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OPIS PRZYPADKU / CASE REPORT
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Multiple iatrogenic syndrome in older women – drug-induced hypothyroidism, memory impairment, hypoglycaemia, bradycardia, syncope and falls

Złożony jatrogenny problem geriatryczny – polekowa niedoczynność tarczycy, zaburzenia poznawcze, hipoglikemia, bradykardia i upadki

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Abstract

Pharmacotherapy in geriatric patients is challenging for all physicians. A proper, individual treatment strategy depends on careful clinical assessment of a patient in terms of present and chronic conditions. Appropriate decisions lead to avoidance of complicated, unnecessary, harmful and duplicated medications. The following case report presents drug-induced multiple iatrogenic syndrome and deficiency in coordinated medical care in a geriatric patient with 31-item therapy. (Gerontol Pol 2019; 27; 83-88)

Key words: *geriatric iatrogenic syndrome, polypharmacy, adverse drug reactions*

Streszczenie

Polifarmakoterapia u pacjentów geriatrycznych jest wyzwaniem dla wszystkich lekarzy. Odpowiednia, indywidualnie dobrana terapia jest zależna od dokładnej oceny klinicznej aktualnych oraz przewlekłych schorzeń. Rozsądne decyzje pozwalają uniknąć skomplikowanych, niepotrzebnych, uciążliwych oraz powielonych schematów leczenia. Poniższy opis przypadku opisuje jatrogenny zespół polekowy o złożonej etiologii oraz wskazuje na deficyty skoordynowanej opieki medycznej w przypadku pacjenta geriatrycznego z 31-lekową terapią. (Gerontol Pol 2019; 27; 83-88)

Słowa kluczowe: *geriatryczny zespół jatrogenny, polifarmakoterapia, polekowe działania niepożądane*

Introduction

The case study presents multiple iatrogenic syndrome induced by inappropriate and duplicated medications, as well as polypharmacy, in older patient admitted to a geriatric ward due to recurrent syncope and falls. Advantages of geriatric approach include drug reduction [1] and treatment optimization according to the Beers [2] and STOPP/START [3] criteria.

Polypharmacy contributes to serious medical errors [4], frequent hospitalization and re-hospitalization, higher risk of death [5], and also puts large economic and social burden on individuals. This case also highlights the difficulties in cooperation between specialists and general practitioners (GP) taking care of older patient with comorbidities.

Case presentation

A 76-year-old woman was referred by geriatric out-patient clinic to the ward in August 2017 due to recurrent past pre-syncope and falls and long-term polypharmacy (31 drugs) for treatment optimization. She was suffering from post-herpetic neuralgia, vertigo, falls, constipations, depressive mood, memory impairment and general fatigue lasting for at least six months. Past medical history revealed diabetes mellitus type two, osteoarthritis,

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glaucoma, depression, chronic sinusitis, and ischemic heart disease with two documented episodes of paroxysmal atrial fibrillation. The first episode occurred in 2014 (arrhythmia was ceased with propafenon), and the second in 2016 (the amiodarone therapy was initiated). As a result hypothyroidism appeared subsequently, and levothyroxine was originated. Due to multimorbidity, the patient was under irregular control of a cardiologist, an endocrinologist, a neurologist, an ophthalmologist, a laryngologist, a pain care specialist, a psychiatrist and all of their prescriptions were continued by a GP. The original list of patient's drugs is presented in Figure 1 and Table I, panel A.

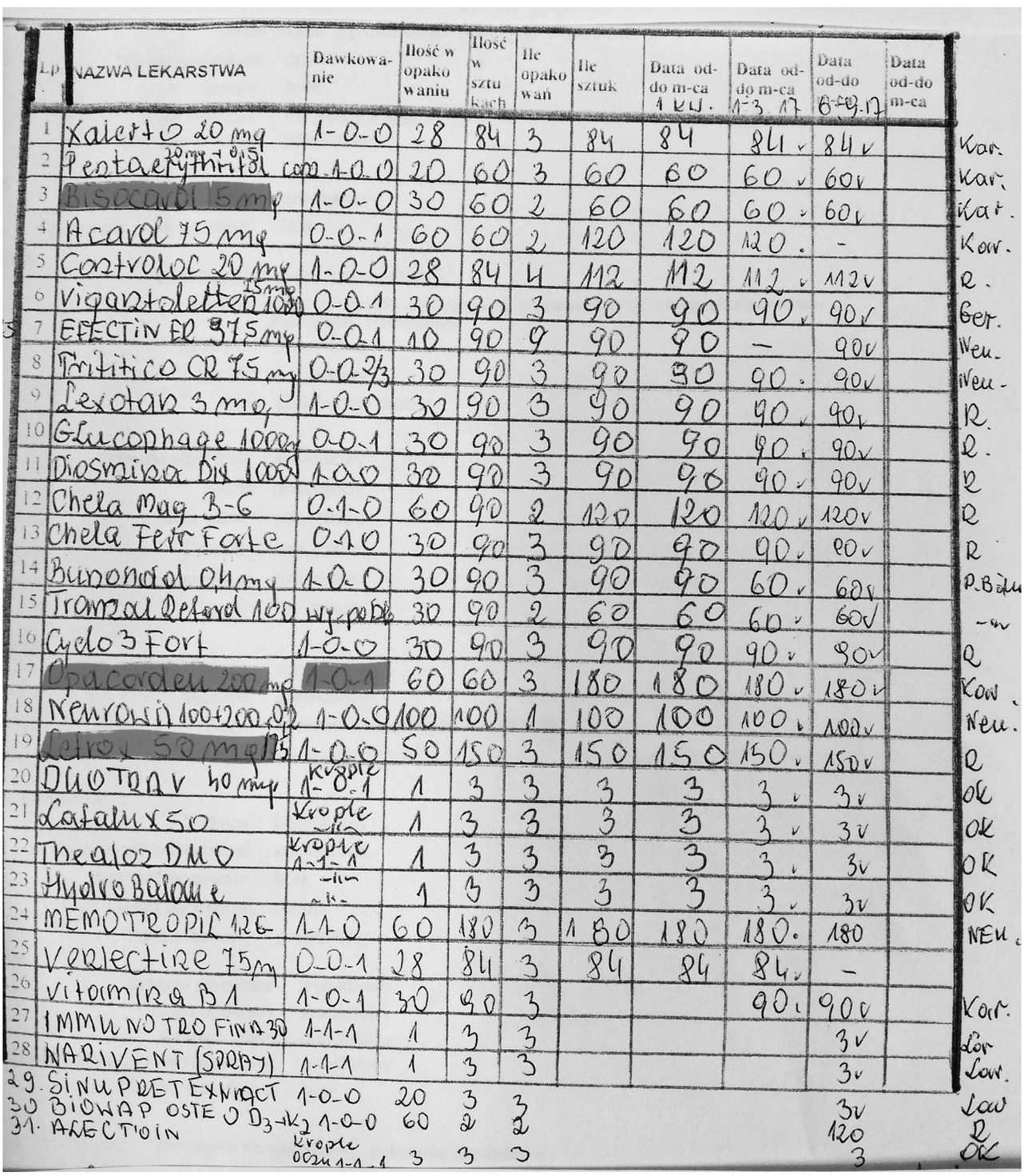

Figure 1. The original list of the patient medications

Table I. Patient's pharmacotherapy

	A. Before geriatric intervention (August 2017)		B. After geriatric intervention September 2017)		C. After cardiological intervention (September 2018)		D. Current prescription (December 2018)	
1	Rivaroxaban (20mg)	1-0-0	Rivaroxaban (20mg)	1-0-0	Rivaroxaban (20mg)	1-0-0	Rivaroxaban (20mg)	1-0-0
2	Nitroglycerin (20mg+ Pentaerythritol 0.5mg)	1-0-0						
3	Bisoprolol (5mg)	1-0-0			Metoprolol (47,5 mg)	1-0-0	Metoprolol (47,5 mg)	1-0-0
4	Acetylsalicylic acid (75mg)	0-0-1						
5	Pantoprazole (20mg)	1-0-0					Pantoprazole (20mg)	1-0-0
6	Cholecalciferol (1000UI)	0-0-1					Cholecalciferol (3000UI)	0-0-1
7	Venlafaxine (37.5mg)	0-0-1			Duloxetine (60 mg)	1-0-0	Duloxetine (60 mg)	1-0-0
8	Trazodone (75mg)	0-0-2/3			Trazodone (75mg)	0-0-2/3	Trazodone (75mg)	0-0-2/3
9	Bromazepam (3mg)	1-0-0						
10	Metformin (1000mg)	0-0-1						
11	Diosmin (1000mg)	1-0-0						
12	Magnesium (100mg) + vitamin B6 (2.1mg)	0-1-0						
13	Iron (14mg) + vit B6 (1.4mg) + vit B12 (2.5 µg) + Folic acid (200 µg)	0-1-0						
14	Buprenorphine (0.4mg)	1-0-0						
15	Tramadol (100mg)	As needed					Tramadol (100mg)	As needed
16	Ascorbic acid (150mg) + Hesperidine (150mg) + Ruscus aculeatus (100mg)	1-0-0					Ascorbic acid (150mg)+ Hesperidine (150mg)+ Ruscus aculeatus extract (100mg)	1-0-0
17	Amiodarone (200mg)	1-0-1					Amiodarone (200mg)	1-0-1
18	Cyanocobalamin (0.2mg)+ Pyridoxine (200mg) + Thiamine (100mg)	1-0-0						
19	Levothyroxine (50 µg)	1-0-0	Levothyroxine (75µg)	1-0-0	Levothyroxine (75 µg)	1-0-0	Levothyroxine (75 µg)	1-0-0
20	Timolol (5mg), Travoprost (0.04mg) (eye drops)	1-0-1	Timolol (5mg), Travoprost (0.04mg)	1-0-1			Timolol (5mg), Travoprost (0.04mg)	1-0-1
21	Latanoprost (50 µg/ml) (eye drops)	1-0-1					Latanoprost (50 µg/ml)	1-0-1
22	Hyaluronic acid (1.5mg) + Trehalose (30mg) (eye drops)	1-1-1						
23	Hyaluronic Acid (eye drops)	1-1-1						

24	Piracetam (1200mg)	1-1-0								
25	Venlafaxine (75mg)	0-0-1								
26	Thiamine (3mg)	1-0-1								
27	Oral herbal spray	1-1-1								
28	Nasal spray for sinusitis	1-1-1								
29	Herbal tablets for sinusitis	1-0-0								
30	Calcium (500mg) + Colecalciferol (25 µg) + Menachinon (15 µg)	1-0-0								
31	Ectoine (drops for eye dryness)	1-1-1	Ectoine (drops for eye dryness)	1-1-1						
32	Acetaminophen (1g)	As needed								
33									Propafenon (150 mg)	As needed
34					Toramide (5 mg)	″-0-0			Toramide (5 mg)	1-0-0
35									Eplerenone (25mg)	1-0-0
36			Pregabalin (150 mg)	0-0-1	Pregabalin (150 mg)	1-0-1			Pregabalin (150mg)	1-0-1
37									Betahistine (24 mg)	″-0-″

The list included: beta-blocker, nitrates, anticoagulant with antiplatelet, proton-pump inhibitor and vasoactive drugs, duplicated venlafaxine and trazodone, oral antidiabetic medications, opioids, vitamins, minerals and other.

On physical examination she presented recurrent bradycardia (heart rate 40 per minute) with the longest RR interval lasting 1796 msec., hypotension (blood pressure 100/60 mmHg), bruises on the skin. Elevated levels of vitamin B12 (1057.0 pg/ml) and TSH (10.23 mIU/l) and lowered HbA1C (5,4%) were found in laboratory findings. The 24-hour Holter-ECG revealed the sinus bradycardia (from minimum 42 beats per minute to maximum 62 per minute). Depression and mild cognitive impairment were confirmed in a neuropsychological examination. The patient required a moderate care assistance in personal and instrumental activities of daily living (housework, shopping, taking own medications, grooming, stair walking, and incidental urine incontinence).

After discontinuation of anti-arrhythmics (β-blocker and amiodarone) heart rate was normalized; however, the post-amiodarone hypothyroidism required an increase in the dosage of levothyroxine. The double anticoagulation (rivaroxaban and acetylsalicylic acid) was shifted into rivaroxaban only. The benzodiazepine (risk of falls) and oral antidiabetics (hypoglycaemia) was withdrawn. Additionally, the analgesic treatment was replaced by acetaminophen and pregabalin (post-herpetic neuralgia) instead of tramadol and oral buprenorphine (constipations and risk of serotonin syndrome in compilation with SSRI and SNRI used by patient). Based on the ophthalmologist consultation, patient's four items of eye-drops were limited to two. Due to overdosing of vitamin B12 and D3 these supplements were discontinued.

On discharge, the patient presented normal blood pressure (120/70 mmHg), slight bradycardia (50/min.), better mood and general improvement without vertigos. Finally, seven indispensable medications were recommended for further treatment (Table I, Panel B). In the meantime, after several months (August 2018), the patient was urgently hospitalized at the Cardiology Department, due to symptomatic tachyarrhythmia and chronic atrial fibrillation that were diagnosed. The β-blocker was initiated again and diuretics were initiated (Table I, Panel C). A further visit to cardiologist caused multiplication of anti-arrhythmic treatment (amiodarone and propafenon) prescribed with recommendation to use as needed.

In the next five months (December 2018), the patient was invited to Geriatric Out-patient clinic to follow-up her treatment and clinical conditions. The final list of 18-item medications is presented in Table I, Panel D. The

patient presented with vertigos, chronic tiredness, however, without any syncope or falls. On physical examination: sinus bradycardia (40 per minute) and hypotension (100/60 mmHg).

Discussion

Pharmacotherapy in a geriatric patient is extremely demanding. The co-incidence of many past and present conditions and co-existing abnormalities prompt a careful clinical assessment and subsequent treatment strategy adjusted to an individual patient. Proper decisions and choices lead to avoidance of unnecessary, harmful, duplicated and inappropriate therapy[6].

The presented case study illustrates a multiple iatrogenic problem following a cascade of unfortunate and single treatment decisions taken by different specialists without any cooperation which led to polypharmacy and drug-induced abnormalities. The position of a GP as a potential therapy coordinator also failed, as the GP was passively prescribing all of 31 medications, confirming the list of prescriptions with his own signature.

Episodes of syncope in course of bradycardia with repeated falls seem to be the most dangerous drug-induced outcome in this patient. The synergic effect of β-blocker and amiodarone usually leads to symptomatic bradycardia that has to be monitored during treatment. For patients with symptomatic paroxysmal or persistent atrial fibrillation, amiodarone is considered as the first line therapy, however, due to long-term drug effectiveness[7], the treatment should be cautiously monitored and if ineffective or harmful, the decision on discontinuation should be taken. Molecular structure of amiodarone contains iodine which is involved in thyroid hormones metabolism. In pharmacokinetics, a great amount of iodide is released in the metabolism and inhibits thyroid hormone biosynthesis[8]. Hypothyroidism is one of amiodarone's side effects [9]. The medical documentation of our patient conclusively confirms the relationship between amiodarone and hypothyroidism. Moreover, three months after initiation of amiodarone therapy, the tenfold increase of TSH serum level (43 uIU/l) was observed. The need for higher and higher levothyroxine supplementation appeared to balance the thyroid metabolism. It constitutes an example of a drug cascade in our patient when one medicine is used for side effect of another. During amiodarone therapy all possible consequences (e.g. symptomatic bradycardia, vertigos, falls, somnolence, thyroid performance, lung fibrosis, ophthalmologic disorders, depression and many other) should be taken into consideration and supervised by the specialist initiating therapy.

Drug duplication referred to venlafaxine taken under two trade names of this substance, as well as to cholecalciferol (3 items of drugs). Furthermore, latanoprost and travoprost, both of the same origin, should not have been taken in parallel to reduce the intraocular pressure in glaucoma. The inappropriate, double anticoagulant therapy (rivaroxaban and acetylic acid), raised the risk of coagulation disorders in our patient (bruises in the skin). The anti-thrombotic prophylaxis in atrial fibrillation according to guidelines is clear, and only one of the oral anticoagulant should have been used, e.g. rivaroxaban in our patient [10].

A combination of SNRI (venlafaxine), SSRI (trazodone) and opiates (buprenorphine and tramadol) causes a potential risk for serotonin syndrome[11]. Luckily for the patient, the dangerous consequences of inappropriate drug therapy did not appear.

Benzodiazepines (bromazepam), especially along with overdosed antiarrhythmics, cumulatively affected the risk of falls, as well as negatively influenced the cognitive performance in our patient (internal anticholinergic activity). The discontinuation of bromazepam contributed to a cognitive improvement (MMSE in 2017 26/30 vs. MMSE in 2018 29/30). Due to depression probably determined by comorbidity and a difficult family situation, our patient became more dependent from other people in activities of daily living than a year earlier.

Despite the fact that the Polish Medical Care System obliges the GP to complex and coordinated care for older adults, it does not work in practice. As a result, the older and comorbid patient remained alone with her medical problems.

Regular verification of patients' drugs lists, asking about understanding of the recommendation will ensure patients health, money and time.

Conclusions

- Side effects of polypharmacy and drug cascades cumulate and generate the multiple iatrogenic syndromes and life-threatening outcomes.
- The geriatric knowledge and specificity of geriatric pharmacotherapy should be developed in all specialists, especially in general practitioners.
- The geriatrician and geriatric approach in health care system should be valued and more available.
- The regular review all of medications taken by an older patient should be systematically verified by physicians, irrespectively of specialty, during each visit.

A written informed consent for publication of clinical details and/or clinical images was obtained from the patient. The case study conforms the Helsinki Declaration.

Konflikt interesów / Conflict of interest
Brak/None

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