the patient is taking an ACEI. In addition, most participants were unaware about how to prescribe aldosterone antagonists when a patient is on an ACEI, with many suggesting replacing it with ACEI or not using aldosterone antagonist if the patient is taking ACEI/ARBs, suggesting that some participants think that both agents have similar effects and mechanisms.

Despite that 72% of participants have general awareness of studies investigating the utility of aldosterone antagonists post-MI and in HF, there was a significant lack of detailed awareness of current guidelines. In particular, only 39.2% agreed on the current AHA/ACC classification of aldosterone antagonists in HF as “useful and recommended.” In contrast, there was greater awareness of their contraindication in the setting of significant renal insufficiency and hyperkalemia.

This study revealed that cardiologists, internal medicine residents and clinical pharmacists were significantly more aware of current guidelines than cardiovascular surgery consultants/residents and pharmacists. The low prevalence of eligible patients, the lack of clinical experience and infrequent interaction of surgery residents or cardiac surgeons with such patients, lack of time to filter the literature, and the lack of detailed knowledge of usage indications, dosing and timing might contribute. In addition, the lack of written protocols on how to use these agents may play a major role, as only 11.7% reported the presence (or awareness) of local usage protocols. Reservations about risk due to hyperkalemia and polypharmacy may also contribute to low prescription rates.¹² In this setting, it may be helpful for clinical pharmacists and pharmacists to take a more active educational and professional role. Clinical pharmacists may improve patient outcomes by discussing the recommended medications and doses with physicians that may have been overlooked. Establishing detailed protocols based on evidence-based medicine, clinical experience therapeutic interchange, and professional judgment could also help.¹³

Limitations

This study is limited by the relatively small number of consultants who participated. To our knowledge, this is the first study in Jordan and the Middle East to investigate current practice and knowledge among health care providers of aldosterone antagonists’ use in post-MI and HF. Collaborative international studies with larger sample size are required to evaluate the prescription of aldosterone antagonists among eligible patients. The findings of this study call for educational programs that emphasize the benefit of aldosterone antagonists, disseminating current guidelines, and encouraging other healthcare professionals to collaborate and prescribe them when needed.

CONCLUSIONS

There is an under-use of aldosterone antagonists in post-MI and HF patients and a lack of detailed awareness of current guidelines related to use of aldosterone antagonists among health care providers. Cardiologists and clinical pharmacists are most aware of guidelines. By more actively disseminating appropriate use of guidelines during their interactions with health care professionals, they may significantly improve patient management and outcomes.

ACKNOWLEDGMENT

We would like to thank Dr. David R. Van Wagoner, Ph.D. for his critical manuscript editing and Doaa Al-hazmi for her great help in completing the study.

CONFLICT OF INTEREST

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

FUNDING

This research was supported by the deanship of research at Jordan University of Science and Technology (#118/2013).

References

1. Mayyas F, Alzoubi KH, Van Wagoner DR. Impact of aldosterone antagonists on the substrate for atrial fibrillation: aldosterone promotes oxidative stress and atrial structural/electrical remodeling. *Int J Cardiol.* 2013;168(6):5135-5142. doi: [10.1016/j.ijcard.2013.08.022](https://doi.org/10.1016/j.ijcard.2013.08.022)

2. Pitt B, Pedro Ferreira J, Zannad F. Mineralocorticoid receptor antagonists in patients with heart failure: current experience and future perspectives. *Eur Heart J Cardiovasc Pharmacother*. 2017;3(1):48-57. doi: [10.1093/ehjcvp/pvw016](https://doi.org/10.1093/ehjcvp/pvw016)
3. Pitt B, Remme W, Zannad F, Neaton J, Martinez F, Roniker B, Bittman R, Hurley S, Kleiman J, Gatlin M. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med*. 2003;348(14):1309-1321. doi: [10.1056/NEJMoa030207](https://doi.org/10.1056/NEJMoa030207)
4. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, Palensky J, Wittes J. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med*. 1999;341(10):709-717. doi: [10.1056/NEJM199909023411001](https://doi.org/10.1056/NEJM199909023411001)
5. Armstrong C. ACCF and AHA Release Guidelines on the Management of Heart Failure. *Am Fam Physician*. 2014;90(3):186-189.
6. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, Drazner MH, Filippatos G, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld J, Masoudi FA, McBride PE, Peterson PN, Stevenson LW, Westlake C. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *J Am Coll Cardiol*. 2016;68(13):1476-1488. doi: [10.1016/j.jacc.2016.05.011](https://doi.org/10.1016/j.jacc.2016.05.011)
7. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Jr., Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;62(16):e147-e239. doi: [10.1016/j.jacc.2013.05.019](https://doi.org/10.1016/j.jacc.2013.05.019)
8. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, Gonzalez-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, Authors/Task Force M. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37(27):2129-2200. doi: [10.1093/eurheartj/ehw128](https://doi.org/10.1093/eurheartj/ehw128)
9. Albert NM, Yancy CW, Liang L, Zhao X, Hernandez AF, Peterson ED, Cannon CP, Fonarow GC. Use of aldosterone antagonists in heart failure. *JAMA*. 2009;302(15):1658-1665. doi: [10.1001/jama.2009.1493](https://doi.org/10.1001/jama.2009.1493)
10. Rassi AN, Cavender MA, Fonarow GC, Cannon CP, Hernandez AF, Peterson ED, Peacock WF, Laskey WK, Rosas SE, Zhao X, Schwamm LH, Bhatt DL. Temporal trends and predictors in the use of aldosterone antagonists post-acute myocardial infarction. *J Am Coll Cardiol*. 2013;61(1):35-40. doi: [10.1016/j.jacc.2012.08.1019](https://doi.org/10.1016/j.jacc.2012.08.1019)
11. Dev S, Lacy ME, Masoudi FA, Wu WC. Temporal trends and hospital variation in mineralocorticoid receptor antagonist use in veterans discharged with heart failure. *J Am Heart Assoc*. 2015;4(12): e002268. doi: [10.1161/JAHA.115.002268](https://doi.org/10.1161/JAHA.115.002268)
12. Maron BA, Leopold JA. Aldosterone receptor antagonists: effective but often forgotten. *Circulation*. 2010;121(7):934-9. doi: [10.1161/CIRCULATIONAHA.109.895235](https://doi.org/10.1161/CIRCULATIONAHA.109.895235)
13. Devine EB, Hoang S, Fisk AW, Wilson-Norton JL, Lawless NM, Louie C. Strategies to optimize medication use in the physician group practice: the role of the clinical pharmacist. *J Am Pharm Assoc* (2003). 2009;49(2):181-191. doi: [10.1331/JAPhA.2009.08009](https://doi.org/10.1331/JAPhA.2009.08009)