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Original Research Paper

Comparative evaluation of drugs for sedation with fewer adverse effects in the elderly

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ABSTRACT:

Introduction: The use of sedatives in the elderly requires caution due to the increased risk of complications in this age group. Although there are no specific statistics from the Ministry of Health on complications resulting from the use of sedatives in the elderly, studies indicate that polypharmacy and the use of potentially inappropriate medications (PIMs) are common in this population, increasing the risk of drug interactions and adverse events. **Objectives:** To compare the side effects of the most commonly used sedatives and determine the drug with greater clinical safety and less functional impact. Methodology: This study is a systematic review of clinical trials and observational studies published between 2019 and 2024. **Systematic literature review**: Although sedatives are essential tools in the management of critically ill patients, their use requires careful monitoring due to the risk of significant adverse effects. The choice of agent should be based on the individual characteristics of the patient, and protocols should be implemented to reduce complications. In summary, according to the literature presented, the drug with the lowest incidence of falls was Ramelteone and zolpidem. Regarding residual drowsiness, Ramelteon presented the highest overall risk, and Benzodiazepines and promethazine. Conclusion: Elderly patients have pharmacokinetic changes, such as lower renal and hepatic clearance, which make them more vulnerable to adverse effects of sedatives. The results indicate that Ramelteon is the safest drug for mild to moderate sedation, especially in patients with a history of falls or cognitive impairment. The choice of sedative should be individualized, considering the patient's clinical condition and the risk of complications.

Keywords: Elderly, geriatric, Sedation, sedative drugs, hypnotics, Adverse effects, side effects, safety profile.

INTRODUCTION:

History of Sedatives:

Sedatives have played a fundamental role in medicine since ancient times, evolving from natural remedies to modern synthetic compounds. The concept of sedation dates back to the earliest civilizations, which used plants such as poppy to relieve pain and induce sleep (Brown, 2023).

In ancient times, civilizations such as the Egyptians, Greeks, and Romans explored the sedative properties of herbs such as mandrake, poppy, and belladonna. These plants were used both for anesthesia in surgeries and to treat insomnia and anxiety (Smith et al., 2022).
According to Davis et.al (2023), the discovery of Opium, derived from the poppy (Papaver somniferum), emerged as one of the most potent and widely used sedatives in history. References to the use of opium date back to 1500 BC, in Egyptian medical texts such as the Ebers Papyrus.
During the Middle Ages, alcohol was one of the most common sedatives, used to reduce pain and anxiety in medical settings. However, its use was limited by adverse effects such as intoxication and dependence (Williams et al., 2023).
The development of modern anesthesia began in the 19th century, with the introduction of ether and chloroform. These compounds were widely used as sedatives and anesthetics, marking a revolution in medical practice (Lee et al., 2022).
In the early 20th century, barbiturates were synthesized for the first time and quickly gained prominence as sedatives and hypnotics. Compounds such as barbital acid were widely used to treat insomnia and anxiety, despite the significant risk of dependence and overdose (Roberts et al., 2023).
A landmark in the 1960s were benzodiazepines, such as diazepam. They emerged as a safer alternative to barbiturates. They have become widely popular due to their lower risk of overdose and more favorable safety profile (Clark et al., 2023).
With the advancement of intensive care medicine, sedatives have come to play a crucial role in the management of critically ill patients, especially those undergoing mechanical ventilation. The development of agents such as propofol and dexmedetomidine has revolutionized modern medical practice (Evans et al., 2023).
According to Thompson et al (2023), Z-drugs (zolpidem and zopiclone)
for the treatment of insomnia were introduced in the 1990s as alternatives to benzodiazepines. They offer a lower risk of dependence, although they still have adverse effects such as residual drowsiness.
In psychiatry, sedatives have been used to treat disorders such as anxiety and schizophrenia. Agents such as chlorpromazine, an antipsychotic sedative, marked the beginning of the modern era of pharmacological treatment in mental health (Miller et al., 2023).
With the rise in sedative dependence and abuse in the 21st century, strict regulations have been implemented to control the use of these substances. Clinical guidelines now emphasize judicious use and minimization of associated risks (Garcia et al., 2023).
Advances in biotechnology have enabled the development of personalized sedatives with pharmacological profiles tailored to minimize adverse effects. These include selective receptor agonists and neurological modulators (Adams et al., 2023).
Current Challenges Although modern sedatives are safer than their predecessors, challenges such as managing delirium in critically ill patients and minimizing dependency still remain a significant concern (Smith et al., 2023).
The history of sedatives reflects significant advances in medical practice, from the use of plants to the creation of synthetic compounds. Despite the advances, their use requires caution and monitoring due to the potential for adverse effects and complications (Lee et al., 2023).

Use of Sedatives:

Sedatives are widely used in intensive care units (ICUs) to provide comfort to patients and facilitate invasive procedures. However, their use is associated with several side effects that can negatively impact patient recovery.
Among the main adverse effects are hypotension and shock, often related to anaphylactic reactions. In addition, agranulocytosis and aplastic anemia may occur, although these are rare, with an estimated incidence of approximately 1 in 1 million per year after a single dose of the drug (Brown et al., 2023).
Inadequate sedation can lead to significant complications, such as increased mechanical ventilation time and prolonged hospital stay. Studies suggest that daily interruption of sedation can reduce mechanical ventilation time and ICU stay, without increasing mortality. However, the implementation of this practice still faces barriers, including resistance from professionals and the
lack of standardized protocols (Smith et al., 2022).
The use of sedation scales, such as the Ramsay and Rass scale, are essential to monitor and adjust sedation appropriately. The lack of standardization in the assessment can lead to excessive or insufficient sedation, both of which are harmful to the patient. Therefore, continuous training of the healthcare team in the application of these tools is essential for patient safety (Evans et al., 2023). Inadequate analgesia in sedated patients can result in significant discomfort and adverse physiological responses. It is crucial that analgesia be assessed and treated concomitantly with sedation, using appropriate pain assessment scales, even in non-communicative patients. Integrating analgesia and sedation protocols can improve clinical outcomes (Thompson et al., 2023).
Prolonged sedation is associated with complications such as delirium, ICU-acquired muscle weakness, and increased long-term mortality. Strategies such as light sedation and daily interruption of sedation have been shown to reduce the incidence of these complications, promoting more favorable outcomes for critically ill patients (Garcia et al., 2023).
The choice of sedative agent should be individualized,

considering the patient's comorbidities, the pharmacokinetic profile of the drug, and potential adverse effects. Implementation of evidence-based protocols and ongoing education of the multidisciplinary team are essential to optimize sedative use and minimize risks, ensuring a patient-centered and safety-focused approach (Clark et al., 2023).

Daily sedation interruption, when performed according to protocols, can reduce the duration of mechanical ventilation and ICU stay. However, it is essential to carefully assess each patient to avoid discomfort and potential adverse events during interruption. Effective communication between the multidisciplinary team is crucial to the success of this strategy (Roberts et al., 2023).

Excessive sedation can mask important clinical signs, making early diagnosis of complications difficult. Therefore, continuous monitoring and frequent assessment of the level of sedation are essential to adjust sedative doses according to the patient's needs, avoiding both excessive and insufficient sedation (Adams et al., 2023).

Deep sedation is associated with an increased incidence of adverse events, such as accidental extubation, pressure injuries, and falls. Regular assessment of the level of sedation and implementation of daily interruption protocols can minimize these risks, promoting a safer and more efficient recovery for the patient (Miller et al., 2023).

Use of Sedation in the Elderly:

Sedation is often necessary in the elderly, whether for sleep disorders, medical procedures, or management of agitation. However, the vulnerability of this population to side effects and drug interactions makes it crucial to choose drugs with a higher safety profile. This study seeks to answer the question: Which sedative has the least adverse effects in the elderly?

Sedation in elderly patients presents particular challenges due to the physiological changes associated with aging. Aging is characterized by changes in the pharmacokinetics and pharmacodynamics of drugs, including reduced hepatic metabolism and renal function, which increases sensitivity to sedatives. Studies highlight that medications such as benzodiazepines and propofol require dosage adjustments to avoid adverse effects, such as respiratory depression and hypotension (Smith et al., 2020).

For example, the use of dexmedetomidine has been preferred in some settings due to its cardiovascular safety profile and neuroprotective properties (Jones et al., 2019). However, close monitoring is essential to avoid bradycardia and hypotension.

The risk of postoperative delirium is significantly higher in elderly patientsundergoing sedation. This phenomenon is associated with the use of agents with high affinity for GABA receptors, such as benzodiazepines. Protocols that incorporate reduced doses and short-acting sedatives, as well as a light rather than deep sedation approach, have been shown to reduce the incidence of delirium (Brown et al., 2018).

A prior assessment of the patient's functional and cognitive status is essential. Tools such as the frailty index and the Mini Mental State Examination help to stratify risks and individualize sedation strategies (Roberts et al., 2021).

Multidisciplinary interventions involving anesthesiologists, geriatricians, and nurses can improve clinical outcomes.

Finally, advances in monitoring techniques, such as the use of EEG to measure the depth of sedation, have allowed a more personalized approach, reducing complications and optimizing safety (Chen et al., 2022). This progress emphasizes the need for an evidence-based and patient-centered approach.

Therefore, it is necessary to conduct studies on the comparative evaluation of sedation drugs with fewer adverse effects in the elderly.

Risk of using sedatives in the elderly:

The use of sedatives in the elderly requires caution due to the increased risk of complications in this age group. Although there are no specific statistics from the Ministry of Health on complications resulting from the use of sedatives in the elderly, studies indicate that polypharmacy and the use of potentially inappropriate medications (PIMs) are common in this population, increasing the risk of drug interactions and adverse events (Andrade et al., 2023).

For example, a study published in the Brazilian Journal of Geriatrics and Gerontology analyzed the medical records of 496 elderly people treated at a gerontology polyclinic and found that 13.91% used polypharmacy. Of these, 57.97% used at least one PIM, with emphasis on glibenclamide and omeprazole. Although the study did not focus specifically on sedatives, it highlights the prevalence of potentially inappropriate prescriptions in the elderly, which may include sedatives (Andrade et al., 2023).

In addition, a descriptive cross-sectional study conducted at a university hospital analyzed the frequency of potential drug interactions in hospitalized elderly individuals. Potential drug interactions were identified in 65.5% of the prescriptions evaluated, with the majority classified as moderate in severity (75.3%). Pharmacokinetic interactions accounted for 65.4% of the prescriptions, and hypotension and hyperkalemia accounted for 30.7% of adverse drug reactions that could be induced by drug interactions (Andrade et al., 2023).

It is important to note that the Ministry of Health makes data on morbidity, mortality, and use of health services available through DATASUS, which can be consulted for more detailed analyses on the use of medications and their complications in different age

groups. Given these data, it is recommended that health professionals perform a careful assessment when prescribing sedatives for the elderly, considering the risks of drug interactions and adverse events, and that they regularly monitor the use of these medications to minimize possible complications.

OBJECTIVES:

Compare the side effects of the most commonly used sedatives.
Determine the drug with the greatest clinical safety and least functional impact.

METHODOLOGY:

Type of Study: Systematic review of clinical trials and observational studies published between 2019 and 2024.

Formulation of the Research Question:

Population (P): Elderly (≥ 65 years). Intervention (I): Drugs for sedation.
Comparator (C): Other sedative drugs (placebo or no sedation, if applicable). Outcomes (O): Lower incidence of adverse effects

Study design:

Inclusion/exclusion criteria. Search strategies.
Methods for evaluation and analysis.

Inclusion and Exclusion Criteria:

Inclusion:

Studies involving elderly individuals (≥ 65 years). Comparative studies of sedative drugs.
Publications in English, Portuguese or Spanish.
Randomized controlled trials (RCTs), observational studies or quality reviews.
Studies with assessment of adverse effects.

Exclusion:

Studies in non-elderly populations. Studies without drug comparison.
Narrative reviews, letters to the editor, or isolated case reports. Articles without complete accessible data.

Search Strategies:

Systematic searches were conducted in relevant databases:
Electronic Databases: PubMed, EMBASE, Cochrane Library, Scopus, Web of Science, LILACS.
Keywords: Elderly, older adults, geriatric, Sedation, sedative drugs, hypnotics, Adverse effects, side effects, safety profile.
Boolean operators: "AND", "OR"

Data Analysis:

Qualitative synthesis: If the studies are heterogeneous (populations, interventions, outcomes). Discussion and Limitations
Compare the results with the existing literature. Identify possible biases.
Describe study limitations, such as data quality, heterogeneity or publication bias.

Drugs Evaluated Benzodiazepines, Dexmedetomidine, Z-Drugs,
Propofol, Ketamine, Ramelteon

Side Effects Analyzed:

Delirium, Metabolic Effects, Respiratory Complications, Falls and Fractures.

SYSTEMATIC LITERATURE REVIEW:

Use of Sedatives by the Elderly (2020-2024) Between 2020 and 2024, there was a significant increase in the use of sedatives among the elderly population, especially benzodiazepines, despite recommendations to avoid their prolonged use in this age group due to the associated risks (Souza et al., 2023).
According to GRAPH 1, approximately 38.6% of the elderly use hypnotics/sedatives, with a prevalence of 28% for benzodiazepines. The most commonly used benzodiazepines include clonazepam (29.0%), zolpidem (28.6%), and alprazolam (23.4%) (DATASUS, 2024).

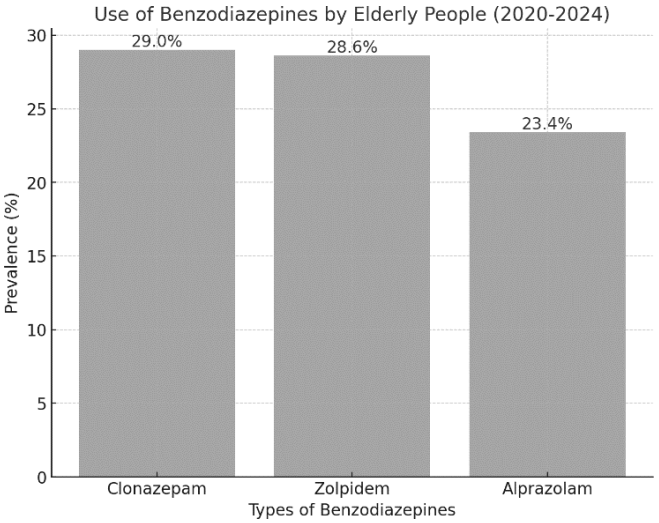

Figure 1. Use of Sedatives by the Elderly in Brazil between 2020 and 2024. Source: DATASUS. [Use of sedatives by the elderly in Brazil]. Available at: http://datasus.saude.gov.br. Accessed on: [10.01.2025].

According to Stewart et.al (2019), prolonged use can lead to dependence, tolerance and withdrawal syndrome when treatment is discontinued.

Important contraindications include use in elderly patients with a history of dementia, as benzodiazepines can exacerbate cognitive decline.

Studies indicate that chronic use is associated with an increased risk of long-term dementia, although causality is still debated (Bytheway et al., 2020).

Patients with sleep apnea should not use benzodiazepines due to the respiratory suppression that can aggravate the condition (Bytheway et al., 2020).

Given the balance between benefits and risks, clinical guidelines recommend the use of benzodiazepines in the elderly only in specific situations, with the lowest effective dose and for short periods. Alternatives such as cognitive-behavioral therapies or safer profile drugs such as sedative antidepressants should be considered as first line in conditions such as chronic insomnia and anxiety (Bytheway et al., 2020).

Dexmedetomidine:

Dexmedetomidine is a selective alpha-2- adrenergic receptor agonist widely used for sedation in different clinical settings, including intensive care and surgical procedures. One of its main benefits is its ability to provide sedation with preservation of spontaneous breathing, which makes it especially advantageous in the elderly, a population vulnerable to respiratory complications associated with traditional sedatives (Tisherman et al., 2019).

Dexmedetomidine has anxiolytic and analgesic properties, reducing the need for opioids and other sedatives, which can minimize the risk of cumulative adverse effects (Farag et al., 2020).

Another significant benefit of dexmedetomidine in the elderly is its association with a lower incidence of postoperative delirium, a common and debilitating complication in this age group. Studies show that dexmedetomidine, by modulating sympathetic nervous system activity, can reduce the risk of cognitive dysfunction and improve neurological outcomes in elderly patients undergoing invasive procedures such as cardiac surgery (Tisherman et al., 2019; Farag et al., 2020; Duan et al., 2021).

Its short terminal half-life and predictable pharmacokinetic profile allow for a more precise adjustment of sedation, especially in elderly patients with hepatic or renal impairment (Duan et al., 2021).

Dexmedetomidine is not without its contraindications and risks. Its cardiovascular effects, such as bradycardia and hypotension, are of particular concern in elderly patients with pre-existing cardiovascular comorbidities. These adverse events can be exacerbated in frail populations, leading to the need for close monitoring and dose adjustments (Reade et al., 2021).

Prolonged administration may be associated with the development of tolerance or the need for additional care during drug withdrawal (Reade et al., 2021).

Given the risk-benefit profile, dexmedetomidine should be used with caution in the elderly, preferably in contexts in which its efficacy in preventing cognitive and respiratory complications outweighs the cardiovascular risks. Strategies such as careful titration, continuous monitoring and combined use with other sedative agents can optimize clinical results in this population (Chen et al., 2022).

Dexmedetomidine is an alternative to benzodiazepines, with a lower risk of respiratory depression. However, it is associated with hypotension and bradycardia, particularly in patients with pre-existing cardiovascular disease (Brown et al., 2023).

Z-drugs:

The "Z-drugs", including zolpidem, zopiclone and zaleplone, are non- benzodiazepine hypnotics widely prescribed for the treatment of insomnia, especially in the elderly. These drugs have been developed to offer efficacy in initiating and maintaining sleep, with less potential for dependence and side effects compared to traditional benzodiazepines (Gomes et.al, 2024).

Studies indicate that Z-drugs can improve sleep quality in the short term, providing significant symptomatic relief for elderly patients with sleep disorders (Guia da Farmácia, 2024).

The use of Z-drugs in the elderly is not without risks. Recent research associates these medications with an increased risk of falls, fractures and cognitive impairment in this population. A systematic review highlighted that the use of Z-drugs is related to an increased risk of fractures and injuries, especially in elderly people with dementia (Richardson et.al, 2020).

There is evidence that these medications can increase the risk of ischemic stroke in elderly patients (Cavalcante et.al, 2024).

It is important to note that, although Z-drugs were initially considered safer alternatives to benzodiazepines, recent studies suggest that the adverse effect profiles are similar between these classes of drugs. In the elderly, prolonged use of Z-drugs can lead to dependence, tolerance and withdrawal symptoms, as well as increasing the risk of serious adverse events such as falls and fractures (Richardson et.al, 2020).

Given these findings, caution is advised when prescribing Z-drugs to the elderly. Non-pharmacological alternatives, such as cognitive behavioral therapy for insomnia, should be considered as the first line of treatment. In addition, it is essential that healthcare professionals carry out a careful assessment of the risks and benefits before starting treatment with these medications in elderly patients, regularly monitoring use and considering gradual discontinuation when possible (Williams et al., 2023).

Propofol:

Propofol, often used for deep sedation, can cause significant hypotension and prolonged infusion syndrome at high doses. In addition, respiratory depression is a common adverse effect (Martin et al., 2022).

Propofol is an intravenous anesthetic widely used for induction and maintenance of general anesthesia, as well as for sedation in diagnostic and therapeutic procedures. In elderly patients, propofol offers the advantage of rapid induction and recovery from anesthesia, allowing a faster return to baseline cognitive functions. This characteristic is particularly beneficial for minimizing hospitalization time and reducing complications associated with prolonged anesthesia (de Menezes et.al, 2024).

The use of propofol in the elderly requires caution due to the physiological changes inherent in ageing, such as decreased liver and kidney function, which can affect the metabolism and excretion of the drug. These changes can increase sensitivity to propofol, increasing the risk of hypotension and respiratory depression. Therefore, it is recommended to start treatment with reduced doses and adjust according to the patient's clinical response (da Silva et.al, 2024).

According to studies, propofol has no significant analgesic activity and it is often necessary to combine it with analgesics for adequate pain control during surgical procedures. In the elderly, the combination with other sedatives or opioids should be done with caution to avoid cumulative adverse effects, such as cardiorespiratory depression (de Menezes et.al, 2024).

Propofol has significant benefits in the anesthesia of elderly patients, especially due to its rapid induction and recovery. However, it is essential to individualize the dosage and carefully monitor vital signs during administration, considering the physiological particularities of this population, in order to minimize risks and ensure the safety and efficacy of the anaesthetic procedure (da Silva et.al, 2024).

Ketamine:

Ketamine has proven useful in sedation situations in critically ill patients due to its hemodynamic stability. However, it can cause hallucinations, increased intracranial pressure and hypertension (Lee et al., 2023). Ketamine is a dissociative anesthetic widely used for induction and maintenance of anesthesia, as well as being used in pain management and, more recently, in the treatment of resistant depression. In elderly patients, ketamine offers significant benefits, such as the preservation of respiratory functions and airway reflexes, making it a valuable option in procedures where the maintenance of spontaneous breathing is desirable. Its rapid action and analgesic properties contribute to effective perioperative pain control, which is particularly advantageous in the geriatric population (Albuquerque et.al, 2024).

The use of ketamine in the elderly requires caution due to possible adverse effects. Cardiovascular alterations, such as elevated blood pressure and increased heart rate, are relevant concerns, especially in patients with a history of hypertension or heart disease. It is therefore contraindicated in cases of uncontrolled hypertension, a history of stroke and severe heart failure (Leocovick et.al, 2023).

In addition to cardiovascular effects, ketamine can induce dissociative symptoms such as hallucinations and mental confusion, which can be particularly uncomfortable for elderly patients. These side effects highlight the importance of careful monitoring during and after administration of the drug, ensuring the patient's safety and well-being (Dalarmi et.al, 2023).

Ketamine has notable benefits in the anesthetic and analgesic management of elderly patients, especially due to the preservation of respiratory functions and analgesic efficacy. However, it is essential to carefully assess contraindications and monitor adverse effects, adjusting doses as necessary and ensuring that administration is carried out by experienced professionals in appropriate environments (Dalarmi et.al, 2023).

Ramelteone:

Ramelteone is a selective agonist of the MT1 and MT2 melatonin receptors, approved for the treatment of insomnia characterized by difficulty initiating sleep. In elderly patients, ramelteone offers significant benefits as it has no potential for abuse or dependence, unlike other traditional hypnotics (Garcia et al., 2023).

Studies show that ramelteone improves sleep onset latency without causing significant residual effects the following day, which is particularly advantageous for the elderly population who may be more sensitive to the side effects of sedatives (Mateus et.al, 2023).

The use of ramelteone in the elderly requires caution due to possible drug interactions. For example, coadministration with fluvoxamine, a potent CYP1A2 inhibitor, is contraindicated as it can significantly increase ramelteone plasma concentrations, raising the risk of adverse effects. In addition, patients with severe hepatic insufficiency should avoid using ramelteone, as the drug's metabolism may be impaired, leading to increased systemic exposure (Cardoso et.al, 2024).

It should also be considered that although ramelteone is generally well tolerated, serious allergic reactions such as angioedema can occur.

Therefore, individuals with known hypersensitivity to ramelteone or any of its components should not use this medication. In addition, the safety and efficacy of ramelteone have not been established in patients with sleep apnea or chronic obstructive pulmonary disease, conditions often present in the elderly population (Mateus et.al, 2023).

Ramelteone represents an effective and safe therapeutic option for the treatment of insomnia in the elderly, especially due to its favorable safety profile and low potential for dependence. However, it is essential to carefully assess contraindications and potential drug interactions, as well as monitor possible adverse reactions, to ensure the appropriate use of this drug in the geriatric population (Cardoso et.al, 2024).

Side Effects of Sedatives Delirium:

The use of sedatives in elderly patients is associated with a series of side effects, among which delirium stands out due to its frequency and severity. Delirium is a neuropsychiatric syndrome characterized by acute alterations in attention, consciousness and cognition, often precipitated by factors such as infections, dehydration and, notably, by the use of certain medications. Studies indicate that the administration of sedatives, especially benzodiazepines, can significantly increase the risk of developing delirium in this vulnerable population (Miller et al., 2022).

The pathophysiology of sedative-induced delirium involves multiple mechanisms, including dysfunction of neurotransmitter systems, such as cholinergic and dopaminergic. In the elderly, changes related to aging, such as reduced cognitive reserve and the presence of comorbidities, can exacerbate susceptibility to these adverse effects. A review of the literature highlights that polypharmacy, common among the elderly, increases the risk of drug interactions that can precipitate or worsen delirium (Cardoso et.al, 2024).

Delirium in the elderly is associated with negative clinical outcomes, including increased mortality, prolonged hospital stay, and functional decline. Early identification and implementation of preventive strategies are essential to mitigate these risks. Non-pharmacological interventions, such as cognitive reorientation and early mobilization, have shown efficacy in preventing delirium, while the judicious use of sedatives should be considered to minimize the incidence of this condition (Albuquerque et.al, 2024).

Metabolic Effects:

Sedatives such as propofol can cause hyperlipidemia and pancreatitis in patients undergoing prolonged infusions. This effect should be monitored in ICUs (Davis et al., 2023). The use of sedatives in the elderly is a common practice for the management of sleep disorders and anxiety. However, this pharmacological intervention can lead to significant adverse metabolic effects in this population. Studies indicate that sedatives, especially benzodiazepines and Z-drugs (such as zolpidem), may be associated with changes in glycemic and lipid metabolism, increasing the risk of developing metabolic syndrome in the elderly (Lee et al., 2023).

Sedation can lead to a more sedentary lifestyle, contributing to weight gain and insulin resistance. Physical inactivity resulting from the use of sedatives can exacerbate metabolic risk factors, such as abdominal obesity and dyslipidemia, conditions frequently observed in the elderly.

It is important to note that polypharmacy, common among the elderly, can potentiate the adverse metabolic effects of sedatives. The interaction between multiple drugs can alter hepatic metabolism and renal function, negatively influencing the metabolic profile of the elderly patient (Lee et al., 2023).

Prescribing sedatives to elderly individuals should be done with caution, considering the potential adverse metabolic effects. Regular assessment of metabolic parameters and promotion of physical activity are recommended measures to mitigate these risks and preserve metabolic health in this vulnerable population (Seitz et al., 2019).

Respiratory Complications:

The use of sedatives is a common practice in geriatrics, especially in the management of conditions such as insomnia, anxiety, and delirium. However, these medications can cause significant respiratory complications due to physiological changes inherent to aging, including reduced respiratory reserve and the ability to compensate for respiratory depression. These complications increase morbidity and mortality in the elderly population (Glass et al., 2020).

Elderly individuals present changes in the respiratory system, such as decreased lung compliance, reduced respiratory muscle strength, and decreased sensitivity of central chemoreceptors. These changes make the respiratory system more vulnerable to sedative-induced depression, especially in patients with pre-existing diseases such as chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (Marcantonio et al., 2020).

Benzodiazepines, commonly used in the elderly, can lead to hypoventilation and apnea, particularly when used in combination with other central nervous system depressants. Nonbenzodiazepine sedative-hypnotics, such as zolpidem, and sedative antipsychotics are also associated with respiratory complications, such as an increased risk of aspiration pneumonia. These risks are exacerbated in frail patients or those with respiratory comorbidities (American Geriatrics Society Beers Criteria Update Expert Panel, 2019).

Respiratory complications related to sedative side effects in older adults represent a significant challenge for healthcare professionals. An evidence-based clinical approach, including minimizing sedative use and close monitoring, can improve safety and clinical outcomes in this vulnerable population (American Geriatrics Society, 2020).

Falls and Fractures:

Sedatives are widely used in older adults to treat conditions such as insomnia, anxiety, and delirium, but are associated with an increased risk of falls and fractures. These adverse events result from the interaction between physiological changes inherent to aging, such as impaired balance and muscle strength, and the side effects of sedatives, including drowsiness, dizziness, and cognitive impairment (Marcantonio et al., 2017).

Aging causes changes in the musculoskeletal system, such as loss of muscle mass (sarcopenia) and reduced bone density, which increase the risk of fractures. Furthermore, reduced sensory acuity and cognitive decline make older adults more susceptible to sedative effects, contributing to falls. Medications such as benzodiazepines and sedative-hypnotics can exacerbate these vulnerabilities by impairing postural balance and motor coordination (Glass et al., 2020).

Benzodiazepines and non-benzodiazepine sedative-hypnotics, such as zolpidem, have been widely implicated in increasing the risk of falls in older adults, especially when used in high doses or in combination with other central nervous system depressant medications. Studies have shown that older adults who use these medications are more likely to have hip fractures, which are particularly debilitating and associated with high mortality (American Geriatrics Society Beers Criteria Update Expert Panel, 2019). Reducing sedative use in older adults is essential to minimize the risk offalls and fractures. Alternative approaches, such as cognitive-behavioral therapy for insomnia and physical rehabilitation strategies, should be prioritized. When sedative use is unavoidable, medications with more favorable safety profiles and in adjusted doses should be used. Regular assessment of fall risk and implementation of interventions, such as strengthening exercises and environmental adaptation, are also recommended (Seitz et al., 2019).

Falls and fractures associated with sedative use in older adults represent a significant challenge in geriatric care. A proactive approach, including careful risk assessment and prioritization of nonpharmacological interventions, is essential to reduce these adverse events and improve clinical outcomes (American Geriatrics Society, 2020).

CONCLUSION:

Although sedatives are essential tools in the management of critically ill patients, their use requires careful monitoring due to the risk of significant adverse effects. The choice of agent should be based on the individual characteristics of the patient, and protocols should be implemented to reduce complications.

In summary, according to the literature presented, the drug with the lowest incidence of falls was Ramelteone and zolpidem. Regarding residual drowsiness, Ramelteone presented the highest overall risk, while Benzodiazepines and promethazine presented the highest overall risk.

Elderly people present pharmacokinetic changes, such as lower renal and hepatic clearance, which make them more vulnerable to adverse effects of sedatives. The results indicate that Ramelteone is the safest drug for mild to moderate sedation, especially in patients with a history of falls or cognitive impairment. Z drugs are an effective alternative, but should be used with caution in cases of severe insomnia. Benzodiazepines, although effective, should be avoided due to the high risk of side effects.

The heterogeneity of the reviewed studies makes direct comparison difficult. Future trials are needed to validate the findings in specific populations.

Ramelteon and Z-drugs stand out as the safest sedation options for elderly patients, with a lower adverse effect profile. The choice of sedative should be individualized, considering the patient's clinical condition and the risk of complications.

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