

Review

A Review of Clinical Influencing Factors in the Selection of Cardiac Medications in the Elderly

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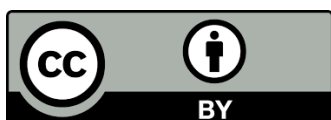
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Abstract

Aging is a stage of the natural life cycle. It is a set of natural and coordinated growth changes all organs and body systems undergo to burnout. It is impossible to determine the exact time of old age for two reasons. First, the aging process is different for humans due to individual, hereditary factors. Second, aging has a set of physiological, psychological and, social factors. This review aimed to gather appropriate clinical information and facts for clinicians when practicing heart medications in elderly patients, preventing potentially inappropriate practices. The absorption of heart medications decreases due to diminished bowel movements in the elderly. In the elderly, the blood flows to the entire gastrointestinal tract decreases and as a result, the entry of the medications into the general bloodstream decreases. Delayed absorption weakens the potency of the medication while prolonging its effects. These effects might be unsafe because most heart medications have a narrow therapeutic index. Factors influencing the selection of alpha & beta blockers, nitrates, CCCBs, ACE-Is, diuretics, and digoxin will be reviewed.

Keywords

Medication selection; elderly; clinical practice



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1. Introduction

In 2015, the WHO under the UN officially revised the age standards. Now, A male or female under forty-four is considered young. Based on the report the young age is from 25 to 44, the middle age is 44-60, the elderly age is 60-75, the senile age is 75-90 and long-livers are after 90. This international standard is made without taking into account the objective regularities of the development of physiology and psychology throughout the whole life in the course of rapid growth in youth, smooth development in mature age and the subsequent gradual aging of the human body. However, aging is a general term that can be defined physiologically, behaviorally, socially, or temporally. From a medical point of view, aging can be considered as a decrease in the body's capacity for physiological functions, which correlates with behavioral, social, and environmental factors.

Aging is a degenerative process that affects everyone and progresses at different speeds in different people. Decreased body weight, dehydration, and run-down liver and kidney functions are the most common phenomena when old. Gradually increasing the ratio of body fat to body mass provides more environments for storing fat-soluble medications. The gradual release of these medications into the bloodstream may increase the duration of the medication's activity especially when an elderly, very elderly, and frail elderly is taking multiple medications, as medication interactions may be delayed for hours [1].

Low albumin level in older adults' serum allows medications to circulate abundantly in the bloodstream without binding to albumin, increasing the risk of side effects with medications such as digoxin and warfarin [2, 3]. The plasma concentration of digoxin increases in these situations. Age-related cardiovascular changes or diseases e.g., heart rate often followed by a heart attack, heart failure, cardiovascular disease, and hypovolemia, reduce medication distribution in the tissues [4, 5] prolonging the onset time and activity duration. In older patients with heart, kidney, and liver diseases it is necessary to reduce the number of medications. However, even in the absence of the diseases, the liver function of an elderly person show reduced capacity due to several structural and microscopic changes occur as the liver ages, resulting in decreased medications metabolism and excretion [6]. Delays in medication metabolism increase the risk of side effects and poisoning because they stay in the bloodstream longer. In the geriatrics renal system, decreased blood flow, decreased glomerular filtration rate, and a gradual decrease in nephron function may lead to slow medication excretion [7].

Older adults often suffer from arthritis, cancer, COPD, depression, diabetes, dyslipidemia, Parkinson, peripheral vascular disease, and osteoporosis. In order to differentiate between the side effects of medications and pre-existing problems, these conditions must first be examined in an interview. In addition, the physician should be aware of any malnutrition, vitamin deficiencies, and long-term use of alcohol, cigarettes, marijuana, or opioid compounds, as well as increased sensitivity to environmental pollutants. Consulting with family and friends is essential if the patient has a poor memory or cognitive impairment.

Furthermore, polypharmacy is an important concern that increases the risk of medication-related problems and it is common in the elderly [8]. An accurate medication history should be used to ensure the possibility of side effects from medication interactions. Many older people may take

several medications simultaneously, including antacid, anticoagulant, anticonvulsant, antihistamine, antihypertensive, anti-parkinsonism, laxative, and sedative. The American Geriatric Society's Beers Criteria® is intended for use in adults 65 years and older in all ambulatory, acute, and institutionalized care settings except for the hospice and palliative care settings.

A clinical reasoning approach and advice to optimized prescribing of heart medications for the elderly in clinical settings will be reviewed in this article.

2. Alpha-Blockers

Alpha 1 receptor blockers such as doxazosin, prazosin, terazosin and, tamsulosin lower blood pressure by reducing peripheral resistance. In the elderly, they are not the first line of treatment and are not used as a single medication treatment. The 2019 American Geriatric Society Beers Criteria® for potentially inappropriate medication use in older adults recommended avoiding use as an antihypertensive. However, they improve the symptoms of benign prostatic hyperplasia (BPH) by reducing the tone of the smooth muscles of the prostate and ureter. Therefore, they are logically, the treatment of choice for patients with hypertension with BPH. Orthostatic hypotension, especially early in treatment, is a known side effect of these medications. Therefore, taking the first dose of the medication at bedtime is recommended. These medications have beneficial effects on fat metabolism.

3. Beta-Blockers

Beta-blockers are widely used in geriatrics [9]. Propranolol can prevent angina, lower blood pressure, and prevent recurrent heart attacks. Beta-blockers block beta1-adrenergic receptors in the heart muscle reducing heart rate and contraction [10]. They also reduce myocardial oxygen demand [11]. Patients need to be closely monitored for bradycardia and hypotension [12]. A specialist should be notified if the apical pulse is less than 60 beats per minute or the systolic blood pressure is less than 90 mmHg [13]. A change in heart rhythm may indicate the onset of heart block and should be evaluated. Beta-blockers in older adults may not be justified because of physiologic changes in people over 60. These include a low cardiac output, bradycardia, high total peripheral resistance, reduced renal blood flow and glomerular filtration rate, and low plasma renin activity [14].

Bronchospasm is a potential side effect and a specific problem of non-selective beta-blockers. For this reason, they should be used with caution in patients with COPD or asthma. Respiratory sounds and lung condition should be monitored if prescribed. Diabetic patients taking beta-blockers should have their blood glucose levels measured, as beta-blockers mask the symptoms of hypoglycemia, such as increased heart rate and changes in blood pressure. Side effects of the central nervous system, such as confusion, depression, drowsiness, fatigue, and sexual dysfunction should be considered in the elderly. Because these side effects are common in the elderly, it is necessary to determine whether these symptoms were present before starting a beta-blocker. Sometimes changing a beta-blocker improves symptoms, while the cardiovascular effects remain beneficial. Changing or discontinuing beta-blockers before surgery should be gradual to avoid withdrawal symptoms such as tremors, sweating, severe headache, weakness, palpitations, and recurrent hypertension. The dose is usually reduced slowly in 3 to 14 days. The patient should avoid heavy physical activity or exercise when beta-blocker is reduced or stopped. β -Blockers have the utmost

impact on the long-term prognosis of patients with HFrEF; consequently, all international guidelines recommend the practice of β -blockers as a first-line therapy for patients with HFrEF. However, to date, they are underused, mostly because of the fallacy that hypotension and bradycardia may worsen the hemodynamic status of patients with HFrEF and because of comorbidities falsely believed to be absolute contraindications to their use. A diffusion of clinical experiences as well as knowledge about the accurate use of β -blockers in clinical practice and drug-disease interaction is necessary for their greater use and titration as well as for the choice of a specific agent given a precisely tailored approach to HFrEF patients [9].

4. Nitrates

Nitrates are effective in preventing and treating angina pectoris [15]. These medications also treat other heart conditions such as ischemia, heart failure, MI, and hypertension emergencies [16]. Nitrates directly affect vascular smooth muscle, dilating peripheral and coronary arteries [17]. Recently, studies have shown that the effectiveness and safety of these medications in the elderly are the same as in young patients [18]. Nitrates are especially helpful in the elderly with chronic persistent angina because they cause fewer side effects than other antiarrhythmic medications [19]. For example, compared with beta-blockers, nitrates do not cause bradycardia or myocardial infarction and, compared with CCCBs, do not cause peripheral edema or constipation [19]. They could be prescribed in the form of subcutaneous, slow-acting sublingual tablets or oral sprays [19]. Slow and gentle skin ointments need less repetition and are acceptable in the elderly [19]. Continued use of nitrates makes them resistant to their effects [17]. For this reason, intermittent treatment is recommended. Although intermittent nitrate therapy is not associated with the development of tolerance, this strategy cannot be recommended for treating unstable angina because rebound angina during nitrate-free periods complicates clinical-decision making. If nitrates are used only to prevent angina, the patient will take them orally during the day or will be instructed to remove the skin ointment from their skin while sleeping at night. An elderly patient who consumes nitrates due to heart failure and has night shortness of breath is instructed to take skin nitrate at night and take it in the morning.

Hypotension and syncope are sublingual and spray nitrates' most common side effects [20]. Patients taking these medications are instructed to sit or lie down immediately when chest pain, dizziness, or lightheadedness occurs to relieve symptoms [21].

In each angina attack, no more than three pills should be used, each five minutes apart. The patient should seek emergency treatment if angina does not go away [22]. People who take long-acting nitrates should monitor their blood pressure regularly [23]. If symptoms of orthostatic hypotension such as dizziness, lightheadedness, and syncope occur, the patient should know that his condition changes slowly over several stages. Slowly get up from a lying or sitting position and stand after a few minutes of rest. Headache is a common side effect of nitrate therapy [20], and as resistance develops, it is less likely to occur, and the patient should be reminded of this. Rest and acetaminophen usually provide relief. Severe headaches require the patient to be referred to a specialist for consultation and examination. Any shortcomings to the detriment of the patient may result.

A dry mouth, which is common in the elderly, could reduce the absorption of sublingual nitrates [24]. Teach these patients to drink a sip of water before using sublingual nitrate. To help absorb oral

nitrate tablets, they should be taken with a full glass of water and on an empty stomach. Teach the patient to swallow the pills safely without chewing or eating. Educate elderly patients not to abruptly discontinue long-term nitrate therapy as it may cause recurrence of chest pain [25]. Nitrates should be discontinued gradually [26].

5. Cardiac Calcium Channel Blockers (CCCBs)

Cardiac calcium channel blockers also known as calcium channel antagonists have been used successfully to treat conditions such as angina pectoris, and some arrhythmias [27, 28]. The two main classes of CCCBs are dihydropyridine, and non-dihydropyridine. The last class consists of phenylethylamine and benzothiazepine structures. While most of CCCBs listed in these two main groups are relatively selective to L-calcium channels, additional medications are considered nonselective. These include mibefradil, bepridil, flunarizine, fluspirilene, and fendiline. CCCBs do not have a protective effect on MI. Instead, BBs and ACEIs are recommended. Inhibition of the passage of Ca^{++} ions through the cell membrane relaxes the smooth muscle of coronary arteries and dilates them, which reduces the risk of angina [29].

They dilate peripheral arteries and therefore have antihypertensive effects in the elderly with arterial stiffness [30]. Verapamil and diltiazem slow the signal conduction from the AV node to SA and are useful in treating supraventricular arrhythmias by slowing the heart rate [31]. But continuous clinical examination is essential to identify the risk of side effects. For example, seniors with a history of sick sinus syndrome or grade 2 or 3 AV block should not take diltiazem or verapamil unless they have a permanent pacemaker [32, 33]. People with a history of heart failure or taking beta-blockers should take these medications cautiously because they suppress myocardial function [32, 33].

Sleep pattern activity levels and physical condition should be monitored frequently for the progression of heart failure. Prolonged fatigue, weight gain, night shortness of breath, and pulmonary or wheezing cracks should be considered by the clinical team and reported to a specialist if observed [34, 35]. Patients taking antihypertensive medications may develop hypotension or orthostatic hypotension, especially if they take nifedipine [28]. Elderly patients taking CCCBs, especially nifedipine, may develop non-cardiac edema finally [36], possibly due to the loosening of the arteries and veins. In some patients, Light aerobic exercise, rest, and keeping the legs high are helpful in some patients. Constipation may occur in 25% of patients taking verapamil or diltiazem [36]. This problem may be exacerbated if a cholesterol-lowering agent such as Cholestyramine is also taken [37]. By encouraging the elderly to drink plenty of fluids and a high-fiber diet, they should be encouraged to prevent constipation and need stool softeners or laxatives. Some CCCBs are taken once a day, slow-releasing, and should be swallowed without chewing or crushing [38]. Esophageal smooth muscle is weakened in some elderly people, making it difficult for the elderly to swallow large pills and capsules. They should be reminded and helped to take their medications with some water and drink half a glass before taking it. This side effect can be beneficial for patients with dysphagia to prevent aspiration pneumonia. ARB will be an alternative. Standing or sitting due to the earth's gravity helps to swallow easily.

Non-dihydropyridines are contraindicated in those with heart failure with reduced ejection fraction, second or third-degree AV blockade, and sick sinus syndrome because of the possibility of causing bradycardia and worsening cardiac output [36].

CCCBs are also contraindicated in patients with known hypersensitivity to the medication or its components [39]. Other contraindications include sick sinus syndrome (except in patients with an artificial pacemaker), severe hypotension, acute myocardial infarction, and pulmonary congestion. CCCBs may cause AV blockade or sinus bradycardia, especially if taken with agents known to slow cardiac conduction. There are reports of dermatologic reactions and hypotension with or without syncope with CCCBs use. Peripheral edema may occur within 2 to 3 weeks of initiating CCCBs therapy. Use with caution in renal and hepatic impairment. Consider starting treatment at a lower dose [29].

6. ACE-Is

The choice of medication for heart failure depends on the patient's underlying heart condition, the degree of heart failure, and the presence of complications such as ischemia and sodium retention. Heart failure is usually treated with diuretics, digoxin, and angiotensin-converting enzyme inhibitors (ACE-Is) [40].

Captopril is given after MI to prevent left ventricular dysfunction. Both captopril and enalapril are used to treat mild to moderate heart failure [40]. In patients with heart failure, this reduces blood pressure and, preloads, and overloads the heart. Elderly patients prescribed ACE-Is for the first time are at risk for severe hypotension [41]. Those previously on long-term diuretic treatment are more likely to experience this complication. ACE inhibitors can be started at a lower dose in the elderly and blood pressure can be controlled for up to 6 hours after the first period or after an increase in dose [42]. Other complications such as decreased hemoglobin and hematocrit, neutropenia, and agranulocytosis have been reported [43]. Cell blood counts should be taken regularly.

About one-third of patients may have a cough, preventing them from continuing treatment [43]. In the first month of treatment, sometimes mild skin rashes appear that should be eliminated by reducing the amount of medication [43]. Severe rashes may accompany joint pain, fever, and itching that require treatment with antihistamines. Elderly people, even with mild renal impairment, may develop severe BUN and creatinine, which may lead to nephrotic syndrome [43]. Potassium should be monitored frequently in elderly patients with diabetes and renal impairment [43]. Potassium-sparing diuretics should be used with ACEIs [44, 45].

Nonsteroidal anti-inflammatory medications reduce the effectiveness of ACE-Is because they inhibit the production of prostaglandins needed to dilate blood vessels [44, 45]. Ibuprofen may cause high blood pressure [46]. These interactions should be considered in the elderly because most of them use nonsteroidal anti-inflammatory medications for their arthritis. If it is impossible to totally avoid these medications, increasing the dose of ACE-Is is necessary.

7. Diuretics

Diuretics are important in the treatment of heart failure. Because they control edema, which is caused by the body's compensatory mechanisms during heart failure [47]. For example, when the heart's pumping activity is disrupted, the nervous and endocrine systems are stimulated to retain water and sodium. This is an adaptive response to maintain circulation to the tissues. Excess fluid enters extracellular spaces and causes edema. When heart failure is mild, weak diuretics such as potassium-sparing medications (spironolactone, triamterene) or thiazides (hydrochlorothiazide) are

commonly prescribed [48]. In severe heart failure, loop diuretics are used that have greater diuretic power, such as furosemide and bumetanide [49]. These diuretics affect nephron cells in the kidney, increasing the excretion of electrolytes such as sodium and chlorine. When urinary sodium increases, excess water is released to dilute the urine. This reduces water throughout the body and blood pressure and increases urination. Although diuretics work in relatively different ways, they have similar properties. All diuretics have the potential to cause hypotension, especially if taken with vasodilators or other antihypertensive agents. This is problematic in the elderly. The patients cannot adapt quickly to venous filling and dizziness, or syncope because patients suffer from high blood pressure. When diuretics are used for the first time, instruct the patient to gradually change their position from lying down to sitting to standing [50].

All diuretics can cause severe electrolyte disturbances if left unattended. Loop and thiazide diuretics excrete potassium, which is dangerous for the elderly who take digoxin. Hypokalemia (serum potassium <3.5 mEq/l) increases the risk of digoxin poisoning [51]. Both hypokalemia and digoxin poisoning can lead to fatal cardiac dysrhythmias [52]. Early signs of hypokalemia include weakness and fatigue. Thiazide diuretics can also increase uric acid levels and symptoms of gout [53]. Control electrolytes, BUN, creatinine, magnesium, calcium, uric acid, glucose, CBC, and blood pH.

If taken with ACE inhibitors and potassium supplements or if kidney disease is impaired, potassium-sparing diuretics may cause hyperkalemia (serum potassium >5 mEq/L. Potassium-rich foods (bananas, dried fruits, tomatoes) Apricots should be consumed in small amounts, but the elderly who take loop or thiazide diuretics should use these foods. Thiazide diuretics increase cholesterol and triglyceride levels [54]. Need a low-fat, low-cholesterol diet, and use cholesterol-lowering medications. Patients taking cholestyramine [55] or colestipol [55] should not be given thiazides because these medications bind to and inactivate thiazides.

Loop diuretics cause hearing loss when taken in large amounts [56]. Intravenous furosemide should be given slowly, at a rate of less than 4 mg/min [57]. Other side effects of diuretics include hypersensitivity with rash and itching, confusion, ataxia, GI distress, and dyskinesia. Patients allergic to sulfonamide antibiotics may be cross-allergic to thiazide diuretics [49].

Tolvaptan, an oral vasopressin-2 receptor antagonist, acts on the distal nephron to reduce volume overload and improve congestive symptoms associated with heart failure through potent diuresis. Recently, early initiation of tolvaptan after hospitalization has been shown to be associated with a shorter length of stay in patients with heart failure regardless of age [58].

8. Digitalis

The main activity of digitalis glycosides is to increase the contractile power of the heart and, consequently, the output of the heart, its other functions include slowing down the electrophysiological activity and reducing the heart rhythm [59]. The most common form of digitalis used in the elderly is digoxin. It is for the first-line treatment of heart failure, which has many side effects [59]. Digoxin has a very narrow therapeutic range (0.8-2 mg/ml) and poisoning occurs above this range [59]. In some patients, toxic effects may occur even at levels less than 2 ng/ml. Mortality from digoxin poisoning is 7 to 50% [60]. Poisoning occurs in 8 to 85% of hospitalized patients and is more likely in the elderly [60]. Careful monitoring and control of the signs of digital poisoning may prevent more serious problems. Vision changes or fatigue are seen in most cases of poisoning [61].

Nausea, dizziness, anorexia, diarrhea, vomiting, abdominal pain, mental problems, abnormal dreams and headaches occur in 40 to 80% of patients [61]. In many elderly patients, anorexia is the first sign. Arrhythmias, especially premature ventricular contractions, are the most common cardiac symptoms. Digoxin poisoning is controlled by discontinuing the medication and treating associated arrhythmias. Digoxin immune Fab is given intravenously if the arrhythmias are dangerous. Improvement can be seen in 15 to 30 minutes. Poisoning or digoxin is especially seen in hypokalemic patients, the patient's diet should be checked for adequate potassium intake. Potassium supplements may be prescribed to patients taking loop or thiazide diuretics. Any weight loss in the elderly should be monitored as digoxin may need to be reduced. Many medications taken by the elderly may interact with digoxin such as cholestyramine [62], decreasing its bioavailability. Antacids, and kaolin-pectin [63] also decrease the bioavailability of digoxin. This binding increase the bioavailability of digoxin [63]. The amount or timing of digoxin or other medications can be changed to control possible interactions. Patients should avoid dairy products for at least two hours before and after eating digoxin, as they reduce medication absorption. Educate patients and family members to control their radial pulse at rest on a daily basis. Dietary fiber, specifically insoluble fiber such as wheat bran, can slow down the absorption of digoxin and lessen its effectiveness. To prevent this, elders should take digoxin at least one hour before or two hours after eating. Some plants containing cardiac steroid glycosides are similar to digitalis compounds and their derivatives. Due to additive effects, such glycosides can lead to cardiotoxicity if used simultaneously with drugs such as digoxin.

The plants that contain digital compounds are licorice, foxglove, oleander leaves, and horizon (tea herb). Other medicinal plants that can induce the toxic effects of digitalis glycosides include those that cause a decrease in serum potassium levels. If consumed chronically as laxatives or used in large quantities, these plants usually cause severe excretion. Potassium is excreted from plants such as senna, rhubarb root, and sorrel root.

Caffeine-containing plants not only exacerbate potassium depletion, but also increase heart rate and blood pressure. Consumption of hawthorn plants or fruit strengthens the function of digoxin. Therefore, he refrained from using it together with digoxin. Ginseng can elevate digoxin blood concentration by as much as 75%, while St. John's Wort decreases blood concentration of it by 25%. "It's important for the patient to recognize signs of digoxin toxicity," says Zive. "These include a yellow tint to vision and the appearance of halos around objects, as well as weakness, confusion, dizziness, nausea and vomiting."

9. Discussion

The elderly in need of care generally suffer from several chronic conditions, so, they receive many medications. Potentially inappropriate medication practices are a common health concern. Therefore, the medication regimen of the elderly should be carefully selected by the clinical specialists. The risk of cognitive impairment and falls in the elderly should be considered, and their companions about their medications should be monitored. The health status of the elderly is constantly fluctuating and changing; therefore, it is necessary to continuously evaluate their medications list. One of the reasons for many mistakes in the selection of medications for the elderly is the lack of knowledge of prescribers about the biology of aging, geriatric medicine, and pharmacotherapy in the elderly regarding inappropriate prescriptions. So, it is necessary to

introduce screening tools for elderly people in in-service training and continuous education programs, these tools should be introduced and taught to all members of the treatment team, and continuous evaluation of elderly people's medication list is also defined as one of the important measures of nursing and be monitored.

It is suggested that because the adverse drug events of the elderly often present themselves with non-specific symptoms, physicians should consider any new symptoms as drug complications when examining the health status of the elderly to confirm other cases.

Electronic prescriptions and suitable software should help physicians to check the prescriptions of the elderly and extract potentially inappropriate drugs electronically instead of extracted manually. By using the right software, information will probably be extracted with more accuracy (e.g., National Service Framework: Medicine and Older People (www.hcsu.org.uk/index.php?option=com_docman&task=doc_download&gid=322%20)-Provides a format for detailed medication review). When lowering blood pressure in the elderly, it should be kept in mind to avoid adverse effects, particularly postural hypotension, which can increase the risk of falls and major fractures. Notably, in elderly patients, cardiovascular disease risk relates directly with the systolic and pulse pressures and inversely with the diastolic pressure. There are several potential limitations to achieving the blood pressure goal in the elderly. Lowering blood pressure has been shown to lead to impaired mental function, confusion, sleepiness, dizziness and syncope with postural hypotension. The observation of the high comorbidity burden among senile age and long-livers with CVD suggests that prescribing must be correct and accurate to better meet the needs of this particularly vulnerable population.

10. Conclusion

The global population is aging rapidly. According to the UN, the elderly population in the world will reach 2.1 billion by 2050. This population is at greatest risk for medication-related harm, partly due to pharmacokinetic and pharmacodynamics changes. CVDs are the leading cause of death globally taking an estimated 17.9 million lives annually. So, it is important to detect these diseases as early as possible and start patients' medications accordingly. Only heart failure affects 26 million people worldwide. Knowing selecting appropriate medications in clinical settings involved in the treatment of CVDs in the elderly would be essential for the prevention of potentially inappropriate medication selection practices.

Author Contributions

B.F. contributed to the idea of this review, writing, editing and approving the final version of the article to be published.

Competing Interests

The author has declared that no competing interests exist.

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