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Case Report

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Analysis polypharmacy in elderly patients with decreased kidney and liver function: A case report

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Abstract: Elderly patients are at a high risk of developing chronic diseases, including cardiovascular disease, cancer, dementia, and diabetes. Additionally, many elderly individuals experience multimorbidity, having more than one chronic condition, contributing to the phenomenon of polypharmacy. This case report aims to analyze polypharmacy therapy in elderly patients with concurrent decreased kidney function and elevated liver enzymes. Polypharmacy in elderly patients with decreased kidney and liver function necessitates a comprehensive study to assess both its benefits and potential side effects. Monitoring should be implemented to detect any emergence of side effects or drug interactions resulting from the prescribed therapy. According to the 2023 Beers Criteria, elderly patients with reduced kidney function face an elevated risk of drug-related side effects, potentially leading to prolonged hospital stays and increased medical costs.

Keywords: Polypharmacy, Renal injury, Liver injury, Beers Criteria.

INTRODUCTION

Elderly patients are defined as individuals aged 60 years and older. In 2017, 9.8% of Southeast Asia's population fell within this demographic, a figure projected to rise to 13.7% and 20.3% by 2030 and 2050, respectively. Notably, Indonesia faces a significant challenge, having the highest number of individuals with limited financial security in old age compared to other low to middle-income countries.[1]

The elderly population is particularly vulnerable to chronic diseases, including cardiovascular disease, cancer, dementia, and diabetes.[2,3] Diabetes mellitus, among the most prevalent chronic conditions in the elderly, affects up to 135.6 million individuals aged 65 years or older worldwide.[4] Other studies indicate that as age increases, the occurrence of comorbidities rises, with patients often experiencing more than one chronic disease.[5,6] This contributes to an upsurge in disease prevalence and a heightened susceptibility to receiving multiple medications, leading to polypharmacy.[7]

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The utilization of five or more medications amplifies the risk of drug side effects and drug-drug interactions.[8] Observational retrospective research demonstrates that polypharmacy can result in one in two elderly individuals experiencing potentially inappropriate medication (PIM), and the complexity of the regimen may lead to hospitalization.[7]

The profound alterations in body composition and the gradual decline in various systems and organs, including changes in renal and liver function, significantly impact the pharmacodynamics and pharmacokinetics of drugs.[2,9] Consequently, optimizing drug regimens becomes imperative in such cases. Several studies advocate the use of PIM assessment instruments, such as the Beers Criteria developed in the United States, to assist healthcare professionals in identifying PIM in elderly patients with specific clinical conditions. Another widely employed instrument is the STOPP/START criteria in Ireland.[10-13]

Decreased kidney function leads to drug and active metabolite accumulation, potentially triggering toxicity. Given the crucial roles of the kidneys, careful attention to drug selection and dose adjustment is essential to ensure the safety of drug use.[14] Dose adjustments in patients with renal failure aim to achieve optimal therapy, preventing undue stress on the kidneys due to elevated drug levels in the plasma.[15,16]

The liver, being the primary site for metabolism, plays a pivotal role in drug inactivation, converting substances through enzymatic processes into inactive metabolites or water-soluble forms for excretion. Some drugs undergo transformation into active metabolites, resulting in an augmented pharmacological response. Liver diseases, such as cirrhosis and hepatitis, significantly impact drug metabolism.[17] Patients with decreased liver function experience elevated drug levels in the plasma, particularly for drugs metabolized by the liver. Consequently, the dosage regimen for specific drugs must be adjusted based on the metabolic rate of individuals with impaired liver function.[18] This case report aims to analyze polypharmacy therapy in elderly patients with concurrent decreased kidney function and elevated liver enzymes.

CASE REPORT

Patient Mrs. P, 74 years old, presented with complaints of abdominal pain, nausea, and vomiting. She was admitted with a diagnosis of type-2 diabetes mellitus, high fat low hemicellulose (HFLH), and dyspepsia, with a history of metformin therapy. In the emergency room, her vital signs were recorded, revealing a blood pressure of 147/88 mmHg, oxygen saturation of 91%, and a pulse rate of 70 beats per minute, along with symptoms of nausea and vomiting. Throughout treatment, the patient reported weakness, with a Glasgow Coma Scale (GCS) of 456. Her laboratory examination results indicated a hemoglobin level of 11.3 g/dL, a leukocyte count of 13,700/µL, and a platelet count of 471,000/µL. Electrolyte values included sodium at 133 mEq/L, potassium at 4.25 mEq/L, chloride at 99.8 mEq/L, and calcium at 9.1 mg/dL. A decline in kidney function was evident with a Blood Urea Nitrogen (BUN) value of 31.1 mg/dL and serum creatinine of 6.66 mg/dL. Liver function assessment revealed elevated Serum Glutamic Oxaloacetic Transaminase (SGOT) at 192 U/L and Serum Glutamic Pyruvic Transaminase (SGPT) at 430 U/L, exceeding five times the normal limit. The patient's Glycated Hemoglobin (HbA1c) was 323 mg/dL. Chest thorax examination revealed cardiomegaly consistent with hypertensive heart disease (HHD) and pulmonary edema. Abdominal ultrasound (BOF) did not detect ileus or pneumoperitoneum.

During hospitalization, the patient received ondansetron injection therapy (8 mg every 12 hours), furosemide injection (20 mg), omeprazole injection (2x40 mg), and multivitamin injection (40 mg every 12 hours). Insulin therapy included Lantus at a dose of 24 units at night and insulin glulisine at a dose of 8 units every 8 hours. The patient was also administered domperidone (10 mg every 8 hours),

spironolactone (25 mg every 24 hours), and candesartan (4 mg every 24 hours). After five days of treatment, the patient's blood sugar levels consistently decreased, reaching the therapeutic target of below 180 mg/dL on the 4th day with the insulin combination. Following six days of treatment, the patient was discharged with improved nausea and vomiting complaints and a random blood sugar level of 143 mg/dL. Notably, no drug interactions were identified in this case.

RESULTS AND DISCUSSION

The examination of kidney and liver function results reveals a decline in kidney function and alterations in liver function. A longitudinal study involving 916,619 elderly patients over 65 years old demonstrated that alterations in kidney and liver function were correlated with multimorbidity. Renal function changes were observed in patients with cardio-renal disorders (OR 2.19; 95% CI 2.15–2.23) and those with metabolic diseases (OR 2.16; 95% CI 2.12–2.20). On the other hand, impaired liver function was identified in patients with gastrointestinal disorders (OR 3.39; 95% CI 3.30–3.49) and cardio-renal conditions (OR 1.96; 95% CI 1.91–2.02).[19] Age-related changes in liver function exert a significant influence on drug clearance and variability in response to most drugs.[3] Consequently, ensuring appropriate therapy for patients is crucial to prevent the occurrence of potentially inappropriate medications.

During the patient's hospitalization, ondansetron and domperidone therapy were administered to address complaints of nausea and vomiting. Ondansetron is the preferred choice for elderly patients (>60 years) due to its absence of extrapyramidal syndrome side effects, unlike metoclopramide. According to the 2023 Beers Criteria, metoclopramide, an antiemetic, should be avoided (except in cases of gastroparesis lasting no more than 12 weeks) as it carries the risk of extrapyramidal syndrome, including tardive dyskinesia, which is more prevalent in the elderly population.[20] However, caution is required in the use of ondansetron, as it may cause QT prolongation occurring 1-2 hours post-administration, necessitating ECG monitoring.[21] Ondansetron does not require dose adjustment in patients with decreased renal function. In contrast, if liver function is compromised, ondansetron should be administered at a maximum daily dose of 8 mg.[22]

The patient was additionally prescribed domperidone as antiemetic therapy since complaints of nausea persisted. Domperidone facilitates peristalsis and gastric emptying by inhibiting dopamine D2 receptors in the gastrointestinal tract and various central and peripheral nervous systems. This prokinetic agent serves as a second-line therapy for gastroparesis in patients who have not responded to metoclopramide.[23]

It also increases esophageal and gastric motility, thereby expediting gastric emptying and elevating lower esophageal sphincter (LES) pressure, effectively alleviating symptoms of vomiting and regurgitation. Notably, domperidone stands out among prokinetic groups for its milder extrapyramidal effects.[24]

Metabolism of domperidone occurs during its passage through the liver and gastrointestinal tract, employing a first-pass elimination mechanism (first-pass metabolism); thereby, caution is warranted when administering this drug to patients with compromised liver function.[22] With high oral bioavailability, domperidone is absorbed orally and excreted through the kidneys, boasting a half-life (T1/2) of approximately 7-12 hours.[25] In individuals with decreased kidney function, the recommended dose of domperidone is 10–20 mg, administered 1-2 times per day.[22]

In addition to domperidone, the patient was prescribed omeprazole to address complaints of nausea and vomiting. According to the Beers Criteria, omeprazole use in geriatric patients may heighten the risk of *Clostridium difficile* infection, bone loss, and fractures.[20] The administration of proton pump inhibitors (PPIs) should

be approached with caution in geriatric patients, especially for prolonged therapy exceeding eight weeks. Careful consideration is also necessary when using omeprazole in patients with decreased liver function, as decreased drug metabolism processes may increase its bioavailability. Conversely, in patients with decreased kidney function, omeprazole can be administered at a standard dose without adjustment.[22]

To manage blood sugar levels, the patient received insulin hormone therapy. Insulin, synthesized by the β cells of the islets of Langerhans from proinsulin, plays a crucial role in stimulating the utilization and storage of amino acids, intracellular fatty acids, and glucose. It regulates blood glucose levels in the liver, muscles, and adipose tissues. In cases of hyperglycemia, reduced insulin levels impede the entry of blood glucose into muscle cells, adipose tissue, and the liver, disrupting metabolism.[26]

Insulin therapy for type-2 diabetes mellitus is initiated when oral therapy fails, blood glucose control is poor (A1c > 7.5%), or fasting blood glucose levels exceed 250 mg/dL. All insulin types are suitable for patients with reduced kidney function, and no specific insulin dosages are recommended. The selection of insulin type, dosage, and usage must be tailored to the patient's condition to achieve therapeutic goals without inducing hypoglycemia.[26]

Insulin glulisine, a rapid-acting insulin, is quickly absorbed in the body and can promptly reduce insulin levels for prandial insulin needs. It has an onset of action of 5-15 minutes, peak action at 30-90 minutes, and an average duration of 5 hours. In patients with stage 4-5 chronic kidney disease (CKD) or those undergoing dialysis, who often experience delayed gastric emptying, administering rapid-acting insulin helps synchronize insulin peaks with postprandial blood glucose peaks.[27]

For patients requiring constant basal insulin, long-acting insulin therapy is employed. The patient, in this case, received insulin glargine (Lantus). Long-acting insulin begins working within 1-2 hours, has almost no peak effect or evenly distributed peaks over 24 hours and maintains its effect for more than 24 hours. This insulin's advantage lies in its once-daily administration, typically at night, as it minimizes the risk of nocturnal hypoglycemia due to its lack of a pronounced peak effect.[28]

The patient is prescribed a combination of furosemide and spironolactone as diuretic therapy. However, the use of spironolactone with a GFR < 30 mL/min is not recommended according to the 2023 Beers Criteria due to the potential risk of hyperkalemia.[20] Spironolactone, an aldosterone antagonist, proves beneficial in cases of volume overload associated with heart problems, cirrhosis, and kidney disorders.[29]

Diuretics, particularly furosemide, play a crucial role in treating acute heart failure, characterized by excess fluid leading to peripheral edema. Diuretics effectively alleviate shortness of breath, enhancing the patient's capacity for physical activity. By reducing water and salt retention, diuretics diminish extracellular fluid volume, venous return, and preload. Typically, a potent diuretic like furosemide is administered at an initial dose of 40 mg, adjusted as needed to achieve sufficient diuresis. In geriatric patients, caution is essential to avoid volume depletion and hypotension, as baroreceptor function tends to decline. Typically, a potent diuretic like furosemide is administered at an initial dose of 40 mg, adjusted as needed to achieve sufficient diuresis.[30] In geriatric patients, caution is essential to avoid volume depletion and hypotension, as baroreceptor function tends to decline. Therefore, diuretics should be administered judiciously, especially in cases of asymptomatic heart failure or when there is no fluid overload.[31,32]

CONCLUSION

Polypharmacy in elderly patients with decreased kidney and liver function necessitates a comprehensive study to assess both its benefits and potential side effects. Vigilant monitoring of adverse effects in elderly patients is crucial.

AUTHORS' CONTRIBUTIONS

Rina Widiyawati and Khoirul Anam took research data and wrote this journal. Nur Oktafiyani, M. Hari Pristantiningtyas, Herya Putra Dharma and Muhammad Muchlis chose cases in the hospital that could be used as case reports, as well as guiding the writing of this journal. Jainuri Erik Pratama, Fauna Herawati, Adji Prayitno Setiadi and Marisca Evalina Gondokesumo reviewed and supervised the journal. All authors have read and approved the final journal.

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DISCLOSURE STATEMENT

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