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Review Article

Optimizing sedation in elderly patients: advantages and challenges of alfentanil-ciprofol for painless gastroscopy

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Abstract: The trend of painless diagnostic and therapeutic procedures is on the increase among older patients as the global population is aging. The pathophysiological changes unique to the aging process are troublesome in terms of sedation management. The use of the traditional narcotic sedation guidelines like fentanyl and propofol is linked to respiratory and circulatory suppression in this at-risk group. Conversely, the new compound of alfentanil-ciprofol has shown potential pharmacological benefits that can maximize sedation in painless gastroscopy in the elderly. This is a systematic literature review discussing the physiological and pharmacological basis for sedation in older individuals, with a focus on the interactions and efficacy of alfentanil and ciprofol. By synthesizing the available evidence, we generalize upon the effectiveness, safety, quality of recovery and benefits of such a combination on the geriatric gastroscopy procedure. Furthermore, we address the challenges inherent to its use in this age group, such as dose individualization and respiratory management, and propose potential solutions. Lastly, we outline future research directions, emphasizing that individualized dosing strategies based on the principles of precision anesthesia will be central to optimizing outcomes for elderly patients.

Keywords: Elderly patients, sedation optimization, alfentanil-ciprofol, painless gastroscopy, advantages and challenges

Introduction

The introduction of non-invasive, relatively comfortable gastroscopy has changed the management of gastrointestinal disorders, as it has become a commonly implemented procedure for some time [1]. Nonetheless, the rapidly growing global aging population has significantly increased the demand for these procedures among the elderly. There is a combination of events that make the elderly especially susceptible (during sedation and anesthesia), which involves multimorbidity, altered pharmacokinetics and pharmacodynamics, lack of physiological reserves and high adverse drug effects tolerance [2]. These peculiarities necessitate special attention in the selection of the right sedation regimens for this cohort.

Recent guideline-based practices of painless gastroscopy in elderly patients under sedation usually presuppose the use of fentanyl or sufentanil along with propofol [3, 4]. Although commonly used, these regimens have several limitations, including an increased risk of respiratory depression, hypotension, injection-site discomfort, and delayed recovery [5, 6]. However, driven by an aging population and increasing numbers of elderly patients on anti-procedural therapy, there is an increasing demand to find safer and more effective sedation methods for gastroscopy and to reduce its risks.

It is increasingly evident that current sedation practices cannot be used in the best way to meet the specific needs of elderly patients undergoing painless gastroscopy [7]. Consequently, there is an urgent need to revise sedation guidelines. The updated protocols should not only act faster and allow quicker recovery but also be gentler on the respiratory and circulatory systems, and, most importantly, be more

specifically tailored to the aged population. The new combination of alfentanil and ciprofol is one of the possible solutions in this case. Alfentanil is a powerful synthetic opioid which is reported to have rapid onset, with short duration of action, while ciprofol, a new-generation sedative, has been reported to have more stable hemodynamics and fewer adverse effects compared to traditional agents [8].

The purpose of the review is not only introduce these two drugs, but also to evaluate the benefits and concerns of the alfentanil-ciprofol combination for sedation in elderly patients undergoing painless gastroscopy. This review will provide a critical, evidence-based assessment of the effects of this new combination on the sedation process for this vulnerable group, integrating pharmacological theory with clinical practice. We explain the potential utility of it, e.g., better safety profiles, reduced recovery time, and small impacts on hemodynamics. In addition, we outline the difficulties connected to its usage, e.g., personalization of the doses, and respiratory management. Overall, this review seeks to provide clinicians with a valuable reference for the future and to facilitate balanced further study that considers both the possibilities and constraints of this promising sedation method.

Considerations for sedation in elderly patients: physiological and pharmacological factors

Age-related physiological changes

The pharmacodynamics and pharmacokinetics of sedatives are crucial to understand in elderly patients, as the physiological changes associated with aging directly alter these properties. These age-related changes require cautious use of sedation in this population to reduce adverse effects and ensure procedural safety.

Old age is characterized by tremendous physiological modifications, which influence various organ systems, thereby altering older patients' responses to sedative agents. The cardiovascular system demonstrates a decline in autonomic nervous regulation, leading to impaired maintenance of vascular tone and reduced myocardial function [9, 10]. This reduces the capability to maintain hemodynamic stability, increases the risk of orthostatic hypotension, and decreases cardiac output, especially during hypotensive episodes [11]. These age-related effects are supplemented by a decrease in vascular elasticity, which makes elderly patients more susceptible to sudden drops in blood pressure during sedation and increases their risk of cardiovascular instability [12]. Equally, the respiratory system is characterized by decreased functional residual volume and inability to exchange gases efficiently, rendering elderly patients highly susceptible to hypoxemia in the state of sedation [13, 14]. The elderly also have a blunted ventilatory response to hypoxia and hypercapnia, which further increases the risk of respiratory depression when central nervous system depressants are administered [15]. Furthermore, the aging process causes the worsening of hepatic and renal functioning, slowing down drug metabolism and clearance. This reduced elimination capacity also prolongs the half-lives of sedatives, which increases the risk of drug accumulation and toxicity, especially when it comes to drugs highly metabolized in the liver and kidney [16]. Lastly, the brains of the elderly are more vulnerable to sedatives, especially the ones that stimulate Gamma-Aminobutyric Acid (GABA) receptors [17, 18]. The sedative effect is further increased by neurotransmitter receptor depletion and brain impairment, which results in delayed recovery and a higher risk of mental problems like delirium. The impact of the aging brain on sedative clearance also complicates sedation management in the elderly, making it essential to consider these age-related changes when determining sedation strategies for this patient population [17-19]. The given physiological changes underline the importance of developing carefully designed sedation plans, accounting for the reduced physiological reserves in the elderly, and ensuring both safety and effectiveness.

In summary, optimal sedative management for elderly patients undergoing painless gastroscopy depends on a thorough understanding of age-related physiological changes (**Figure 1**). The sedative must be fast-acting, have a short-duration, with low-impact on respiratory and cardiovascular systems, have a wide in therapeutic index, be free of active metabolite accumulation, and easy to administer. The alfentanil-ciprofol combination promises to fulfill these requirements and provide a potentially

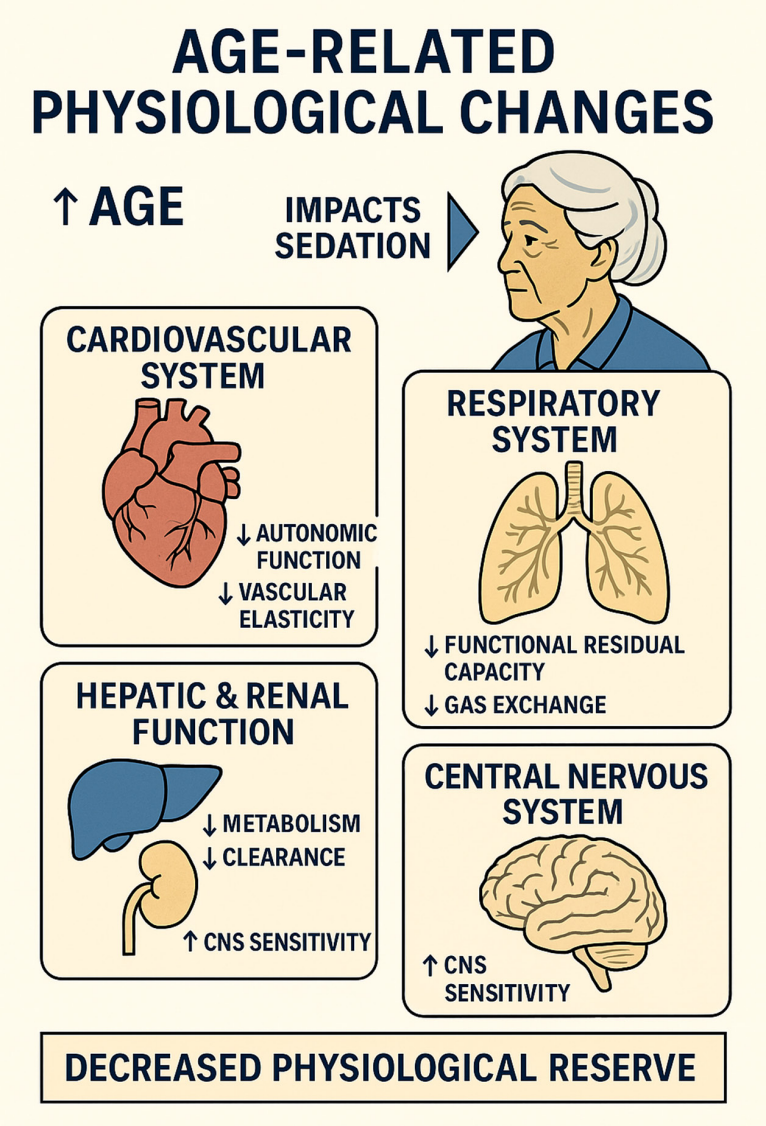

Figure 1. Age-related physiological changes and their impact on sedation in elderly patients. This infographic illustrates how aging affects multiple organ systems, leading to increased sedation risks in elderly patients. Age-related cardiovascular changes, including reduced autonomic function and decreased vascular elasticity, increase susceptibility to hypotension and hemodynamic instability. Respiratory changes, such as reduced functional residual capacity and impaired gas exchange, and heightened vulnerability to hypoxemia and respiratory depression. Hepatic and renal function declines slow drug metabolism and clearance, prolonging sedative effects and increasing the risk of accumulation. Meanwhile, central nervous system sensitivity is enhanced due to receptor changes and reduced processing capacity, resulting in exaggerated sedation and cognitive vulnerability. Together, these physiological alterations reflect a decrease in overall physiological reserve, underscoring the need for individualized, precision-guided sedation strategies in older adults. Note: CNS, central nervous system.

safer and more effective sedation strategy for older patients. Its use, however, requires considerable caution, taking into account the specific challenges presented by this population.

Core drug analysis: alfentanil and ciprofol

Alfentanil: the resurgence of an ultra-short-acting opioid

An effective and ultra-short-acting opioid, Alfentanil, has a bright future in sedation among elderly patients due to its favorable pharmacological profile [20]. In contrast to classical opioids like fentanyl or sufentanil, alfentanil is characterized by a low volume of distribution and a short half-life, resulting in the benefits of rapid onset and quick elimination from the body [21]. This pharmacodynamic property renders alfentanil a perfect choice for short-term procedural sedation, such as during painless gastroscopy. Its rapid onset ensures quick achievement of sedation, while its short duration minimizes the adverse effects associated with prolonged sedation and slow recuperation.

A key strength of alfentanil, compared to fentanyl and sufentanil, is its lower potential for drug accumulation. Due to its high metabolism and short half-life, alfentanil is less likely to accumulate in the body even with repeated dosing, thereby reducing the risks of overdose and prolonged sedation. This is especially necessary in geriatric patients, who tend to have altered pharmacokinetics due to diminished hepatic and renal function [22]. In addition, alfentanil has causes less respiratory depression than fentanyl or sufentanil. This minimizes the occurrence of prolonged hypoxemia and respiratory compromise, making it a safer option for short procedural sedation in elderly patients [23, 24].

Nonetheless, there is a need to adjust the dosage carefully when using alfentanil in geriatric patients due to their altered pharmacodynamic response. Elderly people have a higher sensitivity to opioids and therefore usually need a smaller initial dose, which is then titrated according to clinical response. Moreover, clinicians need to pay closer attention to vital signs, particularly respiratory function, as even short-acting opioids may lead to respiratory depression. Overall, alfentanil offers significant advantages in terms of rapid onset, short duration, and low accumulation, but its use in elderly patients must be managed with attention to individual pharmacological variations and careful monitoring during sedation.

Ciprofol: a new generation GABA-A receptor agonist

Ciprofol is a novel sedative-anesthetic agent and has received much attention due to its advantages over traditional agents such as propofol [25, 26]. Ciprofol, a GABA-A receptor agonist, has high potency and is estimated to be 4 to 5 times stronger than propofol, allowing effective sedation at lower doses. Its enhanced potency allows for better regulation of sedation depth, particularly in patients with varying sensibility to sedatives, such as the elderly [27]. The low lipid solubility of ciprofol causes a low volume of distribution and would reduce tissue retention, probably resulting in a faster onset and offset of action compared to propofol.

Compared to propofol, a key advantage of ciprofol is its improved safety profile. Ciprofol has been demonstrated to cause less respiratory depression and fewer hemodynamic disturbances, such as reduced blood pressure fluctuations, during sedation [28]. They are particularly useful in geriatric patients, who are most vulnerable to cardiovascular instability and respiratory compromise due to age-related physiological alterations. Milder cardiovascular effects of ciprofol help prevent hypotension and bradycardia, which are common side effects of other sedative drugs.

Compared to propofol, Ciprofol has a wider therapeutic index. This is particularly advantageous for aged patients, who often have reduced drug clearance capacity [29]. An expanded therapeutic index indicates that ciprofol is less likely to cause under- or over-sedation, thereby enabling more reliable and controlled sedation [30, 31]. Moreover, ciprofol is linked to negligible injection pain, a frequent side effect of propofol; this significantly enhances patient comfort and reduces procedure-related anxiety [30]. This is especially useful for geriatric patients, who might be more sensitive to the pain associated with sedative drugs.

Ciprofol has a positive pharmacokinetic profile in elderly patients. Unlike many sedatives, its clearance is not significantly influenced by age, suggesting that its effects remain similar and predictable across different age groups [32, 33]. This increases its suitability for elderly patients, whose pharmacokinetics may change considerably with declining liver and kidney performance.

In summary, alfentanil and ciprofol have their unique pharmacological benefits in sedation among the elderly patients. Alfentanil's rapid onset, short duration, and low accumulation potential make it an ideal choice for short procedural sedation. Conversely, ciprofol has strong GABAergic effects, a good safety profile, and minimal side effects, including negligible injection pain, making it highly suitable for elderly patients requiring sedation with little cardiovascular or respiratory degradation. These two agents provide complementary advantages. Their combination may provide the optimal sedation strategy for elderly patients undergoing painless gastroscopy (**Figure 2**). Nevertheless, the administration of these agents in this susceptible group remains crucial and requires cautious dosing and observation to guarantee their safe and effective use.

Synergistic effects: theoretical and practical perspectives of the alfentanil-ciprofol combination

Pharmacological basis of synergy

The rationale for combining alfentanil and ciprofol can be described as the desire to enhance sedation efficacy and reduce potential harm, specifically for geriatric patients undergoing painless gastroscopy [34]. Alfentanil, a short-acting μ-opioid receptor agonist, offers rapid analgesia with a quick onset and short duration, making it suitable for brief surgeries like upper gastrointestinal endoscopy [35]. Ciprofol, a next-generation GABA-A receptor agonist, is

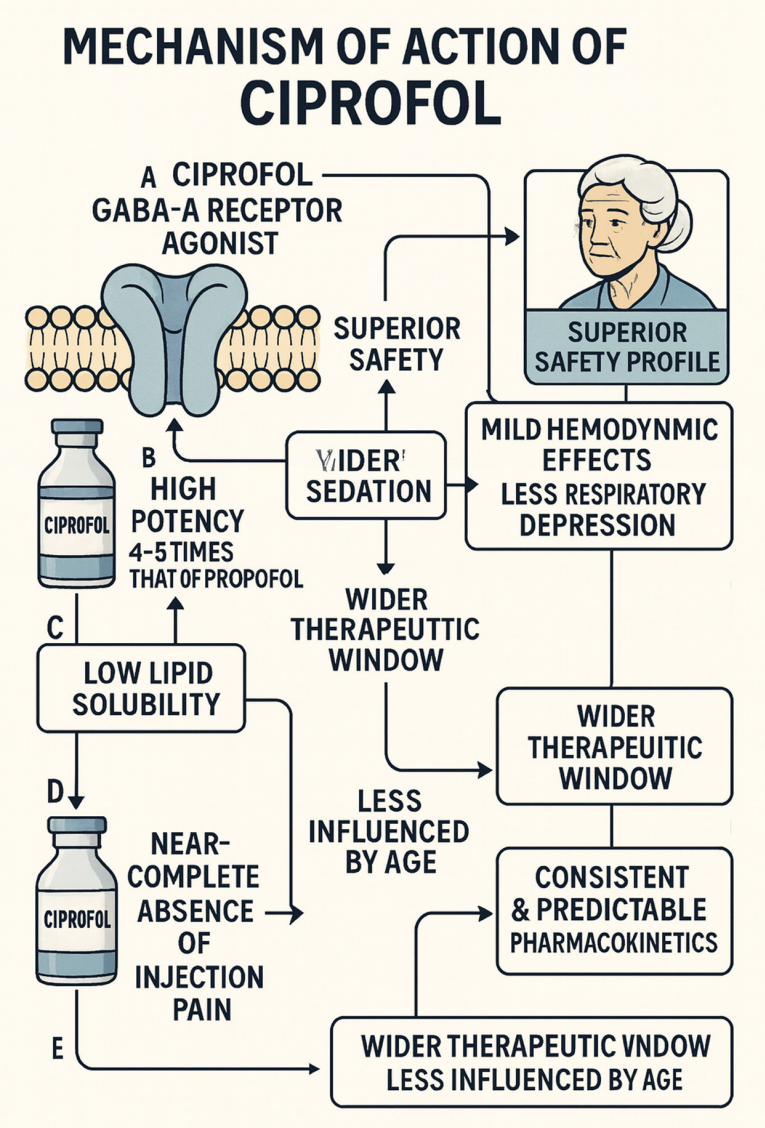

Figure 2. Mechanism of action and pharmacological advantages of ciprofol. Ciprofol is a novel GABA-A receptor agonist with approximately 4-5 times the potency of propofol. Its low lipid solubility leads to a smaller volume of distribution and reduced tissue accumulation, resulting in faster onset and recovery. Compared with propofol, ciprofol exhibits greater hemodynamic stability, less respiratory depression, and a wider therapeutic index. Its pharmacokinetics are largely unaffected by age, allowing for more predictable sedation in the elderly. Furthermore, ciprofol is associated with negligible injection pain, significantly improving patient comfort. Together, these properties position ciprofol as a promising sedative and anesthetic with a favorable safety and efficacy profile for vulnerable populations. Note: GABA-A, Gamma-Aminobutyric Acid A-type.

defined by an substantially greater strength (about 4-5 times that of propofol), reduced lipid solubility, and favorable hemodynamic stability.

These two agents show a dose-sparing synergy. Alfentanil acts at spinal and supraspinal levels to diminish nociceptive input, which successfully decreases the hypnotic dose of ciprofol required for sufficient sedation. This leads to minimization of the ciprofol-caused hypotension, a particular concern in older patients with weak cardiovascular reserve [36]. On the other end, the strong hypnotic and amnestic effects of ciprofol complement alfentanil's sedative-analgesic properties, achieving a more balanced triad of sedation, analgesia, and amnesia (**Figure 3**).

This interaction not only reduces the peak adverse effects of each agent - such as opioid-induced respiratory depression or sedative-induced cardiovascular depression - but also enhances the controllability of sedation depth [37]. The pharmacokinetic properties of the two drugs - characterized by rapid onset, short duration, and low tissue accumulation - facilitate easier titration and faster recovery, which is particularly desirable for procedural sedation in geriatric patients. In addition, the low injection pain and favorable hemodynamic profiles of ciprofol address key limitations of propofol, enhancing patient comfort and procedural efficacy.

To explain the pharmacological synergy further, we have incorporated certain pharmacodynamics and pharmacokinetic processes. Formal plasma concentration interaction studies for alfentanil and ciprofol are limited. However, existing pharmacokinetics and pharmacodynamics data has a clear mechanistic rationale for their combined use. Alfentanil exhibits both rapid plasma-effect site equilibration and a short context-sensitive half-time. This reduces nociceptive transmission

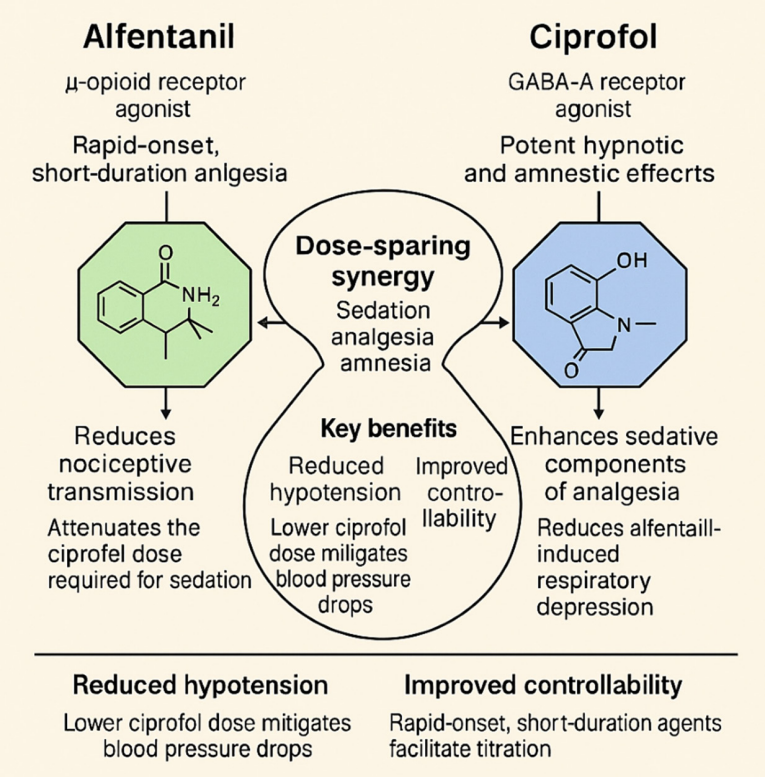

Figure 3. Mechanistic synergy of alfentanil and ciprofol for optimized procedural sedation. This schematic illustrates the complementary mechanisms and dose-sparing synergy of the alfentanil-ciprofol combination during sedation for painless gastroscopy. Alfentanil, a short-acting μ-opioid receptor agonist, provides rapid analgesia and attenuates nociceptive input, thereby reducing the required sedative dose of ciprofol. Ciprofol, a potent GABA-A receptor agonist, enhances the sedative and amnestic components of alfentanil-mediated analgesia while mitigating opioid-induced respiratory depression. Together, these agents achieve a balanced triad of sedation, analgesia, and amnesia, yielding key clinical benefits including reduced hypotension, improved hemodynamic stability, and enhanced titratability. This synergistic interaction provides a rational pharmacological foundation for safer and more effective sedation strategies in elderly patients. Note: GABA-A, Gamma-Aminobutyric Acid A-type.

and consequently, the amount of ciprofol required at the effect site to provide adequate sedation. Clinical pharmacodynamic studies indicate that under optimal analgesia, the hypnotic EC50 for GABA-A agonists decreases. This suggests that alfentanil decreases the plasma concentration threshold of ciprofol required to achieve its sedative effect. On the other hand, the increased strength and the stable hemodynamic rate of ciprofol allow effective hypnosis at lower plasma concentrations and reduces the required dose of opioids to achieve the same hypnotic level, thereby limiting peak alfentanil levels and associated respiratory depression. The combined pharmacokinetics and pharmacodynamics attributes result in a dose-sparing and safety-enhancing synergy, leading to more predictable titration and faster recovery in elderly patients.

Summary of clinical evidence

A growing body of randomized controlled trials (RCTs) and meta-analyses demonstrates the more favorable clinical effectiveness of the alfentanil-propofol combination over the conventional fentanyl-propofol regimen for painless gastroscopy in elderly patients. For example, Zhang et al. found that ciprofol-alfentanil combination significantly reduced induction time (by approximately 35-40% reduction) and achieved higher sedation success rates compared to propofol-alfentanil [38]. The same study showed that ciprofol-alfentanil reduced the required hypnotic dose in elderly patients by approximately 20-30% compared to those aged 18 to 65 years, confirming a clear dose-sparing effect [39, 40]. Regarding efficacy outcome, the application of this sedation regimen demonstrated significant advantages in procedure success rate, induction time, procedural duration, awakening time, and orientation recovery time. The combination facilitates an expeditious and effortless sedation process, reducing the time required for procedure preparation and patient recovery. Several RCTs have demonstrated shorter awakening times (2-4 minutes) and faster full orientation recovery (3-5 minutes) with this combination compared to fentanyl-propofol groups [41, 42]. Patients who received the alfentanil-ciprofol combination regained consciousness and psychomotor function faster, enabling earlier discharge, a decisive advantage in high-volume endoscopy centers.

This alliance is evidently more favorable in terms of safety. The incidence of hypoxemia

(SpO_2 < 90%) and clinically significant respiratory depression requiring airway intervention (e.g., jaw thrust, mask ventilation, or escalated oxygen supplementation) is consistently lower with alfentanil-ciprofol than with fentanyl-propofol. Published trials suggest that the incidence of hypoxemia could be reduced from 12-18% with fentanyl-propofol to 3-7% with alfentanil-ciprofol, and the need for airway maneuvers could be nearly halved [43]. This is partly due to alfentanil's shorter half-life and ciprofol's weak respiratory depressant action compared to propofol. Furthermore, this combination enhances hemodynamic stability, significantly reducing the incidence of hypotension and bradycardia as well as the need for vasopressors during the procedure. Quantitatively, it has been found to reduce procedure-related hypotension by up to 40% and vasopressor requirement by up to 50%, especially in older patients with compromised autonomic reserve [44, 45].

Negative impacts are also reduced in non-respiratory and non-cardiovascular systems. One of the most notable effects of ciprofol is the remarkable reduction of injection pain, which is a common and distressing side effect of propofol that can exacerbate patient anxiety during procedures. Clinically, the incidence of injection pain with ciprofol is 0-2%, compared to the 40-60% typically documented with propofol [46]. Besides, postoperative problems such as nausea, vomiting, dizziness, and delayed recovery appear to be less prevalent and less severe. Studies have demonstrated that the rates of postoperative nausea and vomiting are 20-30% lower compared to regimens using propofol [47]. Patient satisfaction scores consistently favor the alfentanil-ciprofol regimen, reflecting improved comfort and reduced complications during the procedure.

Collectively, the outcomes indicate that the pharmacodynamic interaction between alfentanil and ciprofol is not merely theoretical but is robustly supported by clinical data. This combination achieves an optimal balance between safety and efficacy by enabling enough sedation at lower doses of drugs. It decreases the risk of cardiorespiratory impairment - a major concern in geriatric anesthesia - while improving procedural quality and postoperative outcomes. Future studies should focus on large-scale, multicenter RCTs and individualized dosing trials to refine administration guidelines. Special emphasis should be placed on developing dose-titration methods that account for frailty, comorbidities, and organ reserve in older populations. This evidence will be crucial for establishing the alfentanil-ciprofol combination as standard, precision-directed sedation strategy for geriatric endoscopy.

Challenges and strategies: precision implementation in elderly populations

Challenges in dose individualization

A high extent of inter-individual variability in the elderly poses a significant challenge to the clinical implementation of alfentanil-ciprofol sedation protocols. Unlike younger adults, older individuals present with complex physiological heterogeneity due to factors such as frailty, multimorbidity, sarcopenia, polypharmacy, and impaired organ reserve. These factors significantly alter the pharmacodynamics and pharmacokinetics of sedative-analgesic agents, making it difficult to determine an optimal initial dose. Weight-based dosing schedules might not be effective at explaining changes in volume of distribution, clearance, and central nervous system sensitivity.

To address this, many individualized dosing models that incorporate body weight, age, frailty indices, comorbidity profiles, and hepatic and renal performance are becoming increasingly promoted. For instance, dose adjustments guided by the Clinical Frailty Scale (CFS) enable clinicians to decrease the initial dose of cipro fol by 20-30% in patients with moderate to severe frailty. Similarly, algorithmic tools using indices such as the Charlson Comorbidity Index can facilitate the identification of elderly patients who require slower alfentanil titration because of poor autonomic or respiratory reserve [48]. Equally, a hepatic-function-informed approach suggests using lower doses of alfentanil in patients with low hepatic clearance, while renal assessment tools can prevent drug accumulation in those with chronic kidney disease [49]. These real-life applications are used to describe how multidimensional models can convert the personalized physiological profiles into safer, personalized dosing regimens. Tools such as the CFS, modified American Society of Anesthesiologists classifications, and pharmacokinetic simulations can provide struc-

tured models for determining initial doses and titration rates [50]. Notably, the quick activation and brief elimination half-life of alfentanil, combined with the predictable, low-lipid-solubility-based clearance of ciprofol, make this combination particularly well-suited for careful incremental titration. Essential in the elderly is the so-called titration-to-effect strategy, which is the application of the lowest effective dose in small increments. This allows real-time control of sedation depth, reduces the chance of overfeeding, and decreases the likelihood of hemodynamic or respiratory instability, which can be highly dangerous in patients with a low physiological reserve.

Respiratory management and advanced monitoring

Although alfentanil-ciprofol sedation is associated with a lower incidence of respiratory adverse events compared to fentanyl-propofol, hypoventilation and oxygen desaturation remain a risk in the elderly. Age-related declines in ventilatory drive, chest wall compliance, and upper airway tone predispose these patients to respiratory compromise even with moderate sedation. Traditional low-flow nasal cannula oxygen supplementation, though common, may not be effective enough in discouraging hypoxemia in weak or at-risk patients [51]. There are recent findings indicating that high-flow nasal cannula and transnasal humidified rapid-insufflation ventilatory exchange offer better oxygenation by offering heated, humidified oxygen at high flow rates, generating low-level positive airway pressure, and enabling apneic oxygenation [52]. These techniques can be used to successfully extend the apnea period and reduce the need for airway intervention during endoscopy.

It is also important to identify subclinical respiratory depression in a timely manner, as it often precedes overt oxygen desaturation [53]. Pulse oximetry alone is insufficient for prevention because it is behind real ventilatory events. Capnography, which monitors end-tidal CO_2, provides a more sensitive and earlier sign of respiratory compromise, enabling timely intervention before critical desaturation occurs. Implementing capnography during sedation in the elderly, accompanied by the use of sophisticated oxygen delivery systems, is a crucial step toward safer procedural sedation for this vulnerable population [54, 55].

Considerations in special elderly subgroups

The elderly population is physiologically heterogeneous and does not respond uniformly to sedatives and opioids. Therefore, a subgroup-based dosing strategy that accounts for frailty status, body composition, and organ function can optimize the safety and efficacy of alfentanil-ciprofol sedation.

Frail elderly patients represent a particularly challenging subgroup. Frailty is a biological state characterized by diminished physiological reserve, impaired homeostatic mechanisms, and elevated sensitivity to pharmacological interventions. Age-related declines in receptor density and altered central nervous system responses increase susceptibility to both sedative and opioid effects [56]. In addition, defective autonomic response and reduced hepatic clearance contribute to hemodynamic instability and prolonged drug exposure. Consequently, even a slight dosage of sedatives or opioids can trigger deep hypotension, bradycardia or respiratory depression. In this population, initial doses should be decreased by at least 30-50% compared to standard protocols. Subsequent titration should proceed slowly, with extended intervals between doses to allow for full evaluation of drug effects and to avoid oversedation [57]. For example, recent clinical experience in gastroscopy sedation has indicated that frail elderly patients (CFS $\geq$5) can be adequately sedated with reduced doses: ciprofol at 0.2-0.3 mg/kg (versus 0.4 mg/kg in fit elderly) and alfentanil at 5-7 ug/kg, which helps avoid excessive hemodynamic suppression [39]. Such reduced-dose regimens have been shown in several case series to maintain adequate sedation while minimizing hypotension and extended patient recovery in weak populations [58].

Another complicated subgroup is the obese elderly. The pharmacokinetics of sedatives and opioids are altered in obesity, necessitating dose adjustments. Dosing based on total body weight often overestimates sedative requirements, increasing the risk of drug accumulation and delayed recovery. In the case of ciprofol, which is less lipid-soluble than propofol, dosing in terms of lean body weight (LBW) or adjusted

body weight will give a much more accurate estimate of the effective dose and reduce the risk of oversedation. Since alfentanil has a larger volume of distribution, it must be administered carefully to balance adequate analgesia against the potential for overshoot and prolonged respiratory depression. This is particularly imperative in obese elderly patients, who tend to have comorbid sleep-disordered breathing and diminished functional residual capacity. According to clinical reports, it has been found that administering ciprofol based on LBW dose (0.3-0.4 mg/kg) to obese elderly patients (body mass index ≥30), rather than on total body weight, significantly reduces the incidence of oversedation [59]. Moreover, observational endoscopy studies indicate that low-dose alfentanil titration regimens (5-10 μg/kg based on LBW) can reduce the incidence of desaturation in obese older patients with sleep-disordered breathing [60, 61].

A third subgroup encompasses patients with hepatic or renal failure, in whom drug metabolism and clearance are significantly altered. Alfentanil experiences extensive hepatic metabolism and thus is especially vulnerable to hepatic dysfunction, which can prolong its duration of action and delay recovery. Ciprofol has some benefits in this context due to its short context-sensitive half-time and lack of active metabolites, making its kinetics relatively more predictable even in patients with mild to moderate impairment. However, dose reduction and gradual titration are necessary to prevent excessive accumulation and oversedation. Although renal dysfunction has a less direct impact on ciprofol, it can indirectly potentiate alfentanil's effects due to metabolite retention, necessitating cautious dosing and close monitoring in such patients. For example, elderly patients with Child-Pugh B hepatic impairment have demonstrated sufficient sedation with initial doses of ciprofol and alfentanil reduced by 30-40%, significantly lowering the risk of delayed recovery [62]. Similarly, in cases of renal insufficiency, effective clinical sedation has been reported with reduced alfentanil doses (3-5 μg/kg) due to metabolite retention, while ciprofol doses require minimal adjustment, maintaining safety without compromising efficacy [38].

Considering these subgroup-specific challenges, a precision-based approach to sedation is essential for older patients. By tailoring dosing regimens to the underlying physiological profile - whether frailty, obesity, or organ dysfunction - clinicians can better balance efficacy with safety, reduce adverse events, and optimize procedural outcomes in this vulnerable population.

Cost-effectiveness and health system implications

A practical consideration in implementing alfentanil-ciprofol sedation is cost. Ciprofol, which is a new agent, is more expensive to acquire than generic propofol. Nevertheless, price of drugs is not a good measure of economic feasibility. The combination might generate significant downstream savings, when seen in the light of health systems and procedural efficiency. In clinical research, alfentanil-ciprofol has been shown to permit a reduced internalization and recuperation period, thereby facilitating faster patient turnover and improving operational efficiency. Besides, the decrease in perioperative complications such as hypotension, hypoxemia and injection pain reduce the need for rescue drugs, staff interventions, and post-anesthesia care unit stays.

Notably, greater patient satisfaction and comfort, especially in the older population, might lead to better compliance with screening procedures, including gastroscopy. This, in turn, will positively affect the overall population health by facilitating earlier disease detection. The higher unit cost of ciprofol can be offset (or even outweighed) when a full cost-benefit analysis is conducted, accounting for systemic efficiencies and the expenses associated with managing complications. This approach not only enhances safety but also offers tangible economic benefits, especially in high-volume endoscopy centers.

Conclusion and future perspectives

Summary

The combination of ciprofol and alfentanil is a promising and a clinically significant advancement in procedural sedation for elderly patients undergoing painless gastroscopy. By combining alfentanil's potent, short-acting analgesic with ciprofol's stable and rapidly titratable calming properties, this regimen achieves a better balance of efficacy and safety compared to tradi-

tional sedation therapy like fentanyl-propofol. Its fast onset, hemodynamic stability, lower rates of respiratory depression, and enhanced comfort are especially suited to the physiological peculiarities and the clinical requirements of the elderly. Notably, its capacity to offer sufficient sedation at lower drug doses decreases the chances of adverse cardiovascular and respiratory incidents, which are primary concerns in this susceptible population. These pharmacological and clinical benefits align with the broader objective of providing safer, more efficient, and patient-centered care to a growing global aging population.

Future research directions

Despite these achievements, significant knowledge gaps remain. To begin with, the optimal dosing for the alfentanil-ciprofol regimen requires further refinement. Creating patient-specific target-controlled infusion models that account for age, frailty, body composition, and organ dysfunction potentially allow more personalized and consistent sedation delivery. Second, integrating improved monitoring and closed-loop systems could further improve safety. Real-time dose titration could be assisted by processed electroencephalogram algorithms (e.g., Bispectral Index, entropy) and multimodal physiological analytics. Given its rapid pharmacokinetics, ciprofol may be particularly suitable for automated closed-loop sedation systems, an approach already explored with propofol. Third, more evidence is needed to validate the real-world efficacy and safety of this combination in longer and more complicated endoscopic procedures, such as endoscopic retrograde and endoscopic submucosal dissection, especially in older patients with cardiopulmonary or metabolic comorbidities. Lastly, such long-term effects like postoperative cognition, delirium and quality of life are worth researching especially in geriatric groupings. As precision and individualization represent the future of sedation practice, filling these gaps will be crucial for optimizing patient-centered care.

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Disclosure of conflict of interest

None.

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