Review Article

Medication considerations including safety and its principles in geriatric dentistry

Kuan-Yu Chu[1,2]*

[1]Department of Dentistry, Taipei City Hospital Renai Branch, Taipei, Taiwan. [2]General Education Center, University of Taipei, Taipei, Taiwan.

Correspondence: Kuan-Yu Chu, Department of Dentistry, Taipei City Hospital Renai Branch, Taipei, Taiwan. kyc0321@gmail.com

ABSTRACT

This article explores the safety and principles of medication in geriatric dentistry. Dental care for older adults is becoming increasingly important in the aging society. However, few attempts have been made to suggest medication considerations in the clinical practice of geriatric dentistry. A clinical literature review on three aspects: aging and pharmacology of drugs, polypharmacy in older adults, and commonly used drugs in geriatric dentistry. The pharmacology of older adults is different from that of the young. Adverse drug reactions (ADR) in older people are often caused by polypharmacy. Odontogenic pain treatment focuses on controlling the cause by non-pharmacological treatment. Additionally, non-steroidal anti-inflammatory drugs (NSAIDs) should be used cautiously in older patients with a history of peptic ulcer, renal, or cardiovascular disease. In cases of contraindications to NSAIDs, acetaminophen is used as an alternative. Moreover, the abuse and unreasonable use of antibiotics can cause antimicrobial resistance. In the case of polypharmacy in older people, the geriatric dentist should pay attention to their current medication and medical history. The dentist should determine the cause, diagnose the patient as soon as possible, and treat the cause of pain with non-pharmacological therapy rather than medication. In addition, the dentist should be familiar with the drugs used, their indications, and ADR. Furthermore, educating older patients about the requirement for medication adherence and regular check on the drug used is necessary to confirm its efficacy and adverse reactions.

Keywords: Geriatric dentistry, Pharmacology, Polypharmacy, Adverse drug reactions

Introduction

Medication guidelines are gradually being established for older adults [1]. At the beginning of the development of pharmacoepidemiology, only case-control studies were performed because of adverse drug reaction (ADR) events before randomized controlled trials. Subsequently, excellent randomized controlled trials effectively eliminated bias and provided strong empirical evidence for drug safety and efficacy [2]. Moreover, the scientific evidence provided by modern simulation models and large data such as Health Data has become a powerful driving force for attempting to solve the problems of clinical epidemiology [3-6]. Based on the premarket review and approval system of drugs, the development of pharmacoepidemiology improves the rational use of drugs [7]. Furthermore, understanding age-related pharmacokinetics and pharmacodynamics, as well as commonly prescribed drugs and their indications and ADR, drug interactions, and oral side effects, can help dentists improve the quality of dental care for older patients [8]. However, few attempts have been made to suggest such medication considerations in the clinical practice of geriatric dentistry. This article discusses the safety and principles of pharmacology in geriatric dentistry from three aspects: aging and pharmacology of drugs, polypharmacy in older adults, and the drugs commonly used in geriatric dentistry. This brief and necessarily oversimplified review can improve our understanding of medication in geriatric dentistry practice.

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Chu KY. Medication considerations including safety and its principles in geriatric dentistry. J Adv Pharm Educ Res. 2022;12(4):67-76. https://doi.org/10.51847/BtTsIQwA3d

Aging and pharmacology of drugs

Pharmacodynamics is particularly pronounced for affecting the central nervous system (CNS) and the cardiovascular system.

Some drugs may change the number of specific receptor sites with age. Thereby affecting the efficacy of certain drugs [9].

Pharmacokinetic changes in older adults

The absorption, distribution, biotransformation, and elimination of drugs in older adults differed from those of the younger population. Overuse of antacids and proton pump inhibitors increases gastric pH, affects drug solubility, and may reduce drug absorption [10]. In addition, in the elderly, cardiac output decreases, peripheral blood increases, and drug distribution may decrease [11]. If older adults have hepatitis and cirrhosis, the ability of liver cells to proliferate is reduced, and the slower metabolism and clearance rate will lead to the accumulation of drugs in the plasma, thereby increasing their concentration and prone to toxicity [12]. Apart from reducing the first-pass effect of drugs, aging also increases their bioavailability and blood concentrations. Accordingly, when used in older adults, the dose of some drugs, such as propranolol and morphine, needs to be adjusted [13]. In older adults, kidney mass and nephrons decrease, and the average glomerular filtration rate (GFR) and renal blood flow decrease [14]. Antibiotics with minimal kidney damage should be selected for older patients [15]. Older patients with nephropathy should be tested in agreement with the estimated GFR (eGFR), and the dosing frequency should be adjusted [16].

The overall effect of these pharmacokinetic changes in older adults is to increase the duration of a drug's action and its plasma concentration, possibly resulting in increased potency [17].

Polypharmacy in older adults

Polypharmacy refers to using more than five kinds of drugs, which may be due to multiple comorbidities and complex symptoms that require various drugs to control [18]. In a 2015 US study, polypharmacy accounts for 35.6% of older adults aged 76.9 years on average [19]. In mainland China, among older adults aged between 60 and 91 years in the community, the average number of prescription drugs is 10.1 [20]. In Taiwan, the prevalence of polypharmacy among disabled older adults is 81% [21]. Meanwhile, dentists should be very cautious in increasing the items and quantity of medicines when performing dental consultations for older patients in the hospital [22].

Polypharmacy can also lead to ADR and interactions among drugs. When taking one or two kinds of drugs, ADR incidence is reportedly 5.6%–10.0%. When the number increases to more than nine kinds of drugs, the potential drug risk can be as high as 41%, increasing in related bedridden and mortality cases [23]. Dentists should review their past medical history or cloud medication history to check the patient's current medications, their (oral) side-effects **(Tables 1 and 2)**, and any systemic disease in the first dental visit.

Table 1. Commonly current medications and their side-effects in the past medical history of older adults

Drug Class	Example Drugs	Side-Effects
Anticoagulants	Aspirin [24], warfarin [25]	Bleeding risks
Immunosuppressants	Corticosteroids [26]	Opportunistic infection [26]
Chemotherapy drugs	Combination chemotherapy regimens [27]	Delayed healing [28]
Barbiturates	Valium [29]	Fall risks
Bone Stabilizer	Bisphosphonates [30]	Delayed bone graft, osteonecrosis

Table 2. Current medications that may cause oral side-effects in geriatric dentistry [31]

Oral side-effects	Example Drugs	Drug Class
Dry mouth [32]	Atenolol	Cardiovascular agents
	Oxybutynin	Urological
	Cyclobenzaprine	Muscle relaxants
	Opioids	Analgesics
	Olanzapine	Antipsychotics
	Tricyclics	Antidepressants
Fungal infection	Tetracycline [33]	Antibiotic
Mucositis [33]	Prednisone [34]	Immunosuppressant
Tooth discoloration	5-Fluorouracil [35]	Antitumor
Dysgeusia	Minocycline [36]	Antibiotics
	Glipizide [37]	Oral hypoglycemic drugs
	Enalapril [38]	ACE inhibitor
Gingival overgrowth	Phenobarbitone and Phenytoin [39]	Antiepileptic drugs
	Nifedipine [40]	Calcium channel blockers
	Cyclosporin [41]	Immunosuppressant
Stomatitis [35]	Captopril [42]	ACE inhibitors
Lichen-like reaction	Hydrochlorothiazide [43]	Diuretics

ACE= Angiotensin-converting enzyme

High-risk people are malnourished and have kidney or liver disease [44]. Another cause of ADR in older adults is the inability to comply with complex drug regimens [45]. Cognitive function is an independent predictor of antihypertensive medication adherence in older adults living alone [46]. Avoiding harm from potentially dangerous drug interactions by implementing guidelines for antimicrobial use in older patients is important [47]. Polypharmacy and potentially inappropriate medications (PIMs) create major problems with medication use in older adults, and special attention is required in the training of geriatric dentists. Nationally appropriate PIM lists are also needed to reduce the risk of medication used in this population. Comprehensive geriatric assessment effectively reduces the number of prescriptions and daily drug dosage in older patients and optimizes the efficacy of drug therapy [48].

Commonly used drugs in geriatric dentistry

Anesthetics

Local anesthetics

Among the many local anesthetics available for pain management in dentistry, 4% of articaine solutions are indicated for older adults, patients with hepatic impairment, and renal impairment. In the articaine solution (1:200,000), epinephrine concentrations are lower. Hence, adverse effects are minimized in high-risk patients. However, it should not be used for people allergic to sulphite because it contains sodium metabisulfite as a vasoconstrictor's antioxidant [49, 50].

Clinical trials have shown that phentolamine mesylate can help reverse the numbness of the soft tissue caused by local anesthetics, thereby reducing the self-injury of the lips and tongue after the treatment of older patients [51, 52].

General anesthetics (GA)

Considerable dental treatment is needed for adults in sedation and GA [53]. Conscious sedation is a treatment for moderately anxious patients with intolerance to dental care that must be carefully assessed, adequately monitored, and performed in a well-trained as well as well-equipped condition, with an understanding of its limitations [54-56]. In addition, sedation duration was one of the most important factors assessed, depending on the complexity of the dental procedure [57-59].

Conscious sedation can be performed by administering benzodiazepines, such as Midazolam, or inhaling nitrous oxide. Midazolam has a short half-life of 2 hours, rapid onset of action, and rapid recovery, and is associated with anterograde amnesia, thus requiring skill and experience in intravenous and drug administration. However, sedation techniques require special precautions, thereby ensuring a recovery time of at least 1 hour and post-operative medical supervision. However, it involves using a benzodiazepine antagonist (flumazenil) to manage overdose emergencies [60]. In some cases, invasive dental procedures may be useful to combine the administration of drugs to obtain anxiolysis with local anesthesia [61].

Herein, a thorough evaluation of the patient's medical condition is a standard procedure if a dentist plans to use sedatives or general anesthesia as an adjunct to dental treatment [62]. Ghezzi *et al*. attempt to develop a safe general anesthesia protocol for geriatric dental patients [63]. Meanwhile, according to Prabhu *et al*., standardized screening tools are recommended to assess suitability for treatment under sedation or general anesthesia in patients with special needs [64]. However, older patients are very sensitive to CNS drugs and are affected by comorbidity, and the effects of sedatives may be more profound and long-lasting. These patients are at high risk for perioperative complications [65] **(Table 3)**.

Table 3. Interactions and adverse drug reactions of central nervous system (CNS) related preparations in geriatric dentistry

Drug Class	Common Dental Drugs	Interacting Drugs	Potential Adverse Effects
Anti-Inflammatory/Anesthetic	Prednisone	Acetaminophen, NSAIDs	Hepatotoxicity [66]
	Lidocaine	Beta-blockers [67], H2-blockers [68]	Elevated blood levels lead to toxicity
Vasoconstrictor	Epinephrine [69]	MAOIs, beta-blockers	High blood pressure
Sedative	Diazepam [70]	CNS depressants	Respiratory depression, falling risk

NSAIDs= Non-steroidal Anti-inflammatory Drugs; MAOIs= Monoamine oxidase inhibitors

Analgesics

Odontogenic pain treatment reduces pain by controlling its causes, primarily inflammation. Analgesics should be used as symptomatic pain treatment, and the prescribed dose should be based on the pain severity and the patient's medical history. Acetaminophen and NSAIDs are commonly used for mild to moderate pain in dental practices. Opioids are best avoided in older patients because of their association with severe ADR [71].

Acetaminophen

It is thought that acetaminophen's mechanism of action is via inhibition of COX-3, or cannabinoid receptors in the CNS, that slow transmission of pain signals to the brain. It can also be used to reduce fever but has no anti-inflammatory effect. The recommended dose for adults is 500 mg once every 4–6 h with a maximum daily dose of 4 g [72]. Acetaminophen is the preferred alternative for patients contraindications to non-steroidal anti-inflammatory drugs (NSAIDs) [73]. When acetaminophen is combined with enzyme inducers (such as alcohol, barbiturates, carbamazepine, Phenytoin, primidone, and rifampin), the risk of toxicity increases [74]. Evidence shows that oral warfarin anticoagulation therapy can be enhanced by acetaminophen, and reducing the dose by half is recommended [75]. However, acetaminophen is one of the leading causes of drug overdose and acute liver failure worldwide. Hepatotoxicity results from the

ingestion of a single overdose or accidental treatment [76]. The liver injury caused by acetaminophen is due to the oxidative stress induced by N-acetyl-p-benzoquinone imine, a toxic metabolite formed by drug oxidation [77].

NSAIDs

NSAIDs have anti-inflammatory and analgesic properties and are the most commonly used first-line drugs for toothache and post-operative treatment [78]. NSAIDs include ibuprofen, naproxen, and ketorolac. NSAIDs should be used cautiously in older patients with a history of peptic ulcer disease and those with renal and/or cardiovascular disease [79-81] **(Tables 4 and 5)**.

Table 4. Side-effects of NSAIDs and muscle relaxants in geriatric dentistry [82]

Drugs	Rationale	Recommendation
Diclofenac Ibuprofen Ketoprofen Mefenamic acid Naproxen	Higher risk of upper gastrointestinal ulcers, major bleeding, or perforation in patients > 75 years old or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet drugs; about 1% of patients who use the drugs for 3–6 months; and about 2%–4% for patients who use the drugs for a year. Increased blood pressure and induced kidney damage.	Avoid long-term use unless other alternatives are ineffective. Patients can take gastroprotectants* to reduce but not eliminate the risk.
Carisoprodol Cyclobenzaprine	Some have anticholinergic side effects, sedative effects, and increased fracture risk.	Avoid

NSAID= Non-steroidal Anti-inflammatory Drugs
* Proton-pump inhibitor or misoprostol

Table 5. Drugs and recommendations for drug–drug interactions with NSAIDs in geriatric dentistry [82]

Drug Interaction	Rationale	Recommendation
Oral corticosteroids	Higher risk of peptic ulcer disease or gastrointestinal bleeding	Avoid use. If necessary, provide gastrointestinal protection.
Warfarin	Higher risk of bleeding	Avoid if possible. If used together, monitor closely for bleeding.

NSAIDs= Non-steroidal Anti-inflammatory Drugs

NSAIDs reduce renal blood flow, tubular drug excretion, and prostaglandin production. They also attenuate diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, and other antihypertensive drugs [83]. The use of NSAIDs should be avoided in patients with chronic kidney disease stage four and above (creatinine clearance < 30 mL/min) because they increase the risk of acute kidney disease, renal impairment, and further organ decline [84].

Ibuprofen has a relatively low risk of cardiovascular adverse effects among NSAIDs and is recommended for treating mild to moderate toothache [85].

Diclofenac potassium is more effective than acetaminophen or ibuprofen in reducing post-operative pain associated with tooth extraction or deep-cavity preparation. The use of preoperative analgesics minimizes the degree of pain in older patients [86].

Antibiotics

Older people are more susceptible to microbial infections. In addition, comorbidities such as diabetes and medications can affect the disease severity and response to treatment [87]. Besides special considerations such as preventing infective endocarditis, antibiotic prophylaxis should be limited to established guidelines to avoid the risk of antibiotic resistance, toxicity, and excess costs [88]. Meanwhile, based on currently available evidence, prophylactic antibiotics are recommended for surgical extraction of third molars, comminuted mandibular fractures, temporomandibular joint replacements, complex implants involving transplants or multiple implants, and clean-contaminated tumor resections [89]. The types of antibiotics most commonly used in dentistry are Penicillin, Cephalosporins, Clindamycin, Azithromycin, Clarithromycin, Metronidazole, Erythromycin, and so on [90-93].

Penicillin

The most common types of penicillin used to treat odontogenic infections are penicillin V, amoxicillin, and amoxicillin/clavulanic acid. About 10% of the population may have some allergic reaction to the drug; however, 90% are tolerant to penicillin. Clindamycin may be used instead of penicillin if the patient has a history of allergies to the drug or has a positive skin test [94].

Amoxicillin is the most commonly prescribed antibiotic [95]. Dentists also often use amoxicillin in combination with metronidazole or Amoxicillin with Clavulanic Acid (co-amoxiclav) amoxicillin/clavulanate to treat odontogenic infections [96]. In Germany, co-amoxiclav is the second most used antibiotic in dentist prescriptions [97]. For severe odontogenic infections such as abscesses and pulpitis, high-dose co-amoxiclav(875/125 mg every 12 hours) is an appropriate choice [98]. However, the drug may cause some degree of hepatotoxicity. Furthermore, it can alter the normal microbiota of the oral gastrointestinal tract, thereby causing candidiasis and even clostridium difficile infection [99].

Cephalosporin etc.

Cephalexin and Cefazolin are the most commonly used first-generation cephalosporins in dental practice [100]. Both can be used in penicillin-allergic patients. In clinical practice, the probability of allergic reactions caused by cephalosporins is lower than that caused by penicillin [101]. Meanwhile, Cefazolin is as

effective as anti-staphylococcal penicillin, ASP, but less nephrotoxic [102].

The first consideration for treating simple cellulitis is methicillin-sensitive Staphylococcus aureus, MSSA 1 g Cefazolin (IV) every 6 hours. If methicillin-resistant S. aureus, MRSA is suspected based on previous culture results, replace with clindamycin 600 mg IV every 8 hours or vancomycin 1 g every 12 hours IV. The dose is adjusted based on age, weight, and renal function. When skin pus is obtained, or other infection sites are simultaneously infected, antibiotics are selected based on Gram stain results [103].

Tetracyclines can help fibroblasts attach to the root surface [104]. Tetracycline is recommended for periodontal disease, marginal attachment, and bone graft enhancement. However, tetracycline should not be prescribed for patients with active liver diseases [105]. Clindamycin, broad-spectrum lincomycin, may be prescribed in cases of persistent infection because it is more potent than penicillin and metronidazole [106]. Its properties include bacteriostatic action, inhibition of bacterial protein synthesis, enhancement of neutrophil chemotaxis, and phagocytosis, recommended for periodontal therapy [107]. In addition, this drug is contraindicated in cirrhotic patients and patients with a history of ulcerative and pseudomembranous colitis [108].

Azithromycin shows potent inhibition against Porphyromonas gingivalis [109]. Injecting 0.5% azithromycin gel into periodontal pockets improves the patient's clinical condition [110]. Clarithromycin is a new generation of erythromycin [111]. It is a logical prescription medication for endodontic and periodontal infections [112]. However, Clarithromycin is generally not recommended as first-line therapy but is only used instead of penicillin in patients who cannot tolerate penicillin therapy [113].

Meanwhile, metronidazole combined with amoxicillin can cover most oral bacteria [114].

Moreover, it has shown efficacy in periodontal therapy to improve clinical outcomes of scaling and root planning [115]. Metronidazole can interact with certain drugs, such as alcohol, disulfiram, warfarin, and hydantoin anticonvulsants, causing nausea, vomiting, and abdominal cramp. Furthermore, it can cause serious side effects in some patients, such as seizures, anesthesia, or paresthesia of the limbs in certain patients [94].

Moxifloxacin is a fourth-generation Fluoroquinolones class of drugs. It is a good choice for treating odontogenic and periodontal infections because of its high penetration capacity through periodontal and bone tissue [116]. However, moxifloxacin is not used as a first-line treatment because of its high price and is often prescribed only when first-line antibiotics and surgical procedures have failed [117].

Pseudomembranous colitis is the main complication of antibiotic therapy in older patients and is associated with high mortality **(Table 6)**. Meanwhile, considering that overuse of antibiotics may increase the risk of resistance [118], dentists should gain insight into the role of antibiotic stewardship in oral health importance and use properly prescribed antibiotics based on the guidelines [119].

Table 6. Interactions and adverse reactions induced by antibiotics in geriatric dentistry

Drug Class	Common Dental Drugs	Interacting Drugs	Potential Adverse Effects
Antibiotics	Cephalosporins, Metronidazole	Warfarin [120]	Bleeding risk
		Phenytoin [121]	Increased blood levels of Phenytoin
	Cephalosporins and metronidazole	Alcohol [122]	Disulfiram-like reaction
	Erythromycin or Tetracyclines	Digoxin [123]	Increasing digoxin metabolism
	Tetracycline, etc.	Aluminum, calcium, and sodium [124]	Desorption of antibiotics
Antifungal agent [124]	Ketoconazole	Alcohol [125]	Disulfiram-like reaction
	Fluconazole [125]	Warfarin [126]	Bleeding risk
		Glyburide [127]	Hypoglycemia risk

Hemostatic agents

Patients treated with chitosan dressings as a dental hemostatic agent all had better healing and pain control than controls [128]. Chitosan remains effective in patients with anticoagulant use and is safe for patients with cirrhosis [129].

Studies have shown that although sutures are effective, platelet concentrates leukocyte-platelet-rich fibrin (L-PRF) and advanced platelet-rich fibrin (A-PRF+) are better at promoting coagulation and healing [130].

Tranexamic acid (TXA or Transamin) is a synthetic lysine analog-like antifibrinolytic agent [131]. TXA has hemostatic and anti-inflammatory pharmacological effects and is used by injection or oral administration [132]. Bromelain (Cysteine; trade name, Broen C) significantly reduces pain, edema, inflammation, and platelet aggregation and enhances antibiotic ability, which is beneficial for post-operative healing. This agent should not be used in patients with cases of peptic ulcer, severe liver and kidney dysfunction, or blood coagulation insufficiency [133]. The combination of bromelain and sodium hypochlorite in root canal therapy can reportedly enhance the disintegration action of the pulp [134].

Conclusion

Dentists should know a patient's medical history before prescribing medicine (whether the disease, such as liver disease or kidney affects the drug or if the current medicine presents possible ADR, side effects, or oral symptoms). The cause and diagnosis should be determined as soon as possible. The cause should be treated with clinical dental procedures or non-

pharmacological treatment, and antibiotic drugs should be avoided as much as possible. Dentists should be familiar with the medications such as NSAIDs, used by older patients with peptic ulcers, including their indications and contraindications. The lowest dose should be used first. On the other hand, the hearing, vision, and cognitive ability for adherence of older adults and their body weight should be considered to determine the appropriate dose. Drugs should be regularly checked to confirm their efficacy, ADR, and side effects. If necessary, eGFR should be studied.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

References

1. Wang K, Shen J, Jiang D, Xing X, Zhan S, Yan S. Development of a list of high-risk perioperative medications for the elderly: a Delphi method. Expert Opin Drug Saf. 2019;18(9):853-9. doi:10.1080/14740338.2019.1629416
2. Moore N, Blin P, Droz C. Pharmacoepidemiology. Concepts Princ Pharmacol. 2019;260:433-51.
3. Tanaka S, Seto K, Kawakami K. Pharmacoepidemiology in Japan: medical databases and research achievements. J Pharm Health Care Sci. 2015;1(1):16. doi:10.1186/s40780-015-0016-5
4. Martínez E, Hernandez MT, Hernandez AM, Gabriel JR. Emerging Roles of Pharmacist in Global Health: An Exploratory Study on their Knowledge, Perception and Competency. Arch Pharm Pract. 2020;11(1):40-6.
5. Rezapour A, Moradpour A, Panahi S, Javan-Noughabi J, Vahedi S. Health economic evaluation in Iran (1998–2017), a bibliometrics analysis. Int J Pharm Phytopharmacol Res. 2020;10(4):95-102.
6. Nageeb AN, Alsulami MS, Alshammari MT, Attar AA. An overview on irritable bowel syndrome diagnosis and management in primary health care centers. Pharmacophore. 2020;11(5):151-5.
7. Montastruc JL, Benevent J, Montastruc F, Bagheri H, Despas F, Lapeyre-Mestre M, et al. What is pharmacoepidemiology? Definition, methods, interest and clinical applications. Therapies. 2019;74(2):169-74. doi:10.1016/j.therap.2018.08.001
8. Kratz T, Diefenbacher A. Psychopharmacological Treatment in Older People: Avoiding Drug Interactions and Polypharmacy. Dtsch Arztebl Int. 2019;116(29-30):508-18. doi:10.3238/arztebl.2019.0508
9. Poudel A, Hubbard RE, Nissen L, Mitchell C. Frailty: a key indicator to minimize inappropriate medication in older people. QJM. 2013;106(10):969-75. doi:10.1093/qjmed/hct146
10. Kanno T, Moayyedi P. Proton Pump Inhibitors in the Elderly, Balancing Risk and Benefit: an Age-Old Problem. Curr Gastroenterol Rep. 2019;21(12):65. doi:10.1007/s11894-019-0732-3
11. Corsonello A, Onder G, Maggio M, Corica F, Lattanzio F. Medications affecting functional status in older persons. Curr Pharm Des. 2014;20(19):3256-63.
12. Amarapurkar DN. Prescribing medications in patients with decompensated liver cirrhosis. Int J Hepatol. 2011;2011. doi:10.4061/2011/519526
13. Liu T, Ivaturi V, Gobburu J. Integrated Model to Describe Morphine Pharmacokinetics in Humans. J Clin Pharmacol. 2019;59(8):1070-7. doi:10.1002/jcph.1400
14. Durakovi ć Z, Vitezi ć D. Pharmacodynamics and pharmacokinetics in the elderly. Period Biol. 2013;115(4):517-20.
15. Falcone M, Paul M, Tiseo G, Yahav D, Prendki V, Friberg LE, et al. Considerations for the optimal management of antibiotic therapy in elderly patients. J Glob Antimicrob Resist. 2020;22:325-33. doi:10.1016/j.jgar.2020.02.022
16. Fahimi F, Emami S, Rashid Farokhi F. The rate of antibiotic dosage adjustment in renal dysfunction. Iran J Pharm Res. 2012;11(1):157-61.
17. Ouanounou A, Haas DA. Pharmacotherapy for the elderly dental patient. J Can Dent Assoc. 2015;80(18):f18.
18. Wang Y, Ng HY, Wu CC, Wang YCL, Lee CT. Polypharmacy and Chronic Kidney Disease. J Intern Med Taiwan. 2021;32(2):98-107. doi:10.6314/JIMT.202104_32(2).03
19. Golchin N, Frank SH, Vince A, Isham L, Meropol SB. Polypharmacy in the elderly. J Res Pharm Pract. 2015;4(2):85-8. doi:10.4103/2279-042X.155755
20. Wang Y, Li X, Jia D, Lin B, Fu B, Qi B, et al. Exploring polypharmacy burden among elderly patients with chronic diseases in Chinese community: a cross-sectional study. BMC Geriatr. 2021;21(1):308. doi:10.1186/s12877-021-02247-1
21. Chan DC, Hao YT, Wu SC. Polypharmacy among Disabled Taiwanese Elderly. Drugs Aging. 2009;26(4):345-54. doi:10.2165/00002512-200926040-00005
22. Ho HY. Potentially inappropriate medications and associated factors among older patients after hospitalization. 2017. doi:10.6342/NTU201804016
23. Ku TL, Chew CX, Lee KW, Lin LY. Importance of Establishing Medication Safety for the Elderly: A Public Health Perspective. Formosa J Clin Pharm. 2018;26(4):266-73. doi:10.6168/FJCP.201810_26(4).0003
24. McNeil JJ, Wolfe R, Woods RL, Tonkin AM, Donnan GA, Nelson MR, et al. Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. N Engl J Med. 2018;379(16):1509-18.
25. Shireman TI, Mahnken JD, Howard PA, Kresowik TF, Hou Q, Ellerbeck EF. Development of a Contemporary Bleeding

Risk Model for Elderly Warfarin Recipients. Chest. 2006;130(5):1390-6.
26. Singh JA, Wells GA, Christensen R, Ghogomu ET, Maxwell LJ, MacDonald JK, et al. Adverse effects of biologics: a network meta-analysis and Cochrane overview. Cochrane Database Syst Rev. 2011;(2):CD008794-CD008794.
27. Corrie PG. Cytotoxic chemotherapy: clinical aspects. Medicine. 2008;36(1):24-8.
28. Anderson K, Hamm RL. Factors That Impair Wound Healing. J Am Coll Clin Wound Spec. 2012;4(4):84-91.
29. Chutka DS, Takahashi PY, Hoel RW. Inappropriate Medications for Elderly Patients. Mayo Clin Proc. 2004;79(1):122-39.
30. Spanou A, Lyritis GP, Chronopoulos E, Tournis S. Management of bisphosphonate-related osteonecrosis of the jaw: a literature review. Oral Dis. 2015;21(8):927-36.
31. Holm-Pedersen P, Walls AW, Ship JA. Textbook of geriatric dentistry. 2015:148.
32. Thomson WM, Smith MB, Ferguson CA, Moses G. The Challenge of Medication-Induced Dry Mouth in Residential Aged Care. Pharmacy. 2021;9(4):162.
33. Oliver BG, Silver PM, Marie C, Hoot SJ, Leyde SE, White TC. Tetracycline alters drug susceptibility in Candida albicans and other pathogenic fungi. Microbiology (Reading). 2008;154(Pt 3):960-70.
34. Baughman RP, Lower EE. Fungal infections as a complication of therapy for sarcoidosis. QJM. 2005;98(6):451-6.
35. Ribeiro RA, Wanderley CW, Wong DV, Mota JM, Leite CA, Souza MH, et al. Irinotecan- and 5-fluorouracil-induced intestinal mucositis: insights into pathogenesis and therapeutic perspectives. Cancer Chemother Pharmacol. 2016;78(5):881-93.
36. Kim JH, Kim Y, Shin SJ, Park JW, Jung IY. Tooth Discoloration of Immature Permanent Incisor Associated with Triple Antibiotic Therapy: A Case Report. J Endod. 2010;36(6):1086-91.
37. Yuan A, Woo SB. Adverse drug events in the oral cavity. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015;119(1):35-47.
38. Unnikrishnan D, Murakonda P, Dharmarajan TS. If It Is Not Cough, It Must Be Dysgeusia: Differing Adverse Effects of Angiotensin-Converting Enzyme Inhibitors in the Same Individual. J Am Med Dir Assoc. 2004;5(2):107-10.
39. Priyadharshini V, Belure VV, Triveni MG, Tarun Kumar AB, Mehta DS. Successful management of Phenytoin and phenobarbitone induced gingival enlargement: A multimodal approach. Contemp Clin Dent. 2014;5(2):268-71.
40. Livada R, Shiloah J. Calcium channel blocker-induced gingival enlargement. J Hum Hypertens. 2014;28(1):10-4.
41. Ciavarella D, Guiglia R, Campisi G, Cosola MD, Liberto CD, Sabatucci A, et al. Update on gingival overgrowth by cyclosporine A in renal transplants. Med Oral Patol Oral Cir Bucal. 2007;12(1):19-25.
42. Gunasekaran V, Ganapathy D. Undesirable Drug Reactions in Orofacial Region. J Pharm Sci Res. 2016;8(7):665-7.
43. Sin B, Miller M, Chew E. Hydrochlorothiazide Induced Lichen Planus in the Emergency Department: A Case Report. J Pharm Pract. 2016;30(2):266-9.
44. Oscanoa TJ, Lizaraso F, Carvajal A. Hospital admissions due to adverse drug reactions in the elderly. A meta-analysis. Eur J Clin Pharmacol. 2017;73(6):759-70. doi:10.1007/s00228-017-2225-3
45. Costa E, Giardini A, Savin M, Menditto E, Lehane E, Laosa O, et al. Interventional tools to improve medication adherence: review of literature. Patient Prefer Adherence. 2015;9:1303-14. doi:10.2147/PPA.S87551
46. Jankowska-Polańska B, Dudek K, Szymanska-Chabowska A, Uchmanowicz I. The influence of frailty syndrome on medication adherence among elderly patients with hypertension. Clin Interv Aging. 2016;11:1781-90. doi:10.2147/CIA.S113994
47. Rohde JM, Jacobsen D, Rosenberg DJ. Role of the Hospitalist in Antimicrobial Stewardship: A Review of Work Completed and Description of a Multisite Collaborative. Clin Ther. 2013;35(6):751-7. doi:10.1016/j.clinthera.2013.05.005
48. Sergi G, Rui MD, Sarti S, Manzato E. Polypharmacy in the Elderly. Drugs Aging. 2011;28(7):509-18. doi:10.2165/11592010-000000000-00000
49. Nizharadze N, Mamaladze M, Chipashvili N, Vadachkoria D. Articaine-the best choice of local anesthetic in contemporary dentistry. Georgian Med News. 2011(190):15-23.
50. Dorofeev A. Assessment of pain perception of elderly patients with different levels of dentophobia during surgical dental appointment. Asian J Pharm. 2018;12(03). doi:10.22377/ajp.v12i03.2643
51. Srikar M, Aravind A, Niranjan B, Khandeparker RVS, Grover S. Phentolamine mesylate in reversal local anesthesia: A review. J Int Oral Health. 2015;7(11):129.
52. Al-Khafaji HHJ, Abass MK, Al-Ameedee AH. Unaddressed local anesthesia reversal action of phentolamine mesylate after plain mepivacaine. Eurasia J Biosci. 2020;14:3883-8.
53. Chanpong B, Haas DA, Locker D. Need and Demand for Sedation or General Anesthesia in Dentistry: A National Survey of the Canadian Population. Anesth Prog. 2005;52(1):3-11. doi:10.2344/0003-3006(2005)52[3:NADFSO]2.0.CO;2
54. Kapur A, Kapur V. Conscious sedation in dentistry. Ann Maxillofac Surg. 2018;8(2):320. doi:10.4103/ams.ams_191_18
55. Cervino G, Fiorillo L, Monte IP, De Stefano R, Laino L, Crimi S, et al. Advances in Antiplatelet Therapy for Dentofacial Surgery Patients: Focus on Past and Present Strategies. Materials. 2019;12(9). doi:10.3390/ma12091524
56. De Stefano R, Bruno A, Muscatello MR, Cedro C, Cervino G, Fiorillo L. Fear and anxiety managing methods during dental treatments: a systematic review of recent data.

Minerva Stomatol. 2019;68(6):317-31. doi:10.23736/s0026-4970.19.04288-2

57. Germano F, Bramanti E, Arcuri C, Cecchetti F, Cicciù M. Atomic force microscopy of bacteria from periodontal subgingival biofilm: Preliminary study results. Eur J Dent. 2013;7(02):152-8. doi:10.4103/1305-7456.110155
58. Lo Giudice G, Cutroneo G, Centofanti A, Artemisia A, Bramanti E, Militi A, et al. Dentin morphology of root canal surface: A quantitative evaluation based on a scanning electronic microscopy study. BioMed Res Int. 2015;2015. doi:10.1155/2015/164065
59. Smiljic S. The clinical significance of endocardial endothelial dysfunction. Medicina. 2017;53(5):295-302. doi:10.1016/j.medici.2017.08.003
60. Dantas LP, de Oliveira-Ribeiro A, de Almeida-Souza LM, Groppo FC. Effects of passiflora incarnata and Midazolam for control of anxiety in patients undergoing dental extraction. Med Oral Patol Oral Cir Bucal. 2017;22(1):e95. doi:10.4317/medoral.21140
61. Fiorillo L. Conscious Sedation in Dentistry. Medicina. 2019;55(12). doi:10.3390/medicina55120778
62. Becker DE. Preoperative Medical Evaluation: Part 1: General Principles and Cardiovascular Considerations. Anesth Prog. 2009;56(3):92-103. doi:10.2344/0003-3006-56.3.92
63. Ghezzi EM, Chavez EM, Ship JA. General anesthesia protocol for the dental patient: emphasis for older adults. Spec Care Dentist. 2000;20(3):81-108. doi:10.1111/j.1754-4505.2000.tb00011.x
64. Prabhu NT, Nunn JH, Evans DJ, Girdler NM. Development of a screening tool to assess the suitability of people with a disability for oral care under sedation or general anesthesia. Spec Care Dentist. 2008;28(4):145-58. doi:10.1111/j.1754-4505.2008.00034.x
65. Lim MAWT, Borromeo GL. The use of general anesthesia to facilitate dental treatment in adult patients with special needs. J Dent Anesth Pain Med. 2017;17(2):91-103. doi:10.17245/jdapm.2017.17.2.91
66. Bessone F. Non-steroidal anti-inflammatory drugs: What is the actual risk of liver damage? World J Gastroenterol. 2010;16(45):5651-61.
67. Khan MG. Effects of Drug Interactions. Cardiac Drug Therapy. 2007:363-79.
68. Bailie GR. Med facts pocket guide of Drug Interactions. In: bone care; 2021.
69. Brown RS, Rhodus NL. Epinephrine and local anesthesia revisited. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol. 2005;100(4):401-8.
70. Varma S. Benzodiazepines and hypnotics. Medicine. 2016;44(12):764-7.
71. Krasniqi S, Daci A. Analgesics use in dentistry. Pharmacology, Toxicology and Pharmaceutical Science-Pain Relief-From Analgesics to Alternative Therapies. 2017:111-39.
72. Blieden M, Paramore LC, Shah D, Ben-Joseph R. A perspective on the epidemiology of acetaminophen exposure and toxicity in the United States. Expert Rev Clin Pharmacol. 2014;7(3):341-8.
73. Bascones-Martínez A, Muñoz-Corcuera M, Bascones-Ilundain C. Side effects of drugs on the oral cavity. Med Clín (English Edition). 2015;144(3):126-31. doi:10.1016/j.medcle.2015.05.004
74. Esh CJ, Mauger AR, Palfreeman RA, Al-Janubi H, Taylor L. Acetaminophen (paracetamol): use beyond pain management and dose variability. Front Physiol. 2017;8:1092. doi:10.3389/fphys.2017.01092
75. Hughes GJ, Patel PN, Saxena N. Effect of acetaminophen on international normalized ratio in patients receiving warfarin therapy. Pharmacotherapy. 2011;31(6):591-7. doi:10.1592/phco.31.6.591
76. Yoon E, Babar A, Choudhary M, Kutner M, Pyrsopoulos N. Acetaminophen-induced hepatotoxicity: a comprehensive update. J Clin Transl Hepatol. 2016;4(2):131. doi:10.14218/JCTH.2015.00052
77. Tan SC, New LS, Chan ECY. Prevention of acetaminophen (APAP)-induced hepatotoxicity by leflunomide via inhibition of APAP biotransformation to N-acetyl-p-benzoquinone imine. Toxicol Lett. 2008;180(3):174-81. doi:10.1016/j.toxlet.2008.06.001
78. Bailey E, Worthington H, Coulthard P. Ibuprofen and/or paracetamol (acetaminophen) for pain relief after surgical removal of lower wisdom teeth, a Cochrane systematic review. Br Dent J. 2014;216(8):451-5. doi:10.1038/sj.bdj.2014.330
79. Sostres C, Gargallo CJ, Arroyo MT, Lanas A. Adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs, aspirin and coxibs) on upper gastrointestinal tract. Best Pract Res Clin Gastroenterol. 2010;24(2):121-32. doi:10.1016/j.bpg.2009.11.005
80. Trelle S, Reichenbach S, Wandel S, Hildebrand P, Tschannen B, Villiger PM, et al. Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. BMJ. 2011;342. doi:10.1136/bmj.c7086
81. Bally M, Dendukuri N, Rich B, Nadeau L, Helin-Salmivaara A, Garbe E, et al. Risk of acute myocardial infarction with NSAIDs in real world use: bayesian meta-analysis of individual patient data. BMJ. 2017;357. doi:10.1136/bmj.j1909
82. 2019 American Geriatrics Society Beers Criteria® Update Expert Panel, Fick DM, Semla TP, Steinman M, Beizer J, Brandt N, et al. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2019;67(4):674-94.
83. Khatchadourian ZD, Moreno-Hay I, de Leeuw R. Nonsteroidal anti-inflammatory drugs and antihypertensives: how do they relate? Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;117(6):697-703. doi:10.1016/j.oooo.2014.02.028
84. Panel Agsbcue, Fick DM, Semla TP, Steinman M, Beizer J, Brandt N, et al. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate

medication use in older adults. J Am Geriatr Soc. 2019;67(4):674-94. doi:10.1111/jgs.15767

85. Varrassi G, Pergolizzi JV, Dowling P, Paladini A. Ibuprofen Safety at the Golden Anniversary: Are all NSAIDs the Same? A Narrative Review. Adv Ther. 2020;37(1):61-82. doi:10.1007/s12325-019-01144-9
86. Gazal G, Al-Samadani KH. Comparison of paracetamol, ibuprofen, and diclofenac potassium for pain relief following dental extractions and deep cavity preparations. Saudi Med J. 2017;38(3):284-91. doi:10.15537/smj.2017.3.16023
87. Yoshizumi J, Anzai H, Mitate E, Obayashi Y, Mori S, Yokoo Y, et al. Clinical features of odontogenic infection requiring extraoral drainage in elderly patients. A single-institution retrospective study. Oral Sci Int. 2021;18(2):120-5. doi:10.1002/osi2.1092
88. Dammling C, Abramowicz S, Kinard B. Current Concepts in Prophylactic Antibiotics in Oral and Maxillofacial Surgery. Oral Maxillofac Surg Clin North Am. 2022;34(1):157-67. doi:10.1016/j.coms.2021.08.015
89. Milic T, Raidoo P, Gebauer D. Antibiotic prophylaxis in oral and maxillofacial surgery: a systematic review. Br J Oral Maxillofac Surg. 2021;59(6):633-42. doi:10.1016/j.bjoms.2020.09.020
90. Perić M, Perković I, Romić M, Simeon P, Matijević J, Prpić Mehičić G, et al. The pattern of antibiotic prescribing by dental practitioners in Zagreb, Croatia. Cent Eur J Public Health. 2015;23(2):107-13. doi:10.21101/cejph.a3981
91. O'Rourke VJ. Azithromycin as an adjunct to non-surgical periodontal therapy: a systematic review. Aust Dent J. 2017;62(1):14-22. doi:10.1111/adj.12448
92. Segura-Egea J, Gould K, Şen BH, Jonasson P, Cotti E, Mazzoni A, et al. Antibiotics in Endodontics: a review. Int Endod J. 2017;50(12):1169-84.
93. Isola G, Matarese M, Ramaglia L, Cicciù M, Matarese G. Evaluation of the efficacy of celecoxib and ibuprofen on post-operative pain, swelling, and mouth opening after surgical removal of impacted third molars: A randomized, controlled clinical trial. Int J Oral Maxillofac Surg. 2019;48(10):1348-54.
94. Dar-Odeh NS, Abu-Hammad OA, Al-Omiri MK, Khraisat AS, Shehabi AA. Antibiotic prescribing practices by dentists: a review. Ther Clin Risk Manag. 2010;6:301. doi:10.2147/tcrm.s9736
95. Thornhill MH, Dayer MJ, Durkin MJ, Lockhart PB, Baddour LM. Oral antibiotic prescribing by NHS dentists in England 2010-2017. Bri Dent J. 2019;227(12):1044-50. doi:10.1038/s41415-019-1002-3
96. Lafaurie GI, Noriega LA, Torres CC, Castillo Y, Moscoso SB, Mosquera S, et al. Impact of antibiotic prophylaxis on the incidence, nature, magnitude, and duration of bacteremia associated with dental procedures: A systematic review. J Am Dent Assoc. 2019;150(11):948-59. doi:10.1016/j.adaj.2019.06.017
97. Halling F, Neff A, Heymann P, Ziebart T. Trends in antibiotic prescribing by dental practitioners in Germany. J Craniomaxillofac Surg. 2017;45(11):1854-9. doi:10.1016/j.jcms.2017.08.010
98. López-Píriz R, Aguilar L, Giménez MJ. Management of odontogenic infection of pulpal and periodontal origin. Med Oral Patol Oral Cir Bucal (Internet). 2007;12(2):154-9.
99. Rodríguez Martínez S, Talaván Serna J, Silvestre FJ. Dental management in patients with cirrhosis. Gastroenterol Hepatol (English Edition). 2016;39(3):224-32. doi:10.1016/j.gastre.2016.02.020
100. Bui T, Preuss CV. Cephalosporins. StatPearls [Internet]. StatPearls Publishing; 2021.
101. Sutter R, Rüegg S, Tschudin-Sutter S. Seizures as adverse events of antibiotic drugs. Neurology. 2015;85(15):1332. doi:10.1212/WNL.0000000000002023
102. Weis S, Kesselmeier M, Davis JS, Morris AM, Lee S, Scherag A, et al. Cefazolin versus anti-staphylococcal penicillins for the treatment of patients with Staphylococcus aureus bacteraemia. Clin Microbiol Infect. 2019;25(7):818-27. doi:10.1016/j.cmi.2019.03.010
103. Taniguchi T, Tsuha S, Shiiki S, Narita M. Gram-stain-based antimicrobial selection reduces cost and overuse compared with Japanese guidelines. BMC Infect Dis. 2015;15(1):458. doi:10.1186/s12879-015-1203-6
104. Kafle S, Pradhan S, Gupta S. Locally delivered tetracycline fibres in the treatment of chronic periodontitis. J Nepal Soc Periodontol Oral Implantol. 2018;2(2):45-8.
105. Flynn TR. Evidence-based principles of antibiotic therapy. Evidence-Based Oral Surgery. Springer; 2019. p. 283-316.
106. Ahmadi H, Ebrahimi A, Ahmadi F. Antibiotic therapy in dentistry. Int J Dentist. 2021;2021. doi:10.1155/2021/6667624
107. Luchian I, Goriuc A, Martu MA, Covasa M. Clindamycin as an Alternative Option in Optimizing Periodontal Therapy. Antibiotics. 2021;10(7). doi:10.3390/antibiotics10070814
108. Murphy PB, Bistas KG, Le JK. Clindamycin. StatPearls Publishing, Treasure Island (FL); 2022.
109. Kan P, Sasaki H, Inaba K, Watanabe K, Hamada N, Minabe M. Inhibitory effects of azithromycin on the adherence ability of Porphyromonas gingivalis. J Periodontol. 2019;90(8):903-10.
110. Agarwal E, Bajaj P, Naik SB, Pradeep A. Locally delivered 0.5% azithromycin as an adjunct to non-surgical treatment in patients with chronic periodontitis with type 2 diabetes: a randomized controlled clinical trial. J Periodontol. 2017;88(12):1281-7.
111. Dinos GP. The macrolide antibiotic renaissance. Br J Pharmacol. 2017;174(18):2967-83. doi:10.1111/bph.13936
112. Fos P, Forner L, Llena C, Anadon A. Analysis of Clarithromycin in dental pulp with and without inflammation. Int Dent J. 2011;13:50-4.
113. Greenwood M, Meechan JG. Metabolic Disorders and Dental Practice. In: Greenwood M, Meechan JG, editors.

General Medicine and Surgery for Dental Practitioners. Cham: Springer International Publishing; 2019. p. 137-45.
114. DeAngelis AF, Barrowman RA, Harrod R, Nastri AL. Review article: Maxillofacial emergencies: Oral pain and odontogenic infections. Emerg Med Aust. 2014;26(4):336-42. doi:10.1111/1742-6723.12266
115. Zandbergen D, Slot DE, Niederman R, Van der Weijden FA. The concomitant administration of systemic amoxicillin and metronidazole compared to scaling and root planing alone in treating periodontitis: =a systematic review=. BMC Oral Health. 2016;16(1):27. doi:10.1186/s12903-015-0123-6
116. Loyola-Rodriguez JP, Franco-Miranda A, Loyola-Leyva A, Perez-Elizalde B, Contreras-Palma G, Sanchez-Adame O. Prevention of infective endocarditis and bacterial resistance to antibiotics: A brief review. Spec Care Dent. 2019;39(6):603-9. doi:10.1111/scd.12415
117. Holmes CJ, Pellecchia R. Antimicrobial therapy in management of odontogenic infections in general dentistry. Dent Clin. 2016;60(2):497-507. doi:10.1016/j.cden.2015.11.013
118. Moshkowitz M, Ben-Baruch E, Kline Z, Shimoni Z, Niven M, Konikoff F. Risk factors for severity and relapse of pseudomembranous colitis in an elderly population. Colorectal Dis. 2007;9(2):173-7. doi:10.1111/j.1463-1318.2006.01013.x
119. Stein K, Farmer J, Singhal S, Marra F, Sutherland S, Quiñonez C. The use and misuse of antibiotics in dentistry: A scoping review. J Am Dent Assoc. 2018;149(10):869-84. doi:10.1016/j.adaj.2018.05.034
120. Nutescu E, Chuatrisorn I, Hellenbart E. Drug and dietary interactions of warfarin and novel oral anticoagulants: an update. J Thromb Thrombolysis. 2011;31(3):326-43.
121. Martinez V, Caumes E. Metronidazole. Ann Dermatol Vénéréol. 2001;128(8).
122. Maideen NMP. Clinically important and pharmacologically relevant drug interactions with alcohol. Am J Res Med Sci. 2019;6(1):1-7.
123. Stucky MA, Goldberger ZD. Digoxin: its role in contemporary medicine. Postgrad Med J. 2015;91(1079):514.
124. Chang PH, Li Z, Jean JS, Jiang WT, Wu Q, Kuo CY, et al. Desorption of tetracycline from montmorillonite by aluminum, calcium, and sodium: an indication of intercalation stability. Int J Environ Sci Technol. 2014;11(3):633-44.
125. Mergenhagen Kari A, Wattengel Bethany A, Skelly Megan K, Clark Collin M, Russo Thomas A. Fact versus Fiction: a Review of the Evidence behind Alcohol and Antibiotic Interactions. Antimicrob Agents Chemother. 2020;64(3):e02167-19.
126. Turrentine MA. Single-dose fluconazole for vulvovaginal candidiasis: impact on prothrombin time in women taking warfarin. Obstet Gynecol. 2006;107(2):310-3.
127. Schelleman H, Bilker WB, Brensinger CM, Wan F, Hennessy S. Anti-Infectives and the Risk of Severe Hypoglycemia in Users of Glipizide or Glyburide. Clin Pharmacol Ther. 2010;88(2):214-22.
128. Sharma S, Kale TP, Balihallimath LJ, Motimath A. Evaluating Effectiveness of Axiostat Hemostatic Material in achieving Hemostasis and Healing of Extraction Wounds in Patients on Oral Antiplatelet Drugs. J Contemp Dent Pract. 2017;18(9):802-6. doi:10.5005/jp-journals-10024-2130
129. Efeoğlu C, Çalış AS, Karasu Z, Koca H, Boyacıoğlu H. Prospective randomized single-blind study of post-operative bleeding after minor oral surgery in patients with cirrhosis. Turk J Gastroenterol. 2019;30(2):171. doi:10.5152/tjg.2018.18078
130. Brancaccio Y, Antonelli A, Barone S, Bennardo F, Fortunato L, Giudice A. Evaluation of local hemostatic efficacy after dental extractions in patients taking antiplatelet drugs: a randomized clinical trial. Clin Oral Investig. 2021;25(3):1159-67. doi:10.1007/s00784-020-03420-3
131. Ng WCK, Jerath A, Wasowicz M. Tranexamic acid: a clinical review. Anaesthesiol Intensive Ther. 2015;47(4):339-50. doi:10.5603/AIT.a2015.0011
132. Sperzel M, Huetter J. Evaluation of aprotinin and tranexamic acid in different in vitro and in vivo models of fibrinolysis, coagulation and thrombus formation. J Thrombosis Haemost. 2007;5(10):2113-8. doi:10.1111/j.1538-7836.2007.02717.x
133. Mário-Luis-Tavares Mendes EM, do Nascimento-Júnior DMR. Efficacy of proteolytic enzyme bromelain on health outcomes after third molar surgery. Systematic review and meta-analysis of randomized clinical trials. Med Oral Patol Oral Cir Bucal. 2019;24(1):e61. doi:10.4317/medoral.22731
134. da Silva Caetano V, Alves EHP, de Carvalho França LF, di Lenardo D, Martins VBD, Galeno JG, et al. Histomorphometric analysis of pulp submitted to the action of bromelain associated with irrigation solutions. G Ital Endod. 2019;33(1). doi:10.32067/gie.2019.33.01.03