



## A SHORT REVIEW OF DRUGS WHICH PRESENT AN INCREASED IATROGENIC RISK IN ELDERLY PATIENTS

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**Abstract.** Elder patients are cumulating multiple risk factors that are exposing them more for drug-induced iatrogenic events: physiological variations associated to the ageing process, multiple morbidities and multiple medications-taking, are frequent in aged people and can significantly modify the pharmacological properties of the used drugs. Different interactions between these factors are responsible for a high prevalence and for a potential severity of the iatrogenic pathology in this age category. Most of the undesired consequences in patients over 65 years old can be avoided if the clinical situations and the high-risk drugs are pre-identified. For an optimization of the medical prescription in elderly process some of the following measures are to be taken: evaluating of the benefit/risk ratio for each of the recommended drugs, follow-up evaluating and regular updating of the chronic prescription, ranking the therapeutic goals taking into account the evolution of the disorder, its symptoms and their impact on the patient and the etiological or preventing character of the drugs being used. Also, a better therapeutic co-operation between the prescription-writers (general practitioners and specialists) who are consulting and prescribing for the same patient seems to be indispensable.

**Keywords:** drugs, medical prescription, elderly patients

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Within the context of a significant numerical increase of the elderly population in the last few decades and of a higher and higher number of inadequate medical prescriptions for this category of age, pharmacotherapy in elderly patients has become one of the most important public health problems, because of the financial costs which it implies.

Aged people cumulate several risk factors and so they are exposed to an increased risk for drug-related iatrogenic events: age-related important physiological variations (that are affecting the pharmacokinetic properties and the pharmacody-

namic activity of drugs) and multiple drug-taking (very common after the age of 65), are two of these factors.

Different combinations of these factors are responsible for a potential severe iatrogenic pathology in the aged population. Multiple studies have shown that the undesired effects caused by the current drug intake are about 2-4 times more frequent after the age of 65 years and in most of the cases patient's hospitalization is absolutely necessary.

Thus a drug-related cause has to be always taken into consideration when an aged person presents a health alteration without an obvious clinical explanation instead.

In 30-60% of the cases we can talk about an avoidable drug iatrogenic pathology, because the adverse effects of the medicines are predictable and can be avoided.

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Frequently, the undesired manifestations of the medication are consequences of a therapeutic error (inadequate indication of a drug, inconsideration of a contraindication, treatment prescribed for a too long period of time, excessive dosage, low adherence of the patient to the treatment, self-medication – very usual in elders taking multiple medications).

For reducing the incidence of undesired drug effects in geriatric populations and for confining the inadequate drug prescriptions in these patients, this paper presents several specific aspects which refer to the drug classes that nowadays are considered having the highest iatrogenic risk in elderly people.

This information (a non-exhaustive one) tries to turn the prescribers' attention to the importance of ranking the therapeutic goals and of evaluating the benefit/risk ratio before initial or follow-up pharmacotherapy in aged patients.

class for attenuating the symptoms of a cardiac failure in elders and for improving their quality of life. Their goal is to reduce the hyper-volemic charge and to avoid a pulmonary congestion or an acute pulmonary edema. Also, most of the studies have shown that monotherapy thiazides used in low dosage (hydrochlorothiazide – 12.5-25 mg per day) or different associations between thiazides and potassium-sparing diuretics significantly reduce the cardiovascular mortality and the incidence of stroke in hypertensive aged patients.

When choosing the right diuretic, its administration route and its edema-diminishing potency, the therapy must be patient-centered. When the situation is not severe (acute pulmonary edema, hypertensive encephalopathy), diuretics are taken on the oral route.

*Hydrochlorothiazide* has a low natriuretic effect in elderly patients with cardiac failure, because

| Drug - class                 | Substance                   | Geriatric dosage (mg per day) | Observation   |
|------------------------------|-----------------------------|-------------------------------|---|
| Thiazide diuretics           | Hydrochlorothiazide         | 12.5 - 25                     | If CrCl* is < or = 30 mL per minute, it has no efficiency |
| Loop - diuretics             | Furosemide                  | Individualized therapy        | It is efficient even when renal failure is present        |
| Potassium -sparing diuretics | Spironolactone<br>Amiloride | 12.5 - 25                     |   |

\*CrCl – creatinine clearance

**Table I.** Recommended diuretics for elderly patients

## Recommendations on specific therapeutic classes

### A. Cardiovascular drugs

#### 1. Diuretics

The kidney is a target organ for hemodynamic and neurohormonal modifications which occur when a cardiac failure is evolving. In this situation we notice an intra-renal vasoconstriction with a decrease of the glomerular filtration rate.

On short term, this compensatory mechanism has its benefits, because it favors the hydro-saline retention, ensuring a sufficient cardiac flow for the vital organs' perfusion (brain, cardiac muscle). But then on long term, these variations exacerbate cardiac failure and promote edema.

Diuretics remain a much used pharmacologic

sodium reabsorption is high in the proximal convoluted tubule of the nephron, while this diuretic is active on the distal convoluted tubule. Because the renal perfusion is often compromised in these patients, the Na<sup>+</sup> ions' concentration which can be found at distal convoluted tubule level is also reduced.

Hydrochlorothiazide can be used in patients with mild congestive cardiac failure in which the kidney function is not altered, in association with an angiotensin-converting enzyme inhibitor (ACEI).

Dosage will depend on the patient's symptomatology, and will be individualized for a constant maintenance of the patient's body weight and general condition. It is not efficient in patients suffering from kidney failure, having a CrCl lower than 30 mL per minute.

### *Furosemide*

As the cardiac failure is getting worse, it is recommended the use of a powerful diuretic. Furosemide's natriuretic effect is rapid, potent and short-lived (4 to 6 hours). The usual administration route is the oral route and the dosage is individualized based on the clinical condition of the patient.

In aged people with acute pulmonary edema, furosemide is the commonly used diuretic, administered on parenteral route because of its very rapidly settled action and its higher efficiency, in spite of the presence of a kidney failure. Alongside the rapid hydro-saline depletion, intravenous furosemide also reduces tension in the pulmonary capillaries, thus ameliorating the pulmonary congestion and dyspnea of the aged patient suffering from cardiac failure.

Potassium-sparing diuretics are drugs that in certain cases and in a rigorous clinical monitoring can complete the standard treatment of the severe cardiac failure, improving the patient's quality of life and reducing his number of hospitalizations.

For the majority of the patients suffering from cardiac failure, the hypokalemia secondary to the low-dose hydrochlorothiazide or furosemide use is balanced by the administration of an ACEI. Usually, because of the hyperkalemia risk, the concurrent administration of an ACEI and of a potassium-sparing diuretic is an absolute contraindication. It is known that in patients with cardiac failure, the aldosterone concentration sometimes reaches values that exceed ten times the normal level. An increased aldosterone level has adverse effects over the structure and functions of the cardiac muscle, so blocking this hormone contributes to the slowing down of the disorder's evolution. Within this context, recent studies confirm that in aged patients suffering from severe cardiac failure, low doses of spironolactone (less than 25 mg per day), associated with furosemide and an ACEI can be safely administered and mortality and the hospitalization numbers are significantly reduced.

Diuretics are often responsible for dehydration, hydro-electrolyte imbalances, hypotension and pronounced asthenia. That is why an advisedly administration of these compounds has to take into account the degree of edema and the hypo-volemic risk (asthenia, hypotension), when the blood volume decreases rapidly. A disproportional increase of urea towards blood creatinine often indicates an excessive or too rapid diuresis.

Hypokalemia is the most frequent adverse

event induced by hydrochlorothiazides and furosemide. It can be forestalled by a supplementary potassium-ions administration. Hyponatremia and hypomagnesemia which intervene after the administration of these diuretics, constantly predispose the old patient to cardiac arrhythmia, especially if the patient is concomitantly taking digoxin or an anti-arrhythmic drug.

For the aged patients currently taking a diuretic treatment the recommendations are:

- regular check-up of the hydration state, kalemia, natremia and kidney function, particularly when a kidney disorder pre-exists;
- reassessment of the benefit/risk ratio of these compounds at every dosage change and when the patient has fever episodes, vomits and has persistent or severe diarrhea;

If the diuretic treatment is concomitantly administered with other drugs, there are necessary attentive surveys of:

- the hypopotassemia risk – when taking diuretics and laxatives;
- the hyperpotassemia risk – when taking diuretics alongside with spironolactone, ACEIs or angiotensin II receptor antagonists);

### **2. Angiotensin-converting enzyme inhibitors (ACEIs)**

By blocking the angiotensin I - angiotensin II conversion, ACEIs produce vasodilatation (without modifying the cardiac rhythm), they decrease the sympathetic stimulation and they prevent or reduce the ventricular remodeling.

They are considered drugs of first choice in every stage of cardiac failure, because they attenuate the symptoms, they raise the patients' tolerance to effort and their life-span.

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Thiazide diuretics (monotherapy or associated with low doses of potassium-sparing diuretics)  
ACEIs  
Angiotensin II receptor antagonists  
Dihydropyridines

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**Table II** Antihypertensive drugs in elderly patients

Also, the ACEIs represent a rightful therapeutic choice in elderly hypertensive patients, because of the following considerations:

- they have a proven efficacy in patients with associated cardiac failure, coronary heart disease, diabetes mellitus or chronic renal disorders;
- they reduce the left ventricular hypertrophy;

- they decrease the renal function's deterioration (they have a nephro-protective effect, even in patients with diabetes);
- they have a good clinical tolerability;
- when concomitantly administered with low doses of hydrochlorothiazide, they have a synergic effect and they progressively reduce the blood pressure values.

Before starting any treatment with an ACEI compound, it is recommended to check for certain clinical situations when this kind of medication is contraindicated (bilateral renal artery stenosis) or the following conditions which foist a cautious survey of the patient (table II):

- hypotension (in patients with cardiac failure, a significant decrease of the blood pressure values can lead to a systemic blood – hypoperfusion);
- kalemia values upper than 5.5 mmoles per L;
- pre-existent kidney disease.

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| Too low blood pressure: systolic pressure lower than 90 mmHg       |
| Blood potassium level higher than 5.5 mmoles per L                 |
| Blood creatinine level higher than 260 mmoles per L                |
| <u>Bilateral renal artery stenosis (absolute contraindication)</u> |

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**Table III.** Adverse conditions for using an ACEI

Choosing an ACEI and its dosage depends on the severity of the cardiac disease, the blood pressure values and the liver and kidney functionality of the patient (table IV).

| Substance   | Initial dose (mg per dose) | Maximum dose (mg per day) | Frequency of administration per day |
|-------------|----------------------------|---------------------------|-------------------------------------|
| Captopril   | 6.25                       | 75                        | 3                                   |
| Enalapril   | 2.5                        | 20                        | 2                                   |
| Perindopril | 2                          | 4                         | 1                                   |
| Fosinopril  | 5                          | 20                        | 1                                   |
| Lisinopril  | 2.5                        | 20                        | 1                                   |
| Ramipril    | 1.25 – 2.5                 | 10                        | 2                                   |

**Table IV.** Geriatric dosage of ACEIs in cardiac failure

When associating an ACEI compound with other drugs, it is recommended to:

- ensure an appropriate hydration of the patient with renal function surveillance (when ACEIs are associated with non-steroidal anti-inflammatory drugs, because of the risk of functional renal failure);

- perform a regular check-up of blood potassium and creatinine, mostly in aged patients with NYHA III-IV cardiac failure (when ACEIs are associated with spironolactone, if the potassium values are higher than 5.5 mmoles per L or the CrCl is lower than 30 mL per minute, spironolactone administration is not recommended).

### 3. Angiotensin II receptor antagonists (ARA IIs)

These molecules block the negative effects of angiotensin II, following their specific binding to angiotensin's AT<sub>1</sub> receptors, without inhibiting the breakdown of bradykinin.

ARA IIs are recommended in patients that do not tolerate ACEIs because of their adverse effects (persistent dry cough, rash, taste disturbances, anorexia and weight loss).

### 4. Digoxin

This drug is recommended in patients with cardiac failure associated with atrial fibrillation, because it ameliorates the symptoms and raises the tolerance to effort, without having an influence on their life-span. The explanation for this choice relies on the fact that beside its positive inotropic activity, digoxin reduces the automatism of the pacemaker cardiac cells and slows down the atrioventricular conduction velocity.

Digoxin is a drug with a low therapeutic index. Normal levels of blood digoxin are situated in the range of 0.8 to 1.6 mmoles per L. The measurement of digoxin's plasma concentration will be done after

10 to 14 days from the initiation of the treatment, if suspecting a low adherence of the patient or a digitalis poisoning (the toxic concentration of digoxin is much lower in the elderly population) or if other drugs are associated to the digoxin treatment (risk for drug-drug interactions between digoxin and hydrochlorothiazide, furosemide, laxatives, amio-

darone, verapamil, certain macrolides etc.).

In people over 65 years old, some of the symptoms in the digitalis poisoning (asthenia, confusion) may be mistaken as consequences of the aging process. Very often, in this patient category, an arrhythmia or a cardiac coordination disorder is a manifestation of an excessive digitalis dosage, even if the blood concentration of the drug is situated in the therapeutic range.

Digoxin dosage has to be individualized based on some parameters like the patient's age, CrCl and kalemia (the risk for digitalis intoxication is present when the patient has hypokalemia).

### 5. $\beta$ -blockers

In people suffering from cardiac failure, when the cardiac flow is dropping, the sympathetic nervous system is rapidly activated; therefore a  $\beta$ -adrenergic stimulation happens, with a high release in the circulatory system of catecholamines (with a strong vasoconstrictor peripheral effect).

On long term, high levels of norepinephrine determine a continuous stimulation of the  $\beta_1$  receptors, stimulation that leads to desensitization and a diminution of the receptors at the surface of the myocardial cells.

Because the continuous stimulation of the  $\beta_1$  receptors in the heart seems to be one of the main causes of left ventricular dysfunction, favorable effects for the patient can be obtained if this is counteracted by the administration of a  $\beta$ -blocker.

The benefits of most of the  $\beta$ -blockers in cardiac failure are counterbalanced instead by their negative inotropic and chronotropic effects, which expose the patient to a vascular collapse (shock).

Carvedilol is a non-selective beta blocker/alpha-1 blocker (both a beta blocker ( $\beta_1$ ,  $\beta_2$ ) and alpha blocker ( $\alpha_1$ )) and it can be associated to the standard treatment (ACEI + diuretic + digoxin) in patients with mild to moderate congestive heart failure – NYHA II, for improving their quality of life.

The dosage for carvedilol in aged patients with cardiac failure is 50 mg per day (portioned to each 12 hours).

### 6. Calcium channel blockers

Dihydropyridines (amlodipine, felodipine) can be therapeutic alternatives for hypertensive elderly patients, determining a decrease in the number of lethal or non-lethal strokes.

Verapamil and diltiazem are generally contraindicated in aged persons because of the bradycardic side effects and because of the clinical and hemodynamic deterioration which shorten the life-span

in cardiac failure suffering patients, by systolic dysfunction.

## B. Psychoactive drugs

Anxiety and insomnia are frequent motives for medical consultation in geriatrics. Having a multifactor etiology (somatic disorders, psychosocial causes, drug-induced causes) in about 20% of the elder patients, anxiety requires a time-variable pharmacologic therapy.

### 1. Benzodiazepines

Are first-choice drugs for the anti-anxiety and anti-insomnia treatment in aged people (table V). Other compounds with anxiolytic and hypnotic effects (zopiclone, buspirone) have a limited use in the geriatric field.

| Benzodiazepines              |                 |
|------------------------------|-----------------|
| Sedative – anxiolytic effect | Hypnotic effect |
| Diazepam                     | Nitrazepam      |
| Oxazepam                     | Temazepam       |
| Lorazepam                    | Triazolam       |
| Alprazolam                   | Flurazepam      |
| Bromazepam                   |                 |

Table V. Benzodiazepines with sedative-hypnotic effects

When choosing the adequate benzodiazepine and its dosage, the prescriber will have to consider the physiological variations due to the aging process which in consequence change the pharmacokinetic properties of this class, leading to an amplified clinical response. Thus it is important to proceed to a dose reduction in benzodiazepine treatment.

So, in aged population, because of a severe diminution of the muscular mass and because of an augmentation of the body fat tissue, high liposoluble benzodiazepines (e.g. diazepam, flurazepam) rapidly diffuse in the adipose tissue and from there, they slowly enter the systemic circulation, their half-life being thereby prolonged. In order to avoid the emergence of adverse events as a consequence of the benzodiazepine accumulation, in elderly patients it is preferred to use a benzodiazepine with low liposolubility (ex. oxazepam, lorazepam, nitrazepam).

In aged people suffering from malnutrition, because of a 15 to 25% decrease of the serum albumins, the free benzodiazepine fraction increases, determining an exacerbated pharmacological effect and a high iatrogenic risk.

Benzodiazepine use in geriatrics can predispose the patient to specific risks, which are often

underestimated regarding the clinical prospective benefit (table VI).

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| Somnolence<br>(often secondary to an excessive dosage)<br>confusion, vestibular balance disorders<br>(risk for falls and fractures)<br>memory loss<br>attention deficit<br>anterograde amnesia<br>(with alprazolam, midazolam) |
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**Table VI.** The main adverse effects induced by benzodiazepine treatment in elderly patients

These unwanted benzodiazepine effects can significantly affect the autonomous state of the aged person. The prescriber has to reevaluate his choice for a certain benzodiazepine and has to respect the maximum daily doses recommended in geriatrics for that specific compound.

If benzodiazepines are used over a short period of time, in doses adequate for elderly patients, the manifestations of the physical dependence are insignificant. There have been described possible interactions of benzodiazepines with other drugs so this problem has to represent a cautious concern for the prescriber, because a minimal variation of the hepatic biotransformation of benzodiazepines can be translated into an important clinical impact.

**2. Antidepressants**

Depression is a major and frequent problem in the geriatric field, being triggered by the implication of several factors: life events, social factors, consequences of some pharmacotherapies (propranolol, methyl dopa, corticosteroids, etc.).

The goal of the drug treatment is to improve the general condition of the patient, to attenuate the depression-specific symptoms and to prevent relapses.

The *cyclic antidepressants*, by blocking the presynaptic norepinephrine and serotonin uptake at

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| constipation, urine retention, sight disorders<br>dry mouth syndrome, swallowing disorders, gingival lesions – especially in those who have dental prosthesis<br>orthostatic hypotension, cardiac arrhythmias<br>somnolence, confusion, risk for falls and fractures |
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**Table VII.** Adverse effects of tricyclic antidepressants

the brain level, are efficient antidepressant drugs for geriatric use. Currently, they are considered second-choice drugs for elder depressed people, because of their numerous anticholinergic effects and because of the cardiotoxicity they produce, by concomitantly blocking the muscarinic, H1 – histamine and α1 adrenergic receptors (table VII).

Nortriptyline is the tricyclic antidepressant recommended in elder people, because it produces a lower decrease of the blood pressure values and its anticholinergic effects are dimmed. The initial dose is 25 mg per day and it can be progressively increased, every week, depending on the patient’s tolerability and his clinical response to the treatment.

*Selective serotonin reuptake inhibitors* are the first-choice antidepressant drugs today, for depression treatment in elderly. They have an efficacy that is comparable to that of the tricyclic antidepressants in mild to moderate forms of depression and do not have the cardiotoxic or anticholinergic effects.

Among these, only fluoxetine which has a prolonged half-life and an active metabolite (norfluoxetine) with persistent activity in the brain is not recommended for aged persons.

Digestive disorders (nausea, vomiting and diarrhea) and headache, usually transient, remain the adverse events most frequently reported following the administration of this antidepressant class.

Choosing the right antidepressant drug is commonly very hard in geriatrics, because people over 65 years have an increased iatrogenic risk for

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| Class                                   | Substance     | Initial dose (mg per day) | Maximum dose (mg per day) |
|---|---------------|---------------------------|---------------------------|
| Selective serotonin reuptake inhibitors | Sertraline    | 25                        | 150                       |
|   | Paroxetine    | 5                         | 30                        |
|   | Fluvoxamine   | 25                        | 150                       |
|   | Citalopram    | 5                         | 40                        |
| Tricyclic antidepressants               | Nortriptyline | 25                        | 150                       |

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**Table VIII.** Antidepressant medication: dosages in geriatrics

these molecules. The prescriber has to take into account the depression type and its severity, but also the other somatic conditions of the patient, the pharmacokinetic variations due to the ageing process, etc. The antidepressant treatment will be initiated with low doses that will be progressively increased until the therapeutic (efficient) dose will be reached (table VIII).

After the complete remission of the depression-specific symptoms, the administration of the antidepressant will be continued 4 to 6 months more, for preventing relapses. The treatment will be progressively interrupted, during several months, in order to avoid the apparition of the physical dependence symptoms and depression's recidivation.

### 3. Antipsychotics

Behavior disorders (agitation - psychical and physical excitement, physical or verbal aggressiveness, delusions, hallucinations, etc.) are frequently met in elder people with cognitive deficit. These disorders are the main cause for the institutionalization of senior people with dementia syndrome.

The antipsychotic treatment is trying to diminish the intensity and the rate of behavior disorders, to improve the security and the quality of life in such people and their close entourage and to prevent accidents or events associated to a disturbed behavior.

In order to avoid an excessive antipsychotic treatment prescribed in geriatrics and these drugs' transfiguration into "chemical strait jackets", an establishment of the prescribing guidelines for these compounds was clearly necessary (table IX).

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the presence of a symptom that is so severe that it can significantly debase the functional capacity of the patient (ex: continuous crying, continuous shouting etc.)

the apparition of a disturbed behavior which can danger the patient's own security or the security of his entourage (ex: hurting himself, biting, scratching, spitting etc.)

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**Table IX.** Prescribing criteria of an antipsychotic agent in elderly patients with behavior disorders

These symptoms may appear pursuant to dopaminergic hyperactivity into the brain.

By binding to the dopamine receptors, antipsychotic molecules reduce the nervous signaling into the brain and therefore diminish the effects of the dopamine excess from different brain pathways.

According to the past ten years' studies, the administration of a *typical antipsychotic* to aged

people suffering from behavior disturbances is contraindicated, because these drugs often lead to major side effects (extrapyramidal and anticholinergic symptoms) because of the prevalent D1 and D2 dopamine receptors' blocking at the mesolimbic pathway.

Haloperidol, when administered intra-muscular, is the only typical antipsychotic agent proper for reducing the symptoms in aged agitated and aggressive people which can become real dangers for themselves or for their families.

Through the quasi-selective blocking of the 5HT<sub>2</sub> serotonin receptors and because of a low affinity for dopamine receptors in the nigrostriate pathway, the *atypical antipsychotics* much rarely induce side effects such as extrapyramidal symptoms – Parkinson-like syndrome, akathisia, tardive dyskinesia.

Currently, risperidone is the first-choice antipsychotic agent for treating behavior disturbances associated to dementia. Olanzapine is also a rightful therapeutic alternative for aged people suffering from such symptoms, regardless of their etiology.

Table X summarizes the dosages for some of the antipsychotic agents recommended for elderly patients.

| Substance   | Initial dose (mg per day) | Maximum dose (mg per day) |
|-------------|---------------------------|---------------------------|
| Risperidone | 0.25 – 0.5                | 2                         |
| Olanzapine  | 2.5 – 5.5                 | 10                        |

**Table X.** Dosages for antipsychotic agents recommended for elderly patients

The antipsychotic therapy is initiated in low doses that are progressively increased until the minimal efficient dose is reached.

Every 3 to 6 months a reevaluation of the therapy is recommended in order to check for appearance of extrapyramidal syndrome or akathisia (much more frequent in patients suffering from vascular disorders at the brain level) and in order to establish if the therapeutic indication is still valid.

### C. Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs uses by the patients of the third age can be currently found in medical practice (for pain management and subsequently for improving the quality of life), being recommended especially for osteoarticular and musculoskeletal disorders.

Recent multicenter studies show that the pro-

portion of elder persons to whom an NSAID is prescribed over one year ranges between 10 to 15%. According to the epidemiological research, about 3 to 5% of the chronic NSAIDs elderly users are hospitalized during the first year of treatment, because of the severe complications promoted by these drugs (digestive hemorrhage, gastrointestinal perforation, decompensation of some pre-existent cardiac conditions).

Some of the following reasons of these complications must be always taken into consideration by the prescriber:

a. secondary to the aging process, physiological variations that contribute to the increase of the iatrogenic risk, are the following:

- a decrease of the E2 prostaglandins concentration (this prostaglandin type has a gastro-protective effect), with the promotion of the digestive lesions by NSAIDs (including the agents with intrarectal administration);
- a diminution of the kidney synthesis of E2 and I2 prostaglandins (which have a local vasodilation effect), therefore NSAIDs facilitate renal ischemia and functional kidney failure.

b. prostaglandin synthesis is reduced because of the inhibitory effect of NSAIDs on the cyclooxygenase enzyme and the excretion of sodium ions and chloride is decreased, too. So the blood volume is augmented, therefore peripheral edema may occur and the risk for an essential arterial hypertension or a preexistent cardiac failure decompensation is also heightened.

c. NSAIDs can interact with many other drugs, so they can lead to iatrogenic events, especially in elder persons.

Within this context, because of the low digestive tolerance risk, the hemorrhagic syndrome (secondary to their anti-platelet effect) and the functional renal failure, reservation is recommended when prescribing an NSAID drug to patients over 65 years. The following indications must always be followed:

- managing the pain in musculoskeletal or osteoarticular disorders (exception in the case of acute and chronic inflammatory rheumatism); an NSAID compound will be recommended only if the patient's pain is insufficiently controlled with acetaminophen;
- an NSAID compound has to be stopped from

administration before the patient suffers a surgical intervention (preventing the risk for intra- and post-surgery hemorrhage);

- an association between NSAIDs and misoprostol or a proton pump inhibitor is imperative for avoiding the severe digestive complications (especially when the patient is also taking an anti-platelet or an anticoagulant drug);
- indomethacin will be replaced with another NSAID in elder patients suffering from gout, because this drug has frequent side effects such as: confusion, memory loss, dizziness etc.).

## Conclusions

The patient's age can modify the therapeutic goals and the prescription trend for some drugs.

Still, the increased incidence and the potential severity of iatrogenic drug-related incidents in elderly people do not have to determinate the practitioner to refuse to prescribe drugs that can improve health or quality of life for these patients.

Abiding to several administration rules for some drugs can lead to a significant decrease of the iatrogenic risk in the geriatric field. Any physician who is often confronted with third age patients has to theoretically know these rules, but also to apply them when practicing.

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