Case Series

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Assessment of drug prescription practises in chronic hemodialysis patients: case series

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Introduction: The aim of the study was to assess the quality of drugs prescriptions in chronic haemodialysis patients.

Material and methods: The authors conducted a prospective study in chronic haemodialysis patients of two haemodialysis centres in the city of Oujda eastern Morocco, during the year of 2020. The authors identified the drugs prescribed in this population with regards to the product characteristics, in terms of indications, contraindications, dosage and drug interactions. Our data were analyzed by SPSS version 27 software.

Results: The mean number of drugs taken per patient was 8.15 ± 6. Ninety-three percent of patients received treatment for anaemia. Phosphocalcic disorders and hypertension were treated in 89% and 72% of patients, respectively. In 77.6% of the cases, these drugs were taken orally. According to Vidal, the majority of prescriptions met the criteria of good prescription, in 81.54% of the cases, versus 18.46% of the patients with at least one of non-compliant prescription. On the other hand, 6.15% of the patients had at least one inadvisable combination. No contraindicated association was noted in our patients.

Conclusion: Patients undergoing haemodialysis have a higher risk of developing side effects and drug interactions than patients with normal kidney function. Given the paucity of pharmacokinetic studies in this population, nephrologists refer to their own experience to treat his patients effectively. Therapeutic education and regular monitoring of chronic haemodialysis patients can improve clinical outcomes, quality of life and reduce the cost of care.

Keywords: drug interactions, haemodialysis, kidney, therapeutic

Introduction

End-stage chronic kidney disease (ESKD) has been declared a major public health priority in many countries[1].

Haemodialysis only partially corrects the consequences of renal failure, requiring adjuvant treatments to which are added medications for associated pathologies that are common in this population[2].

Prescription problems in dialysis patients are mainly due to the intersection of two constraints, on one hand the need of a large number of various treatments, and on the other hand the absence of data specific to this population[3].

HIGHLIGHTS

- The aim of the study was to assess the quality of drugs prescriptions in chronic haemodialysis patients.
- We conducted a prospective study in chronic haemodialysis patients of two haemodialysis centres in the city of Oujda eastern Morocco, during the year of 2020. We identified the drugs prescribed in this population with regards to the product characteristics, in terms of indications, contraindications, dosage and drug interactions.
- Therapeutic education and regular monitoring of chronic haemodialysis patients can improve clinical outcomes, quality of life and reduce the cost of care.

These considerations led us in this work to study the treatments administered in a population of haemodialysis (HD) patients and to analyze their compliance with international recommendations.

Our work has been reported in line with the SCARE criteria[4].

Material and methods

The study took place in two haemodialysis departments of the city of Oujda-Eastern Morocco, equipped with 90 haemodialysis machines. One hundred eighty-five HD patients undergo chronic HD in these units each.

We have carried out a prospective survey that took place over a 12-month period, from 1 January 2020, to 31 December 2020, involving all adult patients of both sexes treated by haemodialysis during the study period and meeting the inclusion criteria below:

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Patients who had received at least one dialysis session in one of the two haemodialysis departments.

We excluded patients with an unusable record.

We have also analyzed each prescription regarding to the indication, contraindications, dosages and drug interactions.

The data collection comes from patient files archived on which all the information present on the investigation sheet is included.

All the treatments that the patient takes routinely at the time of the survey have been taken into account.

The prescriptions considered to be non-compliant were: drugs that are contraindicated in haemodialysis patients, dosages not consistent with the recommended adjustments, or use in an indication other than that recommended. Drug interactions have also been researched.

These drug interactions are presented in Vidal in four levels of severity, listed in decreasing order: the contraindication, which absolutely defends the combination of two drugs; the inadvisable combination is a relative contraindication, which should preferably be avoided, requiring close monitoring; the precaution of use qualifies a possible association on condition of respecting the described recommendations. Finally, the association to be taken into account draws the prescriber's attention to the risk of the interaction.

Our data were analyzed using SPSS version 27 software.

Results

Our study involved 130 patients including 70 men (53.8%), and 60 women (46.2%), making a sex ratio of 1. The mean age of our patients was 54.08 ± 18.6, with extremes ranging from 16 to 90 years old.

All the patients had at least one associated pathology (in particular hypertension, diabetes and heart disease). Therefore, 72.3% of our patients were hypertensive, 36.15% were monitored for heart disease, 24.61% were diabetic, 10.76% had dyslipidemia, 20.76% had a psychiatric problem and 16.15% had a thyroid dysfunction.

The most represented therapeutic classes correspond to the most frequent complications of ESKD: treatment of anaemia and mineral bone disorders.

Anaemia was observed in 93.07% of patients, of which 81.45% were treated with iron; both intravenous and oral; and 63.8% of the cases were treated with erythropoietin stimulating agents.

Mineral bone disorder treatments were administrated in 89.23% of the cases: calcium carbonates (Calcidia) in 49.23% of the cases, non-calcium phosphorus chelators (Renagel) in 26.92%, calcimimetics (Mimpara) in 2.30%, and vitamin D supplementation (D-cure 60%, Un-alfa in 25.38%, Sterogyl 13.07%).

Antihypertensive treatment concerned 72.3% of dialysis patients, calcium channel blockers were the most prescribed in 43% of the patients, a hypokalaemic treatment (Kayexalate) in 4.61%, and uric acid lowering drug (Zyloric) in 3% of the cases.

Antibiotic therapy was noted in 42.3% of the patients, who received amoxicillin in 16.15% of the prescriptions.

Other drugs were used such as , proton pump inhibitors are prescribed in 27% of the cases, salicylates (Kardegic, cardioaspirin) in 20% of the cases, and antidepressants (Laroxyl, Anafranyl) in 11.53% of the cases.

The mean number of drugs taken per patient was 8.15 ± 6 with extremes ranging from 4 to 14 drugs. In 77.6% of the cases the drugs were taken orally: there were 10.87 ± 7 galenics units per day and per patient with a maximum of 18 units per day. The data are shown in the table below (Tables 1 – 3):

Referring to Vidal, 20.76% (n = 27) of the patients have at least one non-conform prescription, with 21.53% (n = 28) of the prescriptions showing at least one drug interaction.

In the non-conform prescriptions, we have:

(1) Contraindications concern 16.92% of patients (n = 22): It's mainly about magnesium, (Mag 2, Magé B6) that is contraindicated because of its excretion in active form via the kidneys, in 12 patients.
Central antihypertensive drugs are contraindicated in ESKD, were prescribed in one patient in the form of rilmenidine (Hyperium).
Statin are contraindicated in chronic haemodialysis patients: rosuvastatin (Rozat) was used by one patient.
Thecetirizine (Zyrtec), an H1 antihistamine, taken by one patient. The tremitazidine (Vastarel), an anti-angina drug in one patient. And the fibrates in a patient, used as lipid-lowering agents: fenofibrates (Lipanthyl), gemfibrozil (trialmin), these drugs are contraindicated because of lack of trials in haemodialysis.
In addition, acenocoumarol (Sintrom), generally not recommended in patients with ESKD, because of its elimination in an active form by renal route, was prescribed in 5 patients.
(2) No off-label prescription was found in our patients.
(3) The non-compliant dosages concern seven patients. A dosage that does not comply with the recommendations in dialysis patients is either a dosage where it is necessary to reduce the dose, or to lengthen the interval between two doses. We found allopurinol (Zyloric) which; should be prescribed for haemodialysis patients chronic at a dose of 100 mg every other day; dosed at 200 mg ounce a day in two patients. Bactrim forte, administered to a patient at the usual dose, taken in two twice a day, whereas it should be prescribed at a dosage reduced by half among the hemodilysis patients.
Atenolol (Atenor) which is a beta blocker, dosed at 100 mg per day in two patients, while it should not exceed 50 mg every other day after dialysis.
The perindopril (Zynara) an Angiotensin converting enzyme inhibitor that should be prescribed in chronic

Table 1

Therapeutic characteristics of the included patients

Parameters	*n* (%)
Mean number of specialties per patient	8.15 ± 6.4
Mean number of tablets per patient per day	10.87 ± 7.2
Non-conform prescriptions	20.76%
Patients with a drug that is contraindicated in ESKD	16.92%
Non-conform dosages	5.38%
Prescriptions without marketing authorization	0%
Prescriptions with drug interactions	21.53%
Contraindicated associations	0%
Not recommended associations	6.15%
Precautions for use	9.23%
Associations to take in consideration	16.15%

Table 2

Not recommended combinations in the included patients

Not recommended associations		No. cases	Risks
Oral iron: ferrous sulphate (Tardyferon, Folifer)	Intravenous iron: (Venofer, Fermed)	4	Faintness, even shock attributed to rapid release of iron from its complex form and saturation of the transferrin.
Fenofibrates	Simvastatin (Redlip)	1	Risk of rhabdomyolysis
Carbamazépine (Tegretol)	Simvastatin (Redlip)	1	Significant decrease in plasma concentrations of simvastatin.
Phenobarbital (Gardénal)	Sertraline (No-dep)	1	Risk of ineffective treatment antidepressant
lamotrigine (Lamictal)	Sodium valproate (Dépakine)	1	Risk of serious skin reactions: Lyell's syndrome, and on the other hand: increasing concentrations of plasma lamotrigine, by decreased hepatic metabolism.

Table 3

Combinations with precautions for use in the included patients

Combinations with precautions for use		No. cases	Risks
Clomipramine, Amitiptilyne (Anafranil, Laroxyl)	Escitalopram (S-citap)	2	Increased concentrations plasma antidepressant imipramine with risk of seizures and increased effects unwanted
Calcium Carbonates (Calcidia, Cacit)	Ferrous sulphate (Tardyferon)	6	Decreased digestive absorption of iron salts.
Insulin (Mixtard)	Perindopril / amlodipine (Coveram)	1	The use of ACE inhibitors may lead to increased blood sugar lowering effect in diabetics treated with insulin
Acenocoumarol (sintrom)	Amiodarone (Cordarone)	1	Increased effect of anti-vitamin K and haemorrhagic risk
Acenocoumarol (sintrom)	Simvastatin (Redlip)	1	
Acenocoumarol (sintrom)	Allopurinol (Zyloric)	1	
Furosemide (Lasilix)	Amiodarone (Cordarone)	1	Increased risk of ventricular arrhythmias
Furosemide (Lasilix)	Carbamazepine (Tegretol)	1	Risk of symptomatic hyponatremia

ACE, Angiotensin converting enzyme

haemodialysis patients at the dose of 2 mg on haemodialysis days, was taken in a patient at the dose of 4 mg. Alprazolam (Alpraz) an anxiolytic found in a patient at a dose of 1 mg per day, unlike the recommended doses which should be between 0.25 and 50 mg per day in patients with ESKD, overall we only find overdose specialties.

Regarding drug interactions, we have noted:

(1) The absence of contraindicated drug combinations.
(2) 6.15% of the patients had at least one combination that is not recommended.
(3) Precautions for use were found in 9.23% (n = 12) of the patients.
(4) In 16.15% of the cases, there were associations to take into account.

The different types of drug interactions in our patients are reported in the tables below:

Discussion

Drugs prescribed for chronic haemodialysis patients

The quantity of drugs consumed by chronic haemodialysis patients is much greater than that of the general populations (8 specialties and 11 tablets on average). In France, in a 2005 DREES (Research, Studies, Evaluation and Statistics Department) report, a general practitioner's prescription contained an average of 2.9 drugs[5]. In ESKD Patients, the mean number of drugs per prescription compared to patients of the same age[6].

In the United States, the mean number of drugs per patient ranges from 7.7 to 12, while in Japan it is 7.2[7].

Finally, this broad prescription can also be explained by the fact that our patients benefit from a thrice a week medical consultation.

In addition, these specialties are prescribed on the one hand for the treatment of complications of ESKD: such as phosphocalcic disorders in 89.23% of patients, erythropoietin stimulating agents for 93.07%, and on the other hand for associated comorbidities. kidney disease such as high blood pressure (72.3%) or diabetes (21.53%).

These results are comparable to those of the literature; Thus, Manley lists 98% of haemodialysis patients treated for anaemia, 93% for phosphocalcic disorders and 63% for hypertension[8]. In the study by Tozawa[7], 60% of dialysis patients are treated with erythropoietin stimulating agents, 88% with drugs for phosphocalcic disorders and 71% with antihypertensives.

The risks of polypharmacy include exposure to side effects, and non-adherence, which was not investigated in our review. In our sample, patients ingest an average of 11 galenic units each day, with treatment modification as needed.

Admittedly, adherence to therapy is inversely correlated with the duration of the disease[7], it is worse in the case of chronic diseases such as ESKD; and it could be improved by the use of injectable specialties administered at the time of dialysis, but the required active ingredients are not always available in parenteral form or do not have pharmacokinetic characteristics compatible with thrice weekly administration[9].

Prescriptions not in accordance with the summary of product characteristics

By "non-conformities" we mean: drugs that are contra-indicated, prescriptions not listed in the Marketing

Authorization, and dosages that do not comply with the summary of product characteristics. There are frequent, since 21% of prescriptions are inconsistent with the monographs in the Vidal dictionary.

Regarding drugs contraindicated in ESKD, we mainly cite magnesium prescribed in 9% of patients, acenocoumarol (Sintrom), being generally not recommended in ESKD patients, and which is prescribed in five patients, as well as other molecules less frequently prescribed in our patients such as: rilmenidin (Hyperium), rosuvastatin (Rozat), cetirizine (Zyrtec) and fenofibrates (Lipanthyl).

Let us assume that haemodialysis offers patients the advantage of tri-weekly follow-up, which allows prescriptions to be adapted according to efficacy and tolerance. Consequently, the percentage of non-conformities and overdose is reduced and is only observed in only 5.38% of patients. However, dosage adjustments are essential in ESKD patients for drugs which pharmacokinetic parameters are deeply disturbed, and vary according dialysis schedule[10].

Drugs interactions

Drugs interactions are correlated with the number of the prescribed specialties, which was confirmed in our series. We found in increasing order of frequency, associations that are not recommended, precautions for use and interactions that should be taken into account, with the absence of the contraindicated. The later being the most dangerous.

However, "group" interactions, resulting from the association of one specialty with two others, are not taken into account. It is necessary to consider certain associations necessary in these patients, because; On one hand, they present only a minor risk, and on the other hand, the therapeutic goal is often difficult to achieve in their absence.

Finally, we must remain cautious about the risk of the occurrence of interactions linked to self-medication or to the use of drugs prescribed by other doctors, consulted outside the dialysis facility[11]. Hence the importance of good communication between the patient and the healthcare team, in order to detect medication errors.

An often-overlooked notion is that of the interaction of certain treatments with the dialysis membrane. Let us cite the example of anaphylactic shock secondary to the simultaneous use of converting enzyme inhibitors and poly-acrylonitrile membranes, which were described in the early 1990s. Due to its difficulty, this aspect remains little studied[12].

Conclusion

ESKD is a public health issue, with a steadily increasing incidence and prevalence worldwide.

The studies carried out on drug prescription in chronic haemodialysis patients confirm that these patients are taking multiple drugs, this exposes them to the risks of drug interactions with decreased adherence to therapy.

In contrast, nephrologists must rely on their own experience to prescribe and treat their patients appropriately and effectively, due to the lack of clear consensus regarding drug prescription in this population. This can question the responsibility of the caregiver, and emphasize the importance of a good follow-up in order to detect any deleterious event.

Ethical approval

Applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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Author contribution

S.B., K.F., H.M.: conception, literature review, analysis, data collection, writing—review and editing. Y.B., I.H.: conception, methodology, supervision.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

Research registration unique identifying number (UIN)

This is not an original research project involving human participants in an interventional or an observational study but a case report. This registration is not required.

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Data sharing is not applicable to this article.

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