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Energy drinks among young people: trends and pharmacological mechanisms of adverse effects on the cardiovascular system. Review of the literature

Napoje energetyczne wśród młodzieży — tendencja i mechanizmy farmakologiczne niekorzystnego wpływu na układ sercowo-naczyniowy. Przegląd literatury

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Abstract

Energy drinks contain several ingredients with primarily stimulating effects. Consumption of these drinks greatly increased in the last several years, especially among young people. Recently, scientists focused on investigating their safety. Apart from its desirable effects like boosted mental and physical performance, studies show that energy drinks can also cause adverse effects, which currently remain not well described.

The purpose of this article was to present current trends in energy drink consumption among young adults and to describe the mechanisms of adverse effects, which might be caused by it.

The ingredients of energy drinks, like caffeine, consumed in high doses (> 200 mg/day), were shown to cause shaking, dizziness, heart palpitations, and sleep disorders. The excessive consumption of energy drinks can also lead to electrolyte imbalance, and heart-related diseases, e.g. myocardial infarction.

It is essential to familiarise oneself with the composition of the energy drinks and follow the recommendations for maximum daily intake of substances contained in these drinks. In addition, it is necessary to raise awareness of pharmacological mechanisms of possible side effects and to further the research on the consumption of energy drinks, especially among young people.

Key words: energy drink, cardiovascular system, pharmacological mechanism, adverse effect

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Introduction

Energy drinks (EDs) are non-alcoholic products containing caffeine, amino acids (taurine), plant stimulants (guarana), herbs (ginkgo biloba), and vitamins (niacin) [1]. EDs are used to increase energy, reduce fatigue, and improve physical and mental performance, however, they can also cause adverse effects when overused mostly due to the high level of stimulants like caffeine [2, 3]. Since Red Bull® introduced its ED to the Austrian market in 1987 and later to the USA in 1997, the market of EDs has developed at a very rapid pace [4].

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Caffeine is the main active ingredient in EDs, and its excessive consumption can lead to various adverse effects [5]. According to the European Food Safety Authority, teenagers between the age of 10 and 18 are the largest group consuming EDs. The increase in consumption and the risk of side effects influenced the World Health Organization guidelines, in which European Union countries were prompted to introduce regulations prohibiting the sale of EDs to children [6]. The overall mechanisms of ED's side effects are not well understood, with some publications pointing at the negative impact of the individual ingredients of EDs on the cardiovascular system [7]. The main aim of this article is to present the latest information on ED consumption habits among young adults, and the possible side effects. The summary of papers used in the review was collected in Table 1.

The consumption of energy drinks among young people

The popularity of non-alcoholic beverages is increasing at a very fast pace. The recent data showing the growing number of reports of adverse effects following ED consumption can be seen as a cause for some concern, and some governments are starting to take actions aimed at reducing the consumption of energy drinks [20].

A survey conducted among students of 4th and 5th year of faculty of medicine in the Medical University of Lodz, Poland showed, that 59% of women and 86% of men ($p = 0.003$) declared consumption of EDs, citing the support of mental health as one of the main reasons for consumption [8]. Following ED consumption 31% of students reported heart palpitations, which was the most common adverse effect caused by the consumption of EDs. About 20% of the respondents reported trembling hands/tremor and significant stimulation, and 9% of students noticed headaches. In a Canadian survey among adolescents and young adults (2055 respondents ages 12–24), 74% of respondents admitted to having ever consumed energy drinks, of which 55.4% reported that they had experienced at least 1 adverse event, including rapid heartbeat (24.7%), sleep problems (24.1%), and headache (18.3%) [9]. The prevalence of adverse effects was greater in coffee consumers than ED consumers. Another study included 68 volunteers at an average age of 25 years, who consumed 3 ED servings of 250 mL at an interval of 1 hour (total 240 mg of caffeine). Consumption of EDs caused an increase in diastolic blood pressure (BP), blood glucose levels, and increased discomfort in healthy young adults (such as headache, light chest pain, stomachache, excitation, anxiety), which was more prevalent after the second and third ED [10].

The adverse effects of consumption of energy drinks

Heart rate, blood pressure, calcium and magnesium level

Studies show that consumption of EDs can have an impact on heart rate (HR), BP, and calcium and magnesium levels [7, 11]. In the heart and smooth muscles, calcium acts as an intracellular messenger, which is involved in the activation of cardiac myocytes and muscles contraction [21]. In turn, magnesium is mainly involved in adenosine triphosphate (ATP) metabolism, myocardial and smooth muscle contraction, and relaxation through calcium reuptake [22]. In a study conducted by Kozik et al. [11], the authors showed that ED consumption (960 mL) significantly increases the baseline systolic BP by approximately 20 mm Hg (from 132 ± 7.83 to 151 ± 11.21 mm Hg, $p = 0.001$) [22]. Additionally, the magnesium level (change from 2.04, ± 0.09 to 2.13, ± 0.15 mEq/L, $p = 0.05$) and calcium level (change from 9.31, ± 0.28 to 9.52, ± 0.22 mg/dL, $p = 0.018$) were significantly increased compared to baseline. Similarly, Basrai et al. [12] demonstrated that 1-hour post-consumption the EDs caused an increase in systolic BP in a group of young adults (mean age 22 years), which was also observed after consumption of caffeine without taurine or glucuronolactone. The impact of caffeine consumption is mainly based on the antagonism against the adenosine receptors A1 and A2. Activation of adenosine receptors causes sleepiness and fatigue by inhibiting glutamine and dopamine secretion. Moreover, caffeine increases the secretion of norepinephrine and epinephrine by inhibiting phosphodiesterase enzymes [23]. Epinephrine and norepinephrine are synthetic amines that stimulate alpha and beta-adrenergic receptors. Their action is primarily based on peripheral vasoconstriction and increase of heart rate caused by their binding to G protein-coupled receptors on the cellular membrane [24]. The change in calcium level observed after ED consumption may be caused by the activity of taurine, which is one of the main ingredients of energy drinks. Taurine has a stimulating effect on sarcoplasmic reticular Ca^{2+} pump and may increase the exchange activity of Na^{+}/Ca^{2+}. These activities respond to the translocation of calcium from the intracellular to the extracellular space, which causes an increase in calcium level in blood [25]. The pharmacological rationale for the increase in magnesium level after consumption of EDs has not been described yet. High levels of calcium and magnesium are associated with disorders of vascular homeostasis. Magnesium acts by rendering the calcium channels available at sites critical for contraction, which allows for calcium to enter vascular cells resulting in vasoconstriction, which can further

Table 1. The most important studies investigated the adverse effects of energy drinks

Authors	Energy drink type and volume	Examined group	Caffeine content	Sugar/taurine content	Study findings
Chuda et al. [8]	Type not given	131 students (4^{th} and 5^{th} year of medical degree)	–	–	31% of students had heart palpitations, 20% — trembling hands/ /tremor and significant stimulation, 9% noticed headaches after consumption of energy drinks
Hammond et al. [9]	Type not given	2055 (12–17 years)	–	–	Of the respondents who had consumed energy drinks, 55.4% reported that they had experienced at least 1 adverse event, including rapid heartbeat (24.7%), sleep problems (24.1%), and headache (18.3%)
Nowak et al. [10]	Type not given, 3 × 250 mL	68 volunteers (average aged 25 years)	240 mg	–	↑ diastolic blood pressure, ↑ blood glucose levels, ↑ discomfort in healthy young adults after consumption of EDs
Kozik et al. [11]	Monster®, 2 cans	14 healthy young subjects (average age 28.6 years)	–	–	↑ systolic blood pressure, ↑ level of magnesium and calcium 4 h post-consumption
Basrai et al. [12]	Red Bull®, 750 mL and 1000 mL	38 adults (average age 22 years)	32 mg/ /100 mL caffeine	Taurine 400 mg/100 mL, glucuronolactone 31 mg/100 mL	↑ systolic blood pressure and a QTc prolongation 1-h post--consumption
Steinke et al. [13]	Type not given, 500 mL	15 volunteers (average age 25.9 ± 5.9 years)	200 mg	Taurine 2000 mg	↑ HR and systolic blood pressure after ingestion, maximum change 4 h post-consumption
Wajih et al. [14]	Type not given, 7–9 cans daily	25-year-old man	About 1400–1800 mg daily	–	Induction of myocardial infarction after consumption of 7–9 cans of energy drinks daily for one week before admission to the hospital
Scott et al. [15]	Red Bull®, 2–3 cans daily	19-year-old man	400–600 mg daily	–	Induction of myocardial infarction after consumption of 2–3 cans of energy drinks daily for the last week before admission to the hospital
Ünal et al. [16]	Type not given	32-year-old man	–	–	Induction of myocardial infarction after consumption of 5 bottles of energy drinks 5 h before admission to the hospital
Solomin et al. [17]	Type not given	26-year-old male	–	–	Induction of myocardial infarction after consumption of 4 litres of energy drinks per day before admission to the hospital
Mattioli et al. [18]	Type not given, 600–700 mL	3 patients, average aged 24 years	–	–	After consuming a large amount of energy drinks (600–700 mL) developed AF with high ventricular activity (ventricular rate 135–170 beats per minute)
Baum et al. [19]	Red Bull®, 500 mL	13 athletes	160 mg	Taurine 2000 mg, glucuronolactone 1200 mg	↑ systolic blood pressure and stroke volume, ↓ left ventricular end--systolic diameter after exercises

ED — energy drink; HR — heart rate

manifest as hypertension [26]. Additionally, low levels of magnesium, as well as elevated calcium to magnesium ratio, have been shown as an independent risk factor for death in patients with coronary artery disease [27]. These results emphasize the risks associated with the potential taurine-induced Ca^{2+} imbalance.

Shaking, dizziness and sleep disorders

Published studies indicate that the consumption of beverages containing up to 200 mg of caffeine does not cause significant adverse effects on health. However, an increase in the caffeine dose above 200 mg usually leads to shaking, dizziness, heart palpitations, and sleep disorders [8, 13, 23]. Caffeine increases the level of aminobutyric acid (GABA) A receptors and sensitivity which is most likely involved in the onset of shaking and dizziness [28]. Caffeine also stimulates the secretion of adrenaline and noradrenaline causing increased activity of the sympathetic nervous system, which is responsible for attention and arousal, thus possible sleep disorders following caffeine consumption [23]. Steinke et al. [13] showed that daily consumption of EDs (200 mg of caffeine) for 6 days caused adverse effects such as shakiness, gastrointestinal symptoms, increased urination, sleep disorders, and more forceful heartbeats in 47% of the subjects.

Torsade de pointes

Consumption of EDs can impact the cardiovascular system which can be observed in the results of the electrocardiography (ECG), where the different section of graphical heart electric activity presentation is analysed. Consumption of EDs can result in QT section elongation in ECG, which can be caused by disorders of ion channels of heart cells. It leads to ventricular abnormalities of the myocardium, specifically causing *torsade de pointes* (so-called 'ballet of the heart') [29]. Basrai et al. [12] showed that single-use of 320 mg of caffeine, 4000 mg of taurine, and 310 mg of glucuronolactone consumed in energy drinks causes the extension of the QT section from 3 to 8 ms in young adults. An increase in the interval between Q- and T-peaks is considered an indicator of substances capable of inducing arrhythmias. This effect was visible 1 hour after the consumption of EDs. So far, the mechanism of Torsade de Pointes induction following the consumption of EDs has not been discovered due to the complex interactions that occur between the various ingredients [12].

Myocardial infarction

Recently, some case reports pointed towards the existence of a relationship between the consumption of energy drinks and the occurrence of myocardial infarction in young adults [30–32]. In 2018, a 25-year-old patient was admitted to the hospital emergency department with symptoms of chest pain accompanied by nausea, vomiting, and shortness of breath [14]. The severe pain appeared suddenly and radiated to the right arm. The patient has been consuming 7–9 cans of EDs containing caffeine daily for the last week, which equals approximately 1400–1800 mg of caffeine per day. After sublingual application of nitroglycerin and intravenous administration of morphine, the patient's condition markedly improved. ECG examination showed sinus rhythm with ST-segment depression in precordial leads V2–V6, which most likely demonstrates an anterolateral wall myocardial infarction. Additionally, laboratory results showed elevated levels of a marker of myocardial necrosis — troponin I — 32.22 µg/mL (norm < 0.07 µg/mL). A similar case concerned a 19-year-old patient, who was admitted to the hospital emergency department due to a sudden chest pain radiating to his right arm [15]. The pain subsided after sublingual application of nitroglycerin and intravenous administration of diamorphine. The patient disclosed consuming 2–3 cans of Red Bull per day in the week preceding hospital admission. ECG examination revealed 2 mm ST-segment elevation in leads I, II, aVL and V4 to V6, and 2 mm ST-segment depression in leads V1 and V2. Similarly to the previous case, laboratory tests showed an elevated level of troponin I — 34.67 µg/mL The studies showed posterolateral myocardial infarction likely caused by ED consumption. Another case described a 32-year-old male patient who was admitted to the hospital emergency department with retrosternal chest pain and emesis [16]. These symptoms occurred 5 hours before admission to the emergency department, after drinking 5 bottles of EDs, however, the authors did not specify the volume of consumed drinks. The ECG examination showed ST-segment elevation in V2–V6 leads. An emergent coronary angiogram was performed, which showed thrombi occluding 90% of the diameter of the left main coronary artery and proximal left anterior descending artery. Balloon angioplasty was performed in this case to ensure flow through the occluded vessels. Solomin et al. [17] presented a case report of another individual, a 26-year-old male who developed a myocardial infarction after ED consumption. This patient was admitted to the hospital emergency department following consumption of 4 litres of EDs daily. The patient reported pain located in the chest, the left arm, and the jaw. ECG showed significant ST-elevation in the inferior leads. Coronary angiography was performed and showed 100% occlusion of the left circumflex artery which prompted physicians to perform balloon angioplasty and insert a drug-eluting stent.

The risk of myocardial infarction was associated with the consumption of EDs, which is responsible for increasing platelet aggregation and generating endothelial dysfunction [33, 34]. Glucose, which is one of the main components of EDs causes endothelial cell dysfunction which is associated with the possibility of coronary atherosclerosis [35]. The mechanism of endothelial cell injury includes

initiation of apoptosis in endothelial cells, increasing the activity of the proapoptotic protein Bax and causing activation of caspase-3 proteins by phosphorylation of the p38-MAPK pathway [36]. The cases of cardiologic side effects following the ED consumption were observed in patients as young as 19-years-old, which indicates a high risk of ED overuse among young adults, resulting in serious consequences, including myocardial infarction.

Atrial fibrillation

Atrial fibrillation (AF) is a heart arrhythmia caused by a structural remodelling of the atria and ventricles due to previous heart diseases, and the following change of the electrical discharges in the atria. AF causes irregular atrial contractions and ineffective blood flow to the ventricles, which can lead to clot formation and stroke [37]. Mattioli et al. [18] showed an association between consumption of EDs and the possibility of AF induction. After consuming a large amount (600–700 mL) of EDs, 3 patients (mean age 24 years) developed AF with high ventricular activity (ventricular rate 135–170 beats per minute). After electrical cardioversion, ECG and echocardiogram were normalized in all patients [18]. Heart arrhythmia, like AF, is often caused by electrolyte imbalances. High doses of caffeine also reduce the cellular potassium level, which can generate arrhythmia due to the stimulation of the Na/K pump. The increased activity of the Na/K pump causes hypokalemia, increasing the resting potential of myocardial cells which affects the risk of AF [38].

Conclusions

Measures restricting the sale of EDs could be needed due to the increasing number of studies reporting their negative effects on the human body. Studies show that ED consumption can cause a significant increase in BP, heart rate, prolonged QT, and cause electrolyte imbalances [11, 12, 19]. Greater attention should also be paid to the potential risk of myocardial infarction following excessive ED consumption [14]. Recent reports on EDs present the real possibility of their influence on platelet function and coagulation pathways [39, 40]. Studies describing the adverse effects of ED consumption are usually based on small study groups, therefore future efforts should focus on performing research on larger cohorts with emphasis on observed side effects for more comprehensive evaluation.

The expansion of ED consumption is taking place at a rapid pace. One of the main solutions to the potential problems it may cause is rational and responsible consumption. Consumption of EDs can help with concentration, physical and mental performance, and reduce fatigue, but they also should be consumed in moderation due to several adverse effects. Due to the increasing consumption of EDs, it is important to pay increased attention to the adverse effects of the following consumption and to investigate their mechanisms. Therefore, asking about frequency and volume of consumed EDs as well as their ingredients for complete medical history should be considered more often, especially among younger patients, and patients presenting cardiac symptoms.

Author contributions

The roles of authors: Hałasiński Przemysław: was responsible for the conception and design of the study, literature search, writing of the first draft and subsequent drafts. Musielak Marika: was responsible for reviewing the paper for completeness, critical revisions of the manuscript. Piotrowski Igor: was responsible for reviewing the paper for completeness, critical revisions of the manuscript, and approval of the final version submitted for publication.

Conflict interest

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Streszczenie

Napoje energetyczne zawierają wiele różnych składników o działaniu przede wszystkim pobudzającym. Spożycie tego rodzaju napojów znacznie się zwiększyło w ostatnich kilku latach, zwłaszcza wśród młodzieży. Ostatnio naukowcy skupili się na zbadaniu bezpieczeństwa spożywania tych napojów. W badaniach wykazuje się, że oprócz pozytywnych efektów, takich jak zwiększenie wydolności psychicznej i fizycznej, napoje energetyczne mogą również powodować działania niepożądane, które obecnie nie są dobrze opisane.

Celem niniejszego artykułu było przedstawienie aktualnych trendów w konsumpcji napojów energetycznych wśród młodych dorosłych oraz opisanie mechanizmów działań niepożądanych, które mogą być przez nie wywoływane.

Wykazano, że składniki napojów energetycznych, takie jak kofeina, spożywane w dużych dawkach (> 200 mg/d.) powodują drżenia, zawroty głowy, kołatanie serca i zaburzenia snu. Nadmierne spożycie napojów energetycznych może również prowadzić do zaburzeń równowagi elektrolitowej, a także chorób związanych z układem sercowo-naczyniowym, np. zawału serca.

Niezbędne jest zapoznanie się ze składem napojów energetycznych i przestrzeganie zaleceń dotyczących maksymalnego dziennego spożycia substancji zawartych w tych napojach. Ponadto konieczne są zrozumienie mechanizmów farmakologicznych oraz dalsze badania nad możliwymi niepożądanymi skutkami spożywania napojów energetycznych, zwłaszcza wśród młodych osób.

Słowa kluczowe: napój energetyczny, układ sercowo-naczyniowy, mechanizm farmakologiczny, działanie niepożądane

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