CONSISTENCY OF POTASSIUM AND CREATININE MONITORING DURING INITIATION OF MINERALOCORTICOID RECEPTORS ANTAGONIST THERAPY IN HEART FAILURE PATIENTS; THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

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OBJECTIVES

Mineralocorticoid receptor antagonists (MRAs) reduce morbidity and mortality in heart failure (HF), but may induce hyperkalemia. Clinical guidelines recommend close monitoring of renal function and serum potassium levels throughout the initial course of therapy, but the extent to which this occurs in real life is little studied.

We here assess the adequacy of monitoring rates of potassium and creatinine according to guideline recommendations in HF patients initiating MRA therapy in Stockholm, Sweden.

METHODS

Observational study including HF patients initiating MRAs in Stockholm, Sweden, during 2007-2010. HF cases were ascertained by ICD-10 codes. Study baseline was set as the date of the first MRA purchase, and enriched with comorbidity history, concurrent medications and laboratory values.

For the purposes of evaluating monitoring patterns, we excluded new users who died or were hospitalized within 3 months of drug initiation, as these events may have modified the natural laboratory monitoring practice. We only included individuals that continued MRA therapy for more than 3 months, ascertained by a second MRA purchase and an estimated pill supply sufficient for the period. We consider MRA prescribing center as an important predictor, and centers that issued the index MRA prescription were categorized as primary healthcare centers, Hospitals and others, which included other private services not fitting the other categories above.

The study outcome was the adequacy of potassium and creatinine monitoring during the first 3 months of MRA therapy according to current guideline-recommendations (Cooper et al). We considered three distinct monitoring periods:

1) Pre-initiation testing: measurement of potassium and creatinine at least once within the 120 prior to initiate MRA therapy;
2) Early post-initiation testing: measurement of potassium and creatinine at least once within the first 10 days after MRA initiation;
3) Extended post-initiation testing: measurement of potassium and creatinine at least once within 11 and 90 days after MRA initiation.

We defined adequate monitoring as monitoring across all three monitoring periods. Multivariable logistic regressions were fitted to identify baseline predictors.

RESULTS

A total of 4,036 eligible HF patients were initiated on Spironolactone (99% of cases) or Eplerenone. Median age was 79 years and 55% were women. Median eGFR was 65 ml/min and median serum potassium at initiation was 4 mEq/L.1297 individuals were excluded due to death/hospitalization within the first 3 months. After the exclusion, it was observed that 89% of cases receive a correct preinitiation testing (up to 120 days before starting the therapy). Within the individuals left, 28% receive a potassium and creatinine test in the preinitiation and early post initiation, 38% have received an appropriate monitoring at preinitiation and late postinitiation, but only 23% receive a proper monitoring for all level of testing (Table 2).

The proportion of patients adequately monitored was lower among MRA prescriptions issued from primary healthcare centers than those issued from hospitals (13% against 32%, Figure 1).

In multivariable analysis, patients more likely to be adequately monitored (monitoring before and after therapy start) were those with eGFR<60 ml/min and concomitant utilization of other medications that affect potassium balance (OR = 2.4 [1.65;3.56] for eGFR<30 ml/min). Patients less likely to be adequately monitored were women (P<0.05, OR = 0.8 [0.69;0.96]), and patients factors explained a small portion of adequately monitoring testing (c-statistic, 0.64). Along with having a low renal function, Hospital prescription of MRA was the most outcome related covariate (OR = 2 [1.62;2.55], Figure 2).

	No Preinitiation No. 447	Preinitiation and Early Post No. 1,125	Preinitiation and Late Post No. 1,530	Appropriate Monitoring No. 934
Age-cat				
<45	5 (1%)	15 (1%)	27 (2%)	23 (2%)
45-64	73 (16%)	180 (16%)	263 (17%)	212 (23%)
65-74	97 (22%)	230 (20%)	344 (22%)	232 (25%)
>74	272 (61%)	700 (62%)	896 (59%)	467 (50%)
Female	225 (50%)	540 (48%)	699 (46%)	361 (39%)
eGFR-cat				
<30	1 (0%)	29 (3%)	51 (3%)	53 (6%)
30-45	7 (2%)	152 (14%)	187 (12%)	125 (13%)
45-60	13 (3%)	238 (21%)	366 (24%)	186 (20%)
>60	44 (10%)	706 (63%)	926 (61%)	570 (61%)
Missing	382 (85%)	0 (0%)	0 (0%)	0 (0%)
Potassium-cat				
<4	17 (4%)	526 (47%)	734 (48%)	523 (56%)
4-5	4 (1%)	588 (52%)	792 (52%)	406 (43%)
>5	0 (0%)	11 (1%)	4 (0%)	5 (1%)
Missing	426 (95%)	0 (0%)	0 (0%)	0 (0%)
First Prescription				
Hospitals	55 (12%)	442 (39%)	739 (48%)	580 (62%)
Primary Healthcare Centers	252 (56%)	286 (25%)	313 (20%)	126 (13%)
Other	109 (24%)	390 (35%)	470 (31%)	226 (24%)
Missing	31 (7%)	7 (1%)	8 (1%)	2 (0%)
Diabete	130 (29%)	351 (31%)	499 (33%)	298 (32%)
Myocardial Infarction	111 (25%)	334 (30%)	468 (31%)	285 (31%)
Peripheral Vascular Disease	58 (13%)	148 (13%)	213 (14%)	132 (14%)
Cerebrovascular Disease	74 (17%)	239 (21%)	262 (17%)	157 (17%)
ACEs User	282 (63%)	721 (64%)	1,112 (73%)	706 (76%)
ARBs User	178 (40%)	385 (34%)	597 (39%)	384 (41%)
Beta Blockers User	377 (84%)	965 (86%)	1,389 (91%)	878 (94%)
Thiazide Loop Diuretics User	416 (93%)	1,080 (96%)	1,478 (97%)	907 (97%)
Other Blood Pressure drugs User	163 (36%)	440 (39%)	582 (38%)	366 (39%)

Table 1: Baseline characteristics stratified by frequencies of testing

Testing	Frequency	%
No Preinitiation	447	11%
Preinitiation and Early Post	1125	28%
Preinitiation and Late Post	1530	38%
Preinitiation and Early and Late Post	934	23%

Table 2: Frequency and proportions of individuals for all combination of testing

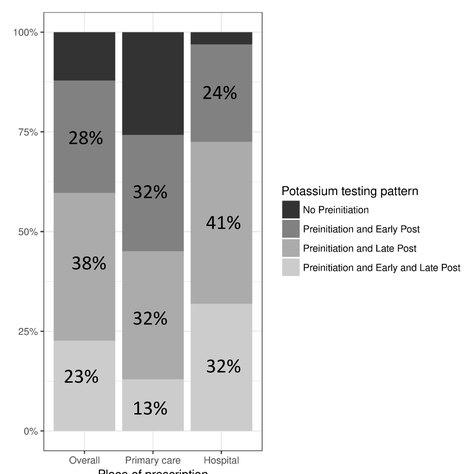

Figure 1: Proportion of individuals with appropriate testing stratified by place of prescription (top right)

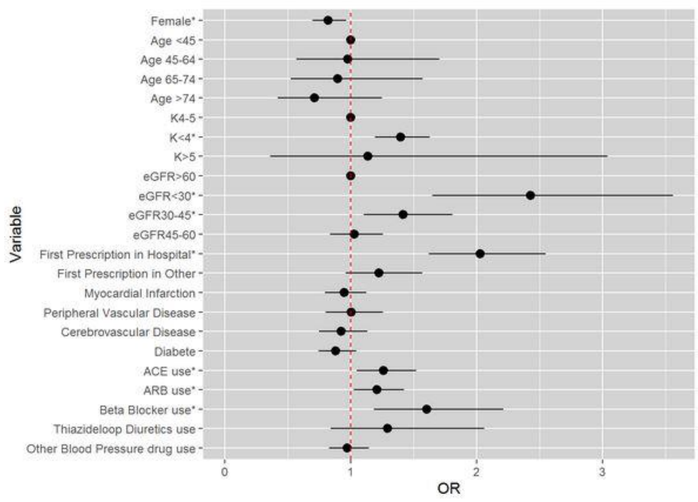

Figure 2: Forest plot with ORs showing risk factors associated with the outcome (appropriateness of testing) in those with correct test at preinitiation (right)

CONCLUSION

Although laboratory monitoring before MRA initiation for HF is frequent in a region-representative healthcare extraction from Sweden, rates of appropriate laboratory monitoring after MRA initiation are suboptimal. Quality improvement initiatives to increase appropriate laboratory monitoring are needed, as they may have direct clinical implications in optimizing MRA dose titration, preventing the risk of hyperkalaemia and potentially influence patient outcome.

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