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Drug handling by elderly kidney: a prospective review to senile kidney physiology

Abstract

Many organs' functional reserve tends to deteriorate as we age. In particular, elderly people have lower lean body mass, serum albumin levels, hepatic perfusion, and filtration rate of residual glomeruli. Furthermore, comorbid processes frequently affect renal patients, who are treated with a variety of medications. Some drug interactions are also altered by the aging process, such as the affinity and number of receptors for certain drugs, as well as cell responses to receptor activation. As a result, Patients with kidney disease who are elderly are more prone to experience adverse drug reactions. The lack of available information on the pharmacokinetic/dynamic profiles of a large number of daily used drugs makes planning a safe pharmacological regimen difficult in this patient group. Finally, many elderly patients are unintentionally disobedient. We will go over the physiological aspects of drug administration in aging kidneys in this literature review.

Keywords: hyponatremia, aging kidney, aldosterone, renin

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Introduction

The term "elderly" refers to people aged 60 and up, who are the world's fastest growing population segment. The percentage of the elderly in developing countries is typically low, despite the fact that the numbers are frequently large.[1] As per the World Population Prospects (1950–2050), the number of elderly people in developing countries is increasing faster than in developed countries.[2] Fertility is rapidly declining, and premature mortality is increasing, which is the primary cause of this changing population aging pattern.[3]

Cellular cumulative damage caused by environmental hazards such as free radicals and radiation, as well as defects in protein synthesis and cross-linking, all contribute to aging.[4,5] It has been reported that the maximal lifetime of a fibroblast varies by species in a variety of animals. There is a linear relationship between the maximum fibroblast population doubling and the maximum lifetime of a species.[6,7]

The kidney's function and structure deteriorate as people age. Due to a decrease in the number of functional glomeruli and an increase in the number of sclerotic glomeruli, GFR decreases by 0.40 to 1.02 mL/min each year.[8] Renal plasma flow stays constant at 600 mL/min until the fourth decade, when it starts to drop by 10% each decade.[10] Reduced glomerular capillary plasma flow rate, glomerular capillary ultrafiltration coefficient, and afferent arteriolar resistance are among the glomerular hemodynamic alterations associated with increasing age.[11]

In addition, renal mass declines with age.[12] the proportion of patients with glomerulosclerosis and tubulointerstitial fibrosis increases[13] and afferent arteriole hyalinization can develop.[14] Additionally, aging changes the activity or responsiveness of hormone systems, creating changes in the elderly's homeostatic processes.[15] The renin-angiotensin system (RAS) is especially important in chronic kidney disease (CKD) because RAS changes predispose the elderly to acute kidney injury and chronic kidney disease as elderly cannot tolerate dehydration or high volume loads.[16,17]

Tubular senescence makes reabsorption and secretion of solutes difficult. Sodium reabsorption, potassium secretion, and hydrogen ion secretion all decrease.[18] In aged individuals, the juxtaglomerular apparatus generates less renin than in young people, blunting the response to aldosterone.[19] As a result, electrolyte and acid-base imbalances are more common in the elderly. Antidiuretic hormone response is also diminished in the elderly, making obvious disturbance in salt and water conservation.[20,21]

The intrarenal renin-angiotensin system (RAS) may not age as well as the systemic RAS[22] and pharmacologic RAS inhibition has been demonstrated to delay the course of age-related CKD.[23] Renin synthesis and release slows as people get older, resulting in decreased levels of total body renin and aldosterone. When the RAS is less sensitive, renin release in response to suitable stimuli is diminished.[24] When these RAS components are present, however, low renin and aldosterone levels may generate an exaggerated renal response.[25]

Systemic hypertension, diabetes, smoking, dyslipidemia[26] lead exposure[27] atherosclerotic disease[28] inflammatory markers, increased levels of advanced glycosylation end products[29] and possibly obesity[30] and male gender may all contribute to the acceleration of age-related renal function loss[31] according to epidemiologic studies. Recent research has shown a history of one or more episodes of acute renal injury as a risk factor for the development or progression of CKD.[32]

Elderly adults who eat a low-salt diet have a harder time conserving sodium and are more prone to hyponatremia due to reduction in plasma renin and reduction in the tubular concentration capacity.[33,34] The risk of hyperkalemia increases when the trans-tubular potassium gradient falls in the elderly[35] are four physiological characteristics that tend to diminish in the elderly.[36] Lean body mass[37] serum albumin concentration[38] blood flow to the liver[39] and kidney function.[40] All of these changes can be exacerbated by concurrent renal illness.

Drug pharmacokinetics

The elderly people have a larger visceral fat tissue to muscle mass ratio. Lipophilic medicines may have a larger volume of distribution and consequently a longer half-life. As GFR diminishes with age, drug clearance of hydrophilic ones may be lowered. As a result, individuals with chronic renal disease should take lower dosages of

lipophilic and hydrophilic medicines.[40–42] Protein-bound medicines circulate freely in plasma at a larger proportion in hypoalbuminemia patients, increasing their volume of distribution.[43]

Drug metabolism

Liver mass and perfusion, as well as metabolic activity, decrease with age.[44] contributing to an increase in lipophilic drug half-life.[45] To screen for gene variants, cytochrome P450 assays are available, with 2D6 being the most widely examined due to its role in the metabolism of several antidepressants and antipsychotic drugs.[46] In older CKD patients, especially those with severe CKD, the starting dose of hepatically metabolized medicines should be lowered to ensure safe dosing.

Drug elimination

As previously mentioned, GFR declines after the age of 30, and it declines much more rapidly after the age of 65.[47,48] Hypertension, coronary heart disease, congestive heart failure, nephrotoxic medication usage, and superimposed renal disease are all factors that might affect the rate and amount of functional deterioration.[49]

According to recent statistics, more than 70% of laboratories now use the Modification of Diet in Renal Disease (MDRD) Study equation to calculate estimated glomerular filtration rate (GFR). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) has developed and verified a novel creatinine equation.[50] which employs the same variables as the MDRD Study but is more accurate. Using eGFR algorithms to calculate medicine dose is both useless and harmful since serum creatinine levels fluctuate. These approaches are affected by malnutrition, obesity, strict vegetarian diets, concomitant medicines, muscle atrophy, age, and underlying illness.[51] Additionally, these techniques do not account for changes in bioavailability, protein binding, or active metabolite destiny that occur with age.[52]

Specific issues in older adults with kidney disease

In the elderly, Renin-Angiotensin-Aldosterone antagonists should be administered with care. Although potassium-sodium ion-exchange resins are commonly used to treat hyperkalaemia, they have been connected to gastrointestinal necrosis.[54] In the elderly, atenolol[54] and short-acting nifedipine[55] have been linked to an increased risk of stroke. A low but considerable risk of diabetes has been documented in elderly people receiving large dosages of statins.[56]

Aminoglycosides, Glycopeptides, Quinolones

Because antibiotics are mostly removed unaltered by the kidneys, using them for a longer period of time raises the risk of toxicity. Quinolones can produce disorientation, weakness, tremor, and depression in the elderly. It has the potential to cause QT interval prolongation, thus it should be taken with caution in those who have had QT interval prolongation, hypokalaemia, or hypomagnesaemia in the past. Tendinitis and tendon ruptures are possible side effects of therapy[57]. Trimethoprim competes with creatinine for the secretion of renal tubules. There have been reports of actual acute renal damage.[58]

Macrolides

In older patients who got both medications at the same time, clarithromycin and erythromycin (but not azithromycin) inhibit cytochrome P450 isoenzyme 3A4, causing bradycardia, shock, heart block, and multiorgan failure.[59]

Anticoagulants (oral)

In the elderly, the combination of NSAIDs and oral anticoagulants raises the incidence of haemorrhagic peptic ulcers by about 13 times.[60]

Lithium

Lithium consumption can cause acute or chronic kidney failure, as well as nephrogenic diabetes insipidus, especially in older people. The length of lithium treatment, the dosage, the level of lithium, the slow-release formulation, and clinical nonresponse were all found to be risk factors.[61]

Antihyperglycemic medications

Antihyperglycemic drugs should be properly titrated in older diabetic persons with CKD. Sulfonylureas increase the risk of hypoglycaemia as people get older. Sodium glucose cotransporter type 2 inhibitors are well tolerated by senior individuals and are a good alternative for those who can't take other drugs.[62]

Anti-Inflammatory drugs (NSAIDs)

In CKD patients over the age of 65, nonsteroidal anti-inflammatory medications (NSAIDs) are among the most routinely mismanaged medicines.[63]

Immunosuppression

Calcineurin inhibitors (CNIs) have a limited therapeutic index, and their usage has been associated to a number of adverse effects, the most serious of which is nephrotoxicity, which is more frequent in older individuals.[64] Over the age of[65] renal transplant patients reported a 34% reduction in total body weight.

Vitamins

Excess vitamin A (retinol) and the transport proteins retinol-binding protein 4 (RBP4) levels in the blood may increase the risk of cardiovascular disease in the elderly.[66]

Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) can cause hyponatremia, which can lead to severe morbidity, particularly in older adults with CKD.[67]

Antihypertensive medications

Angiotensin-converting enzyme (ACE) inhibitors decrease mortality and cardiovascular events in patients with cardiovascular disease or high-risk diabetes and slow the progression of chronic kidney disease (CKD) in patients with proteinuria.[68,69] Dual blockade of the renin-angiotensin pathway with ACE inhibitors in combination with angiotensin receptor blockers (ARBs) has a physiologic basis as standard doses of ACE inhibitors do not fully block the vasoconstrictor response to angiotensin II.

Clinical trials, including ONTARGET, concluded that combination therapy in elderly patients was associated with significantly higher rates of discontinuation, slightly higher rates of hyperkalemia, and no observed benefit in terms of mortality or CKD progression.[70]

Adherence to prescriptions

Noncompliance with prescriptions is a widespread problem among the elderly. Polypharmacy is a major roadblock to adherence. According to a review of research, compliance declined as the number of recommended medicines rose.[71,72]

Conclusion

The term "elderly" refers to people aged 60 and up, who are the world's fastest growing population segment. In 1990, there were more

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than 280 million elderly persons aged > 60 in developing regions of the world. The kidney's function and structure deteriorate as people age. Elderly people do not tolerate dehydration or high volume loads well. They have a slower renin response and are more prone to potassium accumulation.

Because the old patient's filtration reserve is limited, any ischemia or nephrotoxic shocks put him at risk. Renin synthesis and release slows as people get older, resulting in decreased levels of total body renin and aldosterone. Age-related reductions in these components can cause fluid and electrolyte imbalances. Elderly adults who eat a low-salt diet are more prone to hyponatremia.

The aging of the kidney might result in changes in drug affinity and reaction at the cellular level. Kidneys of the elderly are more likely to experience negative drug-drug interactions. The number of pharmaceuticals recommended should be kept to a minimum, with benefits and hazards carefully weighed in senile patients.

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Conflicts of interest

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