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Cover Page Footnote
The author would like to acknowledge the partnership between UNC Eshelman School of Pharmacy and Moses Cone Hospital, which helped guide immersion students through their experience. The author would also like to thank Nita Johnston, Pharm D, for her continual support and advice.

Pharmacy Practice: Exploring the Relationship between SSRIs and Sodium Levels in an Older Adult Population

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Abstract

I was asked to examine the presence of hyponatremia (<130 mEq/L) in older patients (≥65 years) taking Selective Serotonin Reuptake Inhibitors (SSRIs) at Moses Cone Hospital. The presence of hyponatremia in older patients using SSRIs indicates potentially inappropriate use according to the STOPP (Screening Tool of Older Persons' Potentially Inappropriate Prescriptions) and START (Screening Tool to Alert Doctors to Right Treatment) criteria[6]. This study was done to assess possible risk factors for potentially inappropriate use of SSRIs by older patients at Moses Cone Hospital. Data collected included the patient's sex, age, sodium level, and the date the sodium level was drawn. Data also included the specific SSRI and the starting date for the SSRI. The study showed no relationship between age, sex, SSRI prescribed and hyponatremia. However, patients that were prescribed an SSRI for less than a year were more at risk for hyponatremia. Therefore, in order to minimize the risk of hyponatremia, additional monitoring may need to be added at SSRI initiation, three months, six months, and one year, especially in patients with other medications that may lower sodium levels.

Introduction

In the United States, the majority of older adults have multimorbidity, which is the coexistence of multiple chronic conditions. According to Medicare claims data from 2008, 67% of all beneficiaries had two or more chronic conditions. One of the consequences of multimorbidity is the use of multiple medications. As a result, nearly 90% of Medicare beneficiaries were on at least one prescription medication and 46% of beneficiaries were on five or more medications. Using multiple medications increases the number of medication combinations, which can increase the risk of adverse drug reactions and drug-drug interactions[2]. Furthermore, polypharmacy is associated with an increased rate of rehospitalization. The use of seven or more drugs was associated with higher rates of unplanned rehospitalizations. Older adults might be victims of a "prescribing cascade" that might include inappropriate medications, thus leading to an increase in rehospitalization[8]. Adverse drug reactions are prevalent in older adults because typically they are using multiple drug regimens and because an increase in age leads to changes in their pharmacokinetics and pharmacodynamics (Mirko Petrovic, Adverse Drug Reactions in Older People). Hepatic blood flow decreases by 40%, thus decreasing the amount of first-pass metabolism that occurs in the liver[7]. This may result in the need of lowered dosing in medications like warfarin, benzodiazepines, and opiates[5]. Serum proteins, which are capable of binding to drug, decrease due to malnutrition and dietary changes, leading to an increase in unbound drug. This may increase the effects of the drug and lead to unintended consequences. Distribution of drugs within the body is also changed because of a decrease in ratio of lean body weight to body fat. Finally, for the ages 60-60, around 22% have some form of chronic kidney disease (CKD), the majority being Stage 3. For the ages 70 and above, around 47% have some form of CKD, the majority being Stage 3[1]. This means that the process of drug metabolism by the kidney is slowed and the drug will be present in the body for longer periods of time. However, many of these adverse drug events are preventable. In an ambulatory setting, adverse drug events were preventable in around 28% of older adults[3]. One way to avoid these events is by utilizing the STOPP (Screening Tool of Older Persons' Potentially Inappropriate Prescriptions), and START (Screening Tool to Alert Doctors to Right Treatment) criteria[6]. The STOPP criteria was used in this study to identify possible adverse events. Furthermore, the STOPP criteria was used instead of the Beers criteria because STOPP is thought to work better than Beers to identify meds that result in negative outcomes, like in hospital admission[6]. This can help in identifying medications that result in negative outcomes, like adverse events and hospital admissions[6,7].

One class of drugs the START STOPP criteria cautions about are SSRIs. They are potentially inappropriate to use in older adults (≥65 years) per STOPP if they have a history of sodium <130 mEq/L (mmol/L) within the past two months[6,7]. The clinical concern with SSRIs is potential for hyponatremia. In order to prevent adverse drug events, SSRIs should be tapered and discontinued in those that meet these criterion[6,7]. The purpose of the study was to assess what factors other than concomitant medications put older adults more at risk for inappropriate use of SSRIs. Concomitant medications were not addressed because the purpose of the study was only to look at SSRI medications in relation to hyponatremia according to the STOPP criteria. While there

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are other STOPP criteria for other medications, the only STOPP criteria where hyponatremia is a clinical concern is with SSRIs.

Methods

To assess what factors put older patients more at risk for inappropriate use at Moses Cone Hospital, a report was ran on admitted patients that were on one or more SSRIs from June 18th to June 22nd, 2016. A one week period was used to ensure enough patients meeting the STOPP criteria could be analyzed. Inclusion criteria for the study included patients ages 65 years old or older, currently admitted, and on one or more SSRI for two months or greater. Absolute risk was addressed in this study. Patients could have just been newly admitted or been admitted for a longer period of time. Before admission at Moses Cone Hospital, medication reconciliation was done to ensure their medication list was up to date. An audit trail was ran in the report to make sure the patient had been taking the SSRI for two months or greater. The study only investigated if they were taking an SSRI for two months or longer, not if the SSRI was working for them. Moses Cone Hospital represents populations from both the rural and urban settings in Greensboro, North Carolina. From the electronic health record data extracted, patients were identified and data was collected on age, sex, the SSRI they were taking, the start date of their SSRI, their sodium levels, and the date the sodium levels drawn. The sodium levels analyzed were sodium levels taken within two months of the study time period. Having a sodium level below 130 mmol/L meant that the SSRI(s) may require closer monitoring or that perhaps it was inappropriate. Having a sodium level between 131 and 134 mmol/L meant they were at an elevated risk for hyponatremia and the SSRI(s) may require closer monitoring especially if combined with other medications that lower sodium like diuretics. Having a sodium level above 135 mmol/L meant that the SSRI(s) most likely did not cause hyponatremia in this patient and may be appropriate. Comorbidities were address, and there were no comorbidities in patients that affected sodium levels. Out of 257 patients, there were a total of 69 patients that were included in this study and were included only once if their admission was for longer than one day. The data was analyzed for possible correlations between the patient's sex, age, SSRI taken, SSRI start date, and their sodium level.

To understand more about the patients selected for this study, we chose to break down the data into age groups. The six different groups were split into 5 year intervals as follows: 65-69, 70-74, 75-79, 80-84, 85-89, and 90-94 years old.

Results

Patient Demographics

The average age of patients in this study was 76.9 years old, and the age distribution can be seen in Table 1. With respect to patient gender, 46 were female (66.7%) and 23 were male (33.3%). There were 5 patients on two SSRIs (7.2%), while 64 patients received only one SSRI (92.8%). Patients were prescribed a variety of SSRIs with three representing a vast majority (Table 2).

The length of therapy patients had been on SSRIs differed: 55 patients were on an SSRI for less than one year, 11 patients had been on an SSRI for 1-3 years, and 3 patients for more than one year (see Figure 1).

Lastly, patients had varying sodium levels. The lowest sodium level that the patient had in two months was recorded. 9 patients had a sodium level below 130 mmol/L, 12 patients had a sodium level between 131 and 134 mmol/L, and 48 patients had sodium levels above 135 mmol/L (see Figure 2). Hyponatremia is defined as sodium levels below 135 mmol/L, so 21 patients were hyponatremic (30.4% of patients). In total, SSRI prescriptions were even across age groups; females were prescribed more SSRIs than males; most patients were on only one SSRI; Escitalopram and Sertraline were prescribed most often; most patients were on their SSRI for less than one year.

Patients at Risk for Inappropriate Use and Patients with Inappropriate Use

The next step was to look at what factors other than concomitant medications may have contributed to a decrease in sodium levels. Factors analyzed included patient sex, age, duration of SSRI use, and the SSRI used. Patients that were at risk for hyponatremia and potentially inappropriate use as well as patients with hyponatremia and potentially inappropriate use were reviewed to identify a possible correlation between one of these factors and their hyponatremia. Out of 21 patients with hyponatremia, 6 were male (28.6% of patients) and 15 were female (71.4% of patients). The age breakdown is shown in Table 3.

The duration of therapy for the SSRI was reviewed among patients with hyponatremia and 17 patients had been receiving the SSRI for less than one year, 3 patients had been on the SSRI between one and three years, and only 1 patient had been receiving the SSRI for more than three years (see Figure 3).

The SSRIs prescribed among patients with hyponatremia are shown in Table 4. Only one patient had been using more than one SSRI. There appeared to be a trend with more female patients than male patients that had hyponatremia. But this may be because there were more females prescribed SSRIs than males. Out of the 46 older adult females that were prescribed SSRIs, 15 had hyponatremia, meaning that 32.6% of those prescribed developed hyponatremia. Out of the 23 older adult males that were prescribed SSRIs, 6 had hyponatremia, meaning that 26% of those prescribed

developed hyponatremia. A Z-test was run with a significance level of 0.05, leading to a p-value of 0.286, meaning the difference was not significant between the two gender populations. There seemed to be no association between patient age and risk for hyponatremia, as this attribute showed a fairly even distribution between the different age groups. There was no association between the specific SSRI prescribed and a risk for hyponatremia. It appeared that more patients that had been on their SSRI for less than one year seemed to have hyponatremia. Out of the 55 adults prescribed an SSRI for less than a year, 17 adults had hyponatremia, meaning that 30.9% of adults prescribed an SSRI for less than a year developed hyponatremia. Out of 11 adults prescribed an SSRI for one to three years, 3 adults had hyponatremia, meaning that 27.3% of adults prescribed an SSRI for one to three years developed hyponatremia. Out of 3 adults prescribed an SSRI for over three years, 1 adult had hyponatremia, meaning that 1.4% of adults prescribed an SSRI for over three years developed hyponatremia. A Z-test with a significance level of 0.05 was ran to compare adults prescribed an SSRI for less than a year and adults prescribed an SSRI for between one to three years. The result was not significant with a p-value of 0.412. A Z-test with a significance level of 0.05 was ran to compare adults prescribed an SSRI for less than a year and adults prescribed an SSRI for over three years. The result was not significant with a p-value of 0.472. Thus for risk of hyponatremia, the risk was not significant between length of time the SSRI was prescribed.

The last step was to look at what was causing the decrease in sodium levels in patients that had hyponatremia and potentially inappropriate use of their SSRI. Again, the factors analyzed included patient sex, age, duration of SSRI use, and the SSRI used. Out of nine patients with inappropriate SSRI use, three were male (33.3% of patients) and six were female (66.7% of patients).

The age breakdown is shown in Table 5. Of these patients, eight had been on the SSRI for less than one year, 1 patient received their SSRI between one and three years, and no patients in this group had been receiving the SSRI for more than three years (see Figure 4). Only one patient had been receiving more than one SSRI and those used are shown in Table 6. More female patients were affected by hyponatremia than male patients. However, out of 46 females, sex females had inappropriate SSRI use, meaning that 13% of females had inappropriate SSRI use. Out of 23 males, three males had inappropriate SSRI use, meaning that 13% of males had inappropriate SSRI use. A Z-test was ran with a significance level of 0.05, leading to a p-value of 0.5, thus there was no significant difference between the genders with respect to inappropriate SSRI use. There was no association between patient age and risk for hyponatremia, as this attribute showed a fairly even distribution between the different age groups. Patients that had inappropriate use of SSRIs also had Escitalopram and Sertraline due to higher prescription rates, thus was not significant. Much like the previous grouping of patients with hyponatremia, this grouping of patients with inappropriate SSRI use had more patients with hyponatremia if they had been taking their SSRI for less than one year. Of these patients 88.9% had been using it for less than one year. Out of 55 patients that were prescribed an SSRI for less than a year, eight had inappropriate use of the SSRI prescribed, meaning 14.5% of patients prescribed an SSRI for less than a year had inappropriate use. Out of 11 patients that were prescribed an SSRI for between one to three years, one had inappropriate use of the SSRI prescribed, meaning 9.1% of patients prescribed an SSRI for one to three years had inappropriate use. Out of three patients that were prescribed an SSRI for more than three years, zero had inappropriate use of the SSRI. A Z-test with a significance level of 0.05 was ran to compare patients with inappropriate use of SSRI that had been prescribed an SSRI for less than a year and those that had been prescribed an SSRI for one to three years. This resulted in a p-value of 0.298, thus not significant. A Z-test with a significance level of 0.05 was ran to compare patients with inappropriate use of SSRI that had been prescribed an SSRI for less than a year and those that had been prescribed an SSRI for over three years. This resulted in a p-value of 0.001, thus significant. This may indicate a need for closer monitoring with new starts of SSRIs in the older adult population. It may be prudent to obtain basic chemistry bloodwork on initiation, three months, six months, and one year to evaluate for hyponatremia.

Conclusion

The purpose of this study was to assess what risk factors put older adults ($\geq$ 65 years old) at risk for inappropriate use of their prescribed SSRI. Inappropriate used was defined as having a sodium level below 130 mmol/L. Per STOPP criteria, if an older adult patient has an instance of a sodium level below 130 mmol/L while on an SSRI, the SSRI should be tapered and discontinued. Patients were identified and information on age, sex, the SSRI they were taking, the start date of their SSRI, their sodium levels, and date the sodium levels were drawn. The overall findings indicated that there was no relationship between age, sex, the SSRI they were taking and their sodium levels. However, there was a significant relationship with respect to the start date of the SSRI and the sodium levels. Those that had been taking an SSRI for less than a year were more prone to hyponatremia than those that had be on an SSRI for more than three years. While there was not a significant difference in risk for hyponatremia between those that had been taking an SSRI for less than a year and those that had been taking an SSRI for one to three years, there were still more instances of hyponatremia in those taking an SSRI for less than a year.

In order avoid inappropriate use of SSRIs and possible adverse events in older adults, there may need to be closer monitoring with new starts of SSRIs in the older adult population. It may be prudent to obtain basic chemistry bloodwork on initiation, three months, six months, and one year to evaluate for hyponatremia. This is because there was a significant difference in sodium levels between those that were using an SSRI for less than a year and those that were using an SSRI for over three years. Closer monitoring is need in the first year to ensure that the SSRI they are prescribed is appropriate for them. Closer monitoring would indicate early on whether a switch to a different anti-depressant would be more suitable, thus preventing possible adverse events and help decrease the patient's overall health costs[4].

Limitations of this study include a small sample size of patients, use of only one hospital setting, limited review to only SSRIs and not other medications that may have contributed to hyponatremia. Larger studies may be required to delineate between length of SSRI use and increased risk, however, based on the trend the data presents, it appears that those that had been taking the SSRI for less than a year had a higher risk of developing hyponatremia. Additional sodium level monitoring for those on SSRIs has important implications for both hospital and community pharmacist. For hospital pharmacists, additional monitoring allows a chance to ensure the SSRI will not result in hyponatremia, thus ensuring the SSRI is appropriate. If they have additional monitoring done upon initiation of the SSRI and when initiating medications that might potentiate the SSRI's effects, hospital pharmacists will see potentially see less adverse drug events resulting from SSRI use. Depending on if the hospital pharmacist follows up the result, this could provide them with additional consoling time. They could also check in with the patient to ensure that the SSRI is working to control their symptoms after a month. If not, they could recommend that the doctor switch or add an additional agent to better control their symptoms. It will also give community pharmacists a chance to provide additional consoling points when SSRIs are initiated. If additional monitoring in the first year of SSRI use is started, community pharmacists could follow up with them on their results. If their results are abnormal, they would be able to contact their primary care provider to alert them that the patient's SSRI may potentially be inappropriate. Additional monitoring would also have important implications in the healthcare system by preventing adverse drug events that increase overall healthcare costs.

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Conflict of Interest: We declare no conflicts of interest or financial interests that the authors or members of their immediate families have in any product or service discussed in the manuscript, including grants (pending or received), employment, gifts, stock holdings or options, honoraria, consultancies, expert testimony, patents and royalties.

References

1. Anderson S, *et al*. Prediction, Progression, and Outcomes of Chronic Kidney Disease in Older Adults. *Journal of the American society of Nephrology*. 2009;20(6):1199-1209.
2. Fried TR, *et al*. Health Outcomes Associated with Polypharmacy in Community-Dwelling Older Adults: A Systematic Review. *Journal of the American Geriatrics Society*. 2014;62(12):2261-2272.
3. Gurwitz JH, *et al*. Incidence and Preventability of Adverse Drug Events Among Older Persons in the Ambulatory Setting. *Journal of the American Medical Association*. 2003;289(9):1107-1116.
4. Ho MP, Bryson CL, Rumsfeld JS. Medication Adherence, Its Importance in Cardiovascular Outcomes. *Circulation*. 2009;119:3028-3035.
5. Hughes. Prescribing for the Elderly Patient: Why do we need to Exercise Caution?. *British Journal of Clinical Pharmacology*. 1998;46(6):531-533.
6. PL Detail-Document, STARTing and STOPPing Medications in the Elderly. Pharmacist's Letter/Prescriber's Letter. September 2011.
7. Pretorius RW, Gataric G, Swedlung SK, Miller JR. Reducing the Risk of Adverse Drug Events in Older Adults. *American Family Physician.* 2013;87(5):331-336.
8. Sganga F, *et al*. Polypharmacy and Health Outcomes Among Older Adults Discharged from Hospital: Results from the CRIME Study. *Geriatrics & Gerontology International*. 2014;15(2):141-146.

Age	Number of Patients	%
65-69	13	18.8
70-74	16	23.2
75-79	15	21.7
80-84	15	21.7
85-89	6	8.7
90-94	4	5.8

Table 1. Age breakdown of all patients (n=69).

SSRI	Number of Patients
Citalopram	9
Duloxetine	5
Mirtazapine	5
Venlafaxine	3
Venlafaxine XR	1
Amitriptyline	4
Escitalopram	15
Paroxetine	5
Fluoxetine	1
Nefazodone	1
Bupropion	6
Sertraline	19

Table 2. SSRI breakdown of all patients.

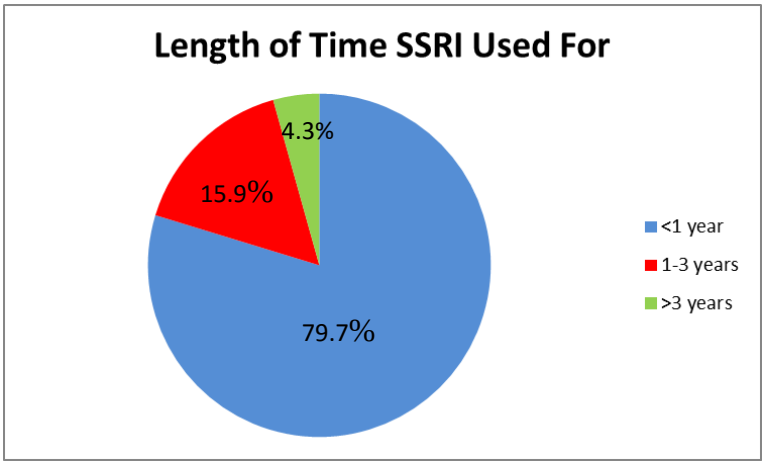

Figure 1. SSRI use breakdown of all patients.

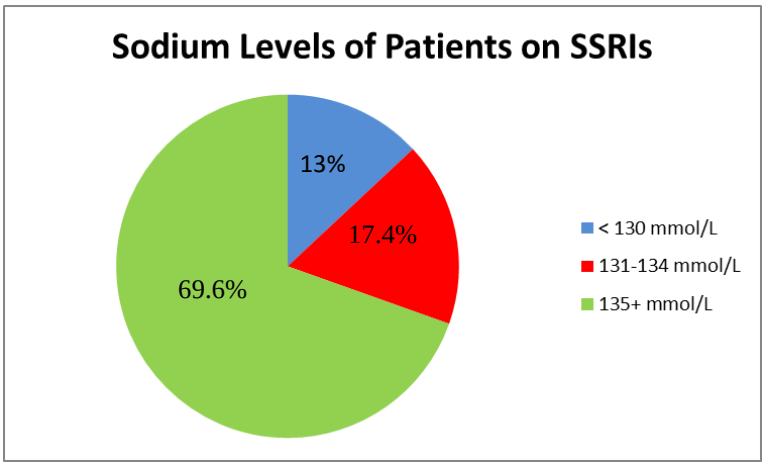

Figure 2. Sodium level breakdown of all patients.

Age	Number of Patients	%
65-69	5	23.8
70-74	6	28.6
75-79	3	14.3
80-84	4	19
85-89	2	9.5
90-94	1	4.8

Table 3. Age breakdown of patients with hyponatremia (n=21).

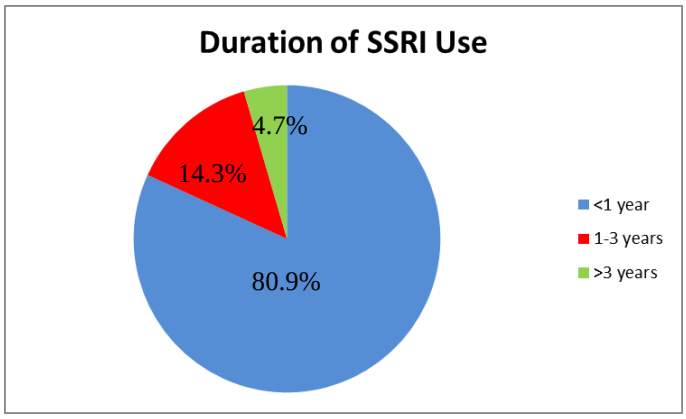

Figure 3. SSRI use breakdown of patients with hyponatremia.

SSRI	Number of Patients
Citalopram	4
Duloxetine	2
Venlafaxine XR	1
Amitriptyline	1
Escitalopram	5
Paroxetine	2
Fluoxetine	1
Nefazodone	1
Bupropion	1
Sertraline	4

Table 4. SSRI breakdown of patients with hyponatremia.

Age	Number of Patients	%
65-69	3	33.3
70-74	2	22.2
75-79	1	11.1
80-84	3	33.3
85-89	0	0
90-94	0	0

Table 5. Age breakdown of patients with inappropriate SSRI use (n=9).

SSRI	Number of Patients
Citalopram	1
Duloxetine	0
Venlafaxine XR	0
Amitriptyline	1
Escitalopram	3
Paroxetine	1
Fluoxetine	0
Nefazodone	1
Bupropion	1
Sertraline	2

Table 6. SSRI breakdown of patients with inappropriate SSRI use.

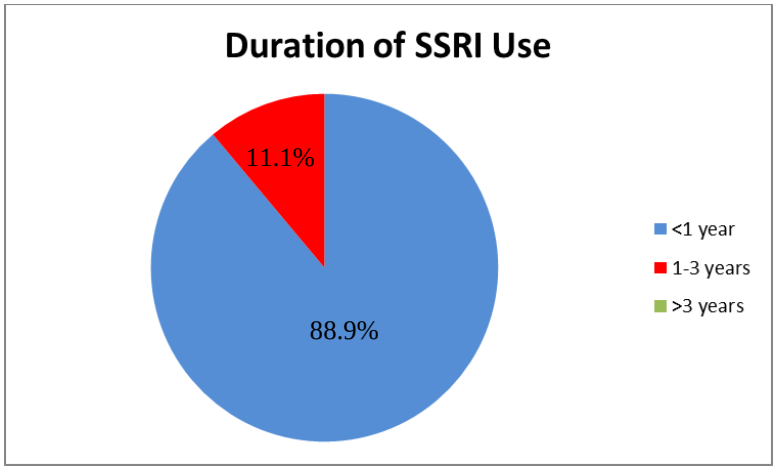

Figure 4. SSRI use breakdown of patients with inappropriate SSRI use.