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Nutrition, Supplements and their Interaction with Drugs in Diets for the Prevention and Treatment of Diseases

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Abstract

The promotion of healthy eating and physical activity is part of the prevention and treatment of diseases in modern medicine. The aim of our research was to study the clinical principles in compiling a diet for patients who are already on drug therapy for a diagnosed disease, guided by the principle of healthy eating. ***Material and method:*** we conducted a study motivated by personal experiences on the interaction of drugs and nutrients in diets prescribed for healthy eating in certain diseases, with a special aspect of anticoagulant therapy. The basic principle of the protocol should include the underlying disease, medications for the same, past diseases with a deficit of certain organs in function and an assessment of the existing diet and supplements to prevent drug interactions. ***Results:*** More than 30% of people take supplements on their own. Knowledge of the interaction of drugs with supplements and nutrients with medications is of crucial importance for preventing the consequences of their synergistic or antagonistic interaction, of which bleeding is the key and most dangerous. ***Discussion:*** Modern management of patients in the perioperative period is crucial to avoid bleeding or thrombosis. The medical team takes into account all possible risks, based on the clinical examination, blood laboratory and possible drug interactions, but there is not always available data on the patients' supplementary therapy, which may be a risk. ***Conclusion:*** When recommending the consumption of supplements and diet for a given disease, the possible interaction of the drug and the condition of the organs that may be damaged should be taken into account.

Keywords: Diet, Supplements, Medications, Interaction.

INTRODUCTION

Nutrition is part of the program for the prevention and treatment of several chronic diseases. In our clinical practice, we accept patients who, due to atherosclerotic changes in blood vessels, the presence of type 2 diabetes, dementia, Parkinson's disease, patients with post-cardiovascular non-invasive and invasive interventions, after stroke, etc. comorbidities and traumas of the musculoskeletal system, need to have an appropriate dietary regimen. Medical professionals, primary care physicians, family doctors, and clinical nutritionists need to know the interactions of antithrombotic therapy drugs with supplements and nutrients, as well as all drug interactions with them, in order to prevent complications from the most benign to intense internal bleeding, especially if patients undergo minor surgical interventions, and importantly if they need to have extensive surgical interventions or invasive methods. Regarding drugs and their interactions, always before surgical or invasive treatment, in high-risk patients, an opinion from a transfusion specialist and cardiologist is required. But patients often do not know that some food or supplement taken on their own can interact with the drugs they are taking. The interaction can be in two directions, to act synergistically and increase the effect of the drug or to reduce the effect of the drug. Here, the most significant and life-threatening are substances that can cause bleeding. Although any drug can interact with food or supplements, the most urgent are substances that cause acute life-threatening conditions, such as drugs for preventing blood coagulation and preventing thrombosis. (Wilkinson,2005; Gelosa, *et al*., 2018; Byon *et al*., 2018)

In clinical practice, three groups of drugs that reduce blood coagulation have been used so far to prevent thrombotic conditions, namely: vitamin K inhibitors, oral antithrombotic drugs, and drugs that prevent platelet aggregation. The first 2 act on the blood coagulation factor system, while the third group acts on

the platelets themselves without affecting the coagulation factors.

The aim of our research was to define the protocol for diet and supplements in patients on anticoagulant therapy as well as for those who are about to undergo surgery, in order to prevent a side effect - bleeding.

MATERIAL AND METHOD

In our research, the key elements were collecting data from patients who took herbal supplements, consulting literature on drug-food and supplement interactions with a special aspect of anticoagulant drugs, as well as the mechanism of action of reducing or increasing the risk of thrombus formation associated with diet and supplements.

We grouped the obtained data according to the following characteristics.

1. Important data that should be included in the personalized diet protocol for patients due to a given disease, as well as the risk of thrombosis with or without anticoagulant therapy. This includes personal data about the patient such as age, gender, past illnesses, current diagnosis, comorbidity and medications they are taking. In addition, laboratory blood tests no older than 5 days are taken.
2. Nutritional history, diet and supplements consumed by the patient and possible interactions with the medications they are taking.
3. Proposal for a personalized diet program.
4. Prescribing supplements that will have a positive effect on the underlying disease, but will not have an effect on blood clotting, as well as interaction with medications.

RESULTS

1. Protocol for assessing the condition as a condition for a personalized diet

After entering personal data and the history of the existing disease with the diagnosis and therapy being received, it is possible to include nutrients and supplements that will improve physical performance, and thus the quality of life as a condition for supporting nutrition in the rehabilitation process. Special attention is paid to patients who are on anticoagulant therapy. (Violi, *et al*., 2020; Popiolek-Kalisz,2025)

1. Most Common Diagnoses of Patients Who are on Anticoagulant Therapy

These data will serve us in practice to immediately select patients at risk or patients where the diet has special specificities. A report from the World Health Organization,(Jankovic, *et al*., 2015) recommends that a healthy diet for adults consists of eating at least 400 g, or 5 servings, of fruits and vegetables per day to reduce the risk of non-communicable diseases and to help ensure an adequate daily intake of dietary fiber. In the energy balance, <30% of total energy intake should come from fat; unsaturated fats (found in fish, avocados and nuts, as well as in sunflower, soy, quinoa) should be preferred over saturated fats (found in fatty meat, butter, palm and coconut oil, cream, cheese and lard). These fats should be <10% of total energy intake as trans fats of all types, and <1% of total energy value.

According to some Public Health Institutions, it is recommended to include 1 to 2 servings per week of seafood rich in Omega-3 fatty acids, to reduce the risk of congestive heart failure, acute myocardial infarction, ischemic stroke and sudden cardiac death, especially when seafood replaces the intake of less healthy foods.(Eckel, *et al*., 2014)

The positive effects of the above nutrients and the recommendations that follow can be based on the antithrombotic activity observed in experimental animal models and from clinical studies. Regarding experimental models, positive effects were obtained when the substances were administered by infusion or orally.

The nutrients that were examined were rich in polyphenols, which are known as antioxidant molecules, although it is not clear whether they participate alone or in combination with other food components as scavengers of free ROS or in reducing the effect of enzymes that generate ROS.

This effect of a nutrient or its molecular component as an antioxidant with a possible antithrombotic effect is positive for patients with CVD. The underlying antithrombotic mechanism appears to be due to inhibition of PA and platelet TxB2 or to an increase in platelet NO. Less common is an inhibitory effect on coagulation activation as a consequence of impaired TF biosynthesis (nuts and wine) or increased fibrinolytic activity. These findings are apparently supported by studies in humans in which supplementation with a single nutrient or nutrient-related molecules resulted in impaired PA biosynthesis, TxB2 or, in very rare cases, reduced coagulation activation. (Marchetti *et al*., 2007)

In clinical studies where different amounts of nutrients and different methods were used, (the studies were not unified) the results suggest that specific nutrients possess antithrombotic properties and the antiplatelet effect may be useful for the primary prevention of Cardiovascular Disease (CVD) or to complement antiplatelet treatment in secondary prevention. It could not be determined whether this nutrient, e.g. polyphenol, can be used as a drug. Further studies have proven that these nutrients, if used, do not reduce the risk of acute episodes of CVD. The exact

doses of the substance that can be used as a drug have not been determined either. For example, Resveratrol from Red Wine, is in such small quantities in one glass as an evening drink that it cannot be attributed to a therapeutic effect. (Gueboudji *et al*., 2021; Behal, *et al*., 2020) Therefore, studies should be repeated using appropriate methodology to compare nutrients, selecting the amount of nutrients that is appropriate for potential CVD prevention, and finally selecting modern markers of platelet activation and coagulation to firmly confirm the results of experimental studies.

The most common diagnoses for which antithrombotic therapy is prescribed are the following:

- patients with chronic thrombophlebitis,
- patients after acute thromboembolism,
- patients with chronic liver failure,
- patients after chemotherapy with or without anticoagulant therapy,
- patients with increased blood coagulability,
- patients with generalized atherosclerosis on anticoagulant therapy,
- patients after stroke, as a consequence of thromboembolism,
- patients with arrhythmia and other cardiac diseases of the cardiac conduction system

One thing is certain, a synergistic effect of these polyphenols and other nutrients with drugs that reduce blood viscosity is possible. (Mendonca, *et al*., 2019)

2. Determining the Scheme for Reducing Anticoagulant Therapy before Surgical Intervention

In clinical practice, the doctor who needs to perform surgical treatment of a patient who is on anticoagulant therapy, seeks the opinion of a transfusion specialist or cardiologist, based on laboratory findings 5-10 days before surgical treatment. (Chen, *et al*., 2022)

Generally, salicylic acid given as Aspirin 100 mg, is excluded 10 days before major surgical intervention in patients who are not on anticoagulant therapy or are not at risk of thrombosis.

The remaining schemes are determined according to a program given by the doctor who gave anticoagulant therapy. Most often 5 days before the intervention.

Managing patients on anticoagulation and anti-aggregation therapy is a daily challenge for physicians. The interruption of therapy can increase the risk of thrombotic events during and after surgery. However, the non-interruption of these medications can heighten the risk of bleeding during surgery and trigger a sequence of undesirable outcomes ranging from minor to uncontrolled bleeding. The optimal management of these patients is thus achieved through a balance between thromboembolic and bleeding risks. Several case-based considerations affect whether or not to interrupt anticoagulation or anti-aggregation therapy before surgery. These include evaluating an individual's underlying bleeding risk, the risk of bleeding associated with the surgical procedure, the timing of interruption and resumption of anticoagulation therapy, and whether to use bridging therapy. These are all typical questions that can be addressed in this topic.

Managing perioperatively the patient receiving anticoagulation therapy is the responsibility across all disciplines of the healthcare team. During the preoperative visit, the surgeon and anesthesiologist are responsible for ensuring this information about the completion of spaces and supplements by the patient. In case they use that, they must control the blood and test on coagulation time. On the day of surgery, operative nurses, physicians, and pharmacy personnel have their usual duties of ensuring the patient receives appropriate operative care per protocol for the procedure. Postoperatively, the physician is responsible for placing orders for either continuing to hold or administering the anticoagulation agent, depending on the drug and the patient's scenario. Additionally, pharmacy personnel are in charge of reviewing the pharmacological conciliation of the patient and with clinical nutritionist to make diet specific for disease but also for medication intake.The periprocedural management of patients who are receiving vitamin K antagonists, direct oral anticoagulants and antiplatelet therapy is a common and challenging clinical scenario as the decision to interrupt or continue these medications is anchored on patient and procedure-related risks for bleeding and thrombosis. Four clinical scenarios will be provided: (1) managing patients in whom anticoagulants can be continued; (2) perioperative management of direct oral anticoagulants; (3) management of patients on dual antiplatelet therapy; and (4) anticoagulant management for emergency or urgent surgery.

3. The Most Common Nutrients That Should be Excluded 15 Days before Surgery as a Supplementary Herbal Therapy for Diabetes, Rheumatic Diseases, Hepatoprotective Drugs

In one study, 45 herbal supplements were listed as part of the treatment of diseases that increase bleeding.(LIJMC,2022) The mechanism of action of the active substance of the herbal ingredient used as a spice or nutrient is mainly due to its activation of the component that prevents blood coagulation or increases. Food and herbal compounds can react with drugs in different stages as follows (Steffel, *et al*., 2021; Auxtero, *et al*., 2021)

i. In the drug release phase, the active substance is released from the pharmaceutical form (e.g., tablets and capsules) and becomes available for absorption in the body. During this process, the drug can bind to food components, which can hinder its release or absorption; also, gastric pH can affect its solubility and subsequent release.

Other important factors include delayed gastric emptying and interactions with digestive enzymes(European Medical Agency,2021)

ii. During the absorption phase, the bioactivity and bioavailability of the drug change, and its concentration changes depending on the type of food consumed. Absorption is influenced by changes in pH (Hakeam, *et al*.2017; Stangier,2008) drug adsorption, complexation, and precipitation. Furthermore, food can alter the rate of bile acid secretion, intestinal metabolism, transport kinetics, gastric emptying time, and drug properties (e.g., solubility, logP, and ionization). (European Medical Agency,2016)

iii. In the distribution phase, the mechanisms that regulate the distribution of the substance are also disrupted. Once absorbed from the site of administration, the drug is distributed into the extracellular fluids, where it can accumulate in significant reserves by binding to plasma proteins; this reservoir can lead to prolonged effects by establishing a mechanism for sustained release (Mueck, *et al*.2013) In addition to various compounds in food, such as cholesterol, which affect, among others, transport proteins, the distribution of drugs is also influenced by the action of drug transporters, in particular P-glycoprotein (Pgp); This plays a significant role in the absorption of drugs in the intestine, its distribution to the brain, lymphocytes and placenta, as well as excretion in urine and bile. In the intestine, Pgp reduces the absorption of toxic compounds from food, while in the liver and kidneys, it mediates the excretion of toxins and metabolites in urine and bile. Therefore, inhibition of Pgp by food and herbal compounds in the intestine may lead to increased drug bioavailability, whereas its induction may reduce bioavailability. (European Medical Agency,2021; Wada, *et al*., 2019)

iv. During the metabolism (biotransformation) phase, the activity of enzymes involved in the metabolism of drugs or components of food and herbals may be impaired or increased.

v. During the excretion phase, both xenobiotics and food can interfere with the elimination of specific compounds. For example, a diet that acidifies the urine (e.g., meat, fish, eggs, and cheese) may reduce the excretion of salicylates, sulfonamides, and ampicillin, while a diet that alkalizes the urine (e.g., milk, vegetables) may reduce the excretion of amphetamines, theophylline, and erythromycin. (Song, *et al*., 2016). Of these phases, phase III is probably the most significant in relation to the externally administered drug and the specific properties of the human body, as it involves biotransformation, which can have dangerous effects on the health and life of patients.

4. Diet and Supplement Protocol for Patients at Risk of Bleeding

This diet should exclude any foods that increase bleeding, teas and supplements for various diseases, such as hepatoprotective (dandelion root, silumarin, turmeric), yarrow, cinnamon, ginkgo biloba, etc.

For almost 60 years, vitamin K antagonists (VKAs) have been the mainstay of anticoagulant therapy, in recent years direct oral anticoagulants (DOACs) have become the anticoagulant treatment of choice. DOACs were initially considered drugs without significant interactions with food, but clinical observations from practice have shown reported interactions with food ingredients. Food, dietary supplements or herbs may contain substances that, when administered simultaneously with DOACs, affect the plasma concentration of drugs. The third group of drugs are those that act on platelet aggregation.

– Vitamin K antagonists

Foods low in vitamin K is good for increased coagulation and for patients on this therapy. Daily intake of vitamin K should not exceed 90 µg. Low vitamin K does not necessarily guarantee safe administration of warfarin (Coumadin). (Booth,2012) However, we list them with their contents in the daily intake (DV).

Vegetables low in vitamin K include:

- Turnips (raw or cooked) 1 cup 0.3µg (0% DV)
- Sweet corn (raw or canned) 1 cup 0.5µg (1% DV)
- Onions (raw or cooked) 1 medium piece (331g) 1µg (1% DV)
- Squash (cooked) 1 cup 2µg (2% DV)
- Potatoes (cooked) 1 cup 3µg (3% DV)
- Sweet potatoes (cooked) 1 cup 7µg (6% DV)
- Eggplant (cooked) 1 cup 3µg (4% DV)
- White mushrooms (raw or cooked) 1 cup 0µg (0% DV)
- Shiitake mushrooms (cooked) 1 cup 0µg (0% DV)
- Tomatoes (raw) 1 cup 14µg (12% DV)
- Tomatoes (cooked) 1 cup 7µg (6% DV)
- Cucumber (raw) 1 cup 17µg (14% DV)

Fruits low in vitamin K

- Watermelon 1 cup 2µg (0% DV)
- Banana 1 medium (105g) 0.6µg (1% DV)
- Pineapple 1 cup 1.2µg (1% DV)
- Apple 1 medium (182g) 4µg (3% DV)
- Nectarine 1 medium (142g) 3µg (3% DV)
- Strawberries 1 cup 3µg (3% DV)
- Peaches 1 medium (150g) 4µg (3% DV)

Foods that reduce clotting in tea form: St. John's wort, ginger, chamomile,

Foods high in vitamin K increase coagulation, bad for patients on anticoagulant therapy with vitamin K antagonists.

- All green leaves (spinach, Swiss chard, parsley, broccoli, cabbage, cauliflower,) beets,
- Soft and hard cheeses, soy and soy products,
- Offal: pâtés and liver products, pork, chicken, bacon, ground beef, kidneys, turkey and all other feathered birds, egg yolk.
- Fruits: plums, kiwi, avocado, blackberry, blueberry, pomegranate, dried figs, grapes, cranberries.
- Legumes: green and red beans, peas, hazelnuts and pistachios,
- Green tea, alcohol.

Interaction of DOACs with Dietary Supplements

In order to reduce the risk of cardiovascular disease, the European Society of Cardiology and the American Heart Association recommend the following:

- An appropriate daily calorie intake should be based on weight, age, and level of physical activity;
- Choosing fiber-rich whole grains, cereals, nuts, and legumes;
- Eating a variety of vegetables, fruits, skinless poultry, and fish and preparing them in a healthful manner;
- Limiting saturated fat, trans fat, sodium, red meat, sweets, and sugar-sweetened beverages;
- Drinking alcohol in moderation and avoiding smoking (Mach, *et al*., 2020; Cosentino, *et al*., 2020; Arnett *et al*., 2019)

Dietary supplements, such as oral products containing ingredients including vitamins, minerals, amino acids, herbs, or botanicals, as well as other substances that may be used to supplement the diet (Regan,2018), may affect blood clotting. On the other hand, European law (Directive 2002/46/CE) defines supplements as vitamins, minerals, herbs and other natural products sold in dosage forms such as tablets, pills or liquid ampoules.

Due to lack of awareness and knowledge, patients misinterpret recommendations, following a diet or using dietary supplements that may cause relevant clinical interactions with anticoagulants and other drugs. Until recently, warfarin was the most commonly used anticoagulant drug. The simultaneous consumption of foods rich in vitamin K (lettuce, broccoli, spinach, green peas)) has been associated with a risk of reduced therapeutic effect of VKA (Nutescu *et al*., 2006) while herbs such as St. John's wort and echinacea as a prolonged effect of the drug.

Currently, DOACs are the most commonly prescribed anticoagulants (Zhu, *et al*., 2018; Ho, *et al*., 2020). According to a US study, 30% of patients treated with warfarin and 20% of patients treated with apixaban (the most commonly used DOAC) take dietary supplements regularly (32). Patients treated with apixaban most commonly use (daily or most days): vitamin D, calcium, fish oil/omega-3 fatty acids/cod liver oil, B vitamins, vitamin E, and various herbal compounds. Respondents also reported consuming herbal teas (11.1%), turmeric (9%), St. John's wort (<1%), and other herbal products (Chinese herbs, ginger, ginkgo biloba - all less than 5%), which potentially modify apixaban exposure. (Tarn, *et al*., 2020)

Sales of dietary supplements are increasing worldwide, and sales of herbal medicines worldwide have doubled in the last 20 years. (Waddington, *et al*., 2015) When choosing these products, patients often accept the suggestions of the marketing service without cross-examination and research on the interaction of these substances with drug.s (Waddington, *et al*., 2015) Dietary supplements are used in the treatment of cardiovascular diseases such as hypertension, hyperlipidemia, coronary artery disease, stroke, and peripheral arterial disease, where patients are receiving drugs that may interact with the supplements to produce undesirable and life-threatening effects. However, their use together with DOAC therapy carries a risk of bleeding or a decrease in the therapeutic effect. (Eikelboom, *et al*., 2017) The potential effect of some of them with DOAC is shown in Table 1.

Table 1: Potential effect of food with DOAC

Substance	Source of substance	Substance	Source of substance
1.Alfa lipoic acid	Supplement's Human body	2.Bilobalide	G. biloba (Ginko)
3.Apigenin	Камилица чај	4.Biochanin A	T. pratense (Црвена детелина)
5.Avenanthramide (A, B, C)	Oats Chamomile	6.Caffein	C. arabica (Coffee, Cocoa)
7.Coumarin	Cassia cinnamon (Cinnamon)	8.Carbolines (Harmine)	L. Meyenii (Maca)
9.Capsaicin	Capsicum- (Chili peppers)	10.Chicoric acid, Alkylamides	G. Echinacea (nine species of echinacea)

Substance	Source of substance	Substance	Source of substance
11.Crocin	C.sativus (Saffron)	12, Curcumin	C. longa (Curcuma)
13.Ephedrine	Angelica sinensis (Apiaceae)	14. Eucalyptus oil	E. globulus (Еукалиптус)
15.Gingerol	Z. officinale Rosc (Ginger)	16.Ginkgolide A, B	G. biloba (Ginkgo)
17.Ginsenoside Rb, Rd	P. ginseng (Ginseng)	18.Glabridin	G. glabra (Licorice)
19.Grapefruit juice	C. paradisi (Grapefruit)	20.Guggulsterone	Guggul (Commiphoramukul)
21.Hyperforin, hypericin	H. perforatum (St. John's wort)	22.Lime extract	C.aurantifolia (Lime)
23.Nobiletin	C.reticulata (Mandarin)	24.Oleanolic acid	M. lucida (Brimstone tree) R. officinalis (Rosemary)
25.Omega-3 polyunsaturated fatty	Fish oil	26.Piperine	P. nigrum (Black pepper) P. longum (Long pepper)
27.Polyphenols	Theaceae (Green tea leaf)	28.Prunus avium extract	P. avium (Wild cherry)
29.Quercetin	A. melegueta (Melegueta pepper) C. sativus (Saffron) C. rotundus (Coco-grass) H. perforatum (St. John's wort) I. R. Nigrum (Black currant) S. costus (Costus) V. uliginosum L. (Bog bilberry)	30.Resveratrol	V. vinifera (Grape)
31.Rosmarinic acid	M. officinalis (Lemon balm) M.spicata (Spearmint) R.officinalis (Rosemary)	32.Silymarin	Silybum marianum (Asteraceae)
33.Vitamin E	Food	34.Valerenic acid	V. officinalis (Valerian)

The Platelet Inhibition Interaction with Food

Ticagrelor is a new antiplatelet agent that was pitted against clopidogrel in the Platelet Inhibition and Patient Outcomes (PLATO) trial. (Holmberg, *et al*., 2012) because ticagrelor is the first oral, reversible, twice-daily agent, sufficient information on drug interactions is not available. Соме Review indicates that renal adverse events (AEs) and renal function AEs were higher in ticagrelor-treated patients who were concomitantly treated with angiotensin receptor blockers (ARBs Clopidogrel-treated patients showed a trend for an increase in adverse renal events with ARB use. Moreover, in patients with a baseline eGFR <30 mL/min, the risk of major bleeding, death, and renal failure was increased in patients on ticagrelor compared to patients on clopidogrel.

Grapefruit juice increased ticagrelor exposure by more than two-fold, leading to an enhanced and prolonged ticagrelor antiplatelet effect. The grapefruit juice–ticagrelor interaction seems clinically important and indicates the significance of intestinal metabolism to ticagrelor pharmacokinetics. Such changes could directly affect the safety and effectiveness of the treatment with ticagrelor. (DiNicolantonio, *et al*., 2012)

5. Clinical Case Report

Case 1:

A 62-year-old patient, preoperatively prepared in the laboratory with a certain blood group and blood count with coagulation factors. The operation was postponed for 2 months due to the patient's work obligations. In the meantime, the patient consumed yarrow tea and hepatoprotective drugs. Before the operation itself, only a blood count was performed. During the gynecological operation itself, bleeding and severe rigidity of the blood vessels occurred, she lost a lot of blood, 2 units of blood and 1 plasma were given. Postoperatively, large hematomas on the surgical suture, anemia, low hemoglobin (before the operation 13, after

the operation with a given transfusion 8.3), hematomas at the site of infusion therapy.

Case 2:

A 62-year-old patient on tablet anticoagulant therapy due to 2 implanted heart valves. Preoperatively, aspirin was excluded for 5 days, 24 hours before the operation and after the operation, a drug from the DOAC group was excluded. A tooth was extracted in a dental office, the postoperative course was normal. During the 10 months postoperatively, episodes of bleeding from the gums 1-2 times a month, difficulties in placing dental bridges. After a dental examination and placed bridges on the upper jaw, 24 hours after the intervention, intense bleeding appeared in the area of the 2nd tooth on the upper right, without stopping. Local vasoconstrictor therapy, vitamin C and Almetex tablets were given. Anamnesis later revealed that the patient was taking cinnamon and turmeric as spices with food. And 7 days before that, he was also taking Eucalyptus tablets for a cold. These 3 supplements reduce coagulation.

Case 3:

A 23-year-old patient is taking Aspirin 100 mg tablets, prescribed by a cardiologist, for the prevention of microthrombosis due to an atrial shunt. When cleaning the ear canal with an earpick, skin damage occurred, which manifested itself as profuse bleeding. Referred to the emergency room and then to an ENT specialist, who after examination determined a skin lesion that stopped bleeding, without damage to the eardrum.

All these patients come from the same family, where turmeric, cinnamon, ginger, thyme, and other spices are regularly used. Concentration in the blood together with anticoagulant therapy can provoke bleeding. Due to the provocation of bleeding during pain, they use the central analgesic Paracetamol.

DISCUSSION

Taking supplements on your own has become very popular, especially with their intensive marketing on social media. Health care workers, on the other hand, stick to basic protocols for treating the disease without sufficient insight into what the patient is taking on their own.

There is no practice in health care institutions, nor among primary care doctors, to educate patients on a diet for a given disease. This is left to nutritionists as well as advice from social media. This leads to the risk of side effects due to synergistic or agonistic effects of food, supplements, and medications.(Grzesk, *et al*., 2021) The risk to patients, including the risk of bleeding, ultimately falls on the doctor who will be faced with this patient's condition.

When purchasing supplements and herbal medicines online, we are faced not only with insufficient assessment of the indication, but also with insufficient purity and organic origin of the supplement.

Physicians' clinical recommendations, which are based on the knowledge of drug indications, pharmacokinetics and pharmacodynamics, form a foundation of a safe and effective therapy. Unfortunately, patients' compliance with these recommendations is sometimes a serious problem. If patients do not take medications as recommended, the expected therapeutic effect may not be achieved. The more patients understand the meaning of diagnostic and therapeutic measures, the more they accept these measures, which significantly improves the effectiveness of therapy. (Djaoudene *et al*., 2023)

Unfortunately, oral direct anticoagulants are not free of side effects, which include gastrointestinal and intracranial hemorrhage. Long-term DOAC therapy may require gastric protection through the use of PPIs. Patients' adherence to therapeutic recommendations is a substantial problem. If the patient does not regularly take medication, the expected therapeutic effect may not be achieved.

CONCLUSIONS

The case studies and reports given in the presented text, providing information on food–drug or herb–drug interactions. The medical community should be more vocal in educating patients not to buy supplements or implement diets without consulting professionals. Patients decide on their own actions, but they are not always correct. Medical professionals should be aware of the interactions of drugs with certain types of foods, and exclude them from diet programs. Interactions between xenobiotics and food are a little-studied branch of science. Despite the everyday ubiquity of food and drugs, the lack of ongoing research or maintenance of specialised health service centres prevents the proper training of medical personnel and patients regarding their interactions.

Finally, it is time for the patient to be discharged. The physician is responsible for writing discharge orders, which may consist of continuing the same anticoagulation regimen prescribed preoperatively, changing the dosage, or even holding medication for some time. Such orders should again be checked by pharmacy personnel. In general, it is the nurse's responsibility to ensure that discharge instructions are received and understood by the patient, thus completing the interdisciplinary care circle for the patient receiving anticoagulation perioperatively. Only by working as an interprofessional team can the morbidity and mortality related to anticoagulation treatments and physician errors be diminished.

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