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Case Report

Could Thiocolchicoside Together With Beta-Blockers Result in Addictive Effects and a Potential Risk of Myocardial Depression?

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Abstract

Thiocolchicoside used for treatment of symptomatic muscular contractures in rheumatic and neurological disorders, may cause the side effects. Cardiotoxicity of thiocolchicoside has never been reported. We report the case of a 66-year-old male patient suffering from hypertension, ischemic heart disease, with a previous acute myocardial infarction in 2000, treated with PTCA on drug-eluting stent. Due to a persistent low back pain, he was treated with intramuscolar injection of a 4mg Tiocolchicoside and simultaneous Ketoprofen 100 mg im, for 12 consecutive days, in addition to the existing treatment with metoprolol 100mg twice a day, amlodipine 5 mg once a day, ramipril 2,5 mg twice a day, rosuvastatin 5 mg once a day, Asa 100 mg once a day.

Seven days after the end of the treatment, the patient had a fainting episode, followed by other disorders, such as chest pressure, palpitations, non-specific chest pain, face flushing, episodes of headache. Thiocolchicoside, in high doses, may act as a nicotinic receptor antagonist and inhibit transmission between preganglionic and postganglionic neurons in the Autonomic Nervous System. The ganglionic blockade reduces both sympathetic and the parasympathetic effects on organs receiving an autonomic innervation. In other words, Thiocolchicoside overdosage may result in a summing of the antagonist effect of the two drugs on sympathetic nervous system. Drugs with similar effects can produce addictive effects.

Keywords: Thiocolchicoside; Cardiotoxicity of Thiocolchicoside; Beta Blockers.

Introduction

Thiocolchicoside is used for treatment of symptomatic muscular contractures in rheumatic and neurological disorders. It acts pharmacologically by means of a selective affinity for the inhibitory gamma-aminobutyric acid and glycine receptors. Side effects, though rare, typically occur within minutes of administration and include anaphylactic reactions, anaphylactic shock, vasovagal syncope, and allergic skin reaction. [1] Thiocolchicoside can also cause seizures in predisposed subjects [2]. The European Medicines Agency's Committee on Human Medicinal Products (CHMP) has recommended that the uses for thiocolchicoside by mouth or injection should be restricted across the European Union (EU). Treatment should now only be given for 7 days by mouth or 5 days by injection into the muscle[3]. Other systemic side effects, such as cardiotoxicity have not been reported [4].

Case Report

We report the case of a 66-year-old male patient suffering from hypertension, ischemic heart disease, with a previous acute myocardial infarction in 2000, treated with PTCA on drug-eluting stent. He has been in therapy for 15 years taking metoprolol 100mg twice a day, amlodipine 5 mg once a day, ramipril 2,5 mg twice a day, rosuvastatin 5 mg once a day, Asa 100 mg once a day.

Due to a persistent low back pain, he was treated with 4mg of Tiocolchicoside i.m. and simultaneous Ketoprofen 100 mg im, for 12 consecutive days. The recommended duration of treatment with Tiocolchicoside is limited to 5 consecutive days. [3]

Seven days after the end of the treatment, the patient had a fainting episode, followed by other disorders, such as chest pressure, palpitations, non-specific chest pain, face flushing, episodes of headache. These symptoms have been persisted for about 15 days after the end of therapy with thiocolchicoside and so the patient had to have a cardiological examination.

In hospital the results of medical examinations and blood tests were : Blood pressure 170/95 mm Hg, heart rate 90bm, SpO2 98%, K 4 mMol/L, Na 143 mMol/L, Creatinin 0,75mg/dL, Troponin I <0,015ng/mL. ECG: sinus rhythm, 89bpm, PR 0,18 sec., q in D3 – AVF: results unchanged compared to those of a check up 6 months before.

The cardiac symptoms resolved spontaneously about 20 days after the end of therapy with Thiocolchicoside and Ketoprofene.

Discussion

Adverse drug reactions are important determinants in inpatient and outpatient morbidity and may be caused by the direct action of the drug, the drug interactions, high doses, or by individual organ or system hypersensitivity , including the age.

The maximum intramuscular dose of thiocolchicoside should be 4 mg every 12 hours, for up to a maximum of 5 days [3]. Our patient was treated with 4mg Tiocolchicoside for 12 consecutive days.

In our case the patient has been suffering from ischemic heart disease for 15 years and he is being treated with beta-blockers and anti hypertensive drugs. He had never suffer from cardiovascular disorders related to existing treatment, in particular, palpitations, episodes of low blood pressure or weight chest.

The palpitations may have been caused by a premature contraction of the heart atrium or ventricle. The most common type of fainting is vasovagal syncope [4] due to a temporary reduction in blood flow to the brain but also to coronary vessels . The chest pressure may be due to a temporary coronary blood flow reduction. Face flushing and episodes of headache are side effects already reported in literature. Cardiotoxicity of thiocolchiside has never been reported [5], however the possibility of unsafe interaction of Thiocolchicoside with beta blockers means that particular attention must be paid when prescribing. Drugs with similar effects can result in additive effects. Drug interactions may reduce metabolic clearance of drugs by the liver. Reduced elimination causes drug accumulation and subsequent toxicity.

Thiocolchicoside acts as a competitive GABA and Glycine receptor antagonist with similar potency, but also as a nicotinic acetylcholine receptors antagonist, even though to a small extent [6].

Nicotinic acetylcholine receptors are ionotropic receptors, responsible for the sympathetic and parasympathetic ganglia trasmission through the Na + and K + permeability.

Thiocolchicoside, in high doses, may act as a nicotinic receptor antagonist and inhibit transmission between preganglionic and postganglionic neurons in the Autonomic Nervous System. The ganglionic blockade reduces both sympathetic and the parasympathetic effects on organs receiving an autonomic innervation.

The sympathetic nervous system is part of the autonomic nervous system. Beta-blockers block the action of the sympathetic nervous system of the heart. The effects of beta blockers, in particular the depression of sinus node function and atrioventricular node conduction, are the consequence of the sympathetic nervous system blockade.

In other words, Thiocolchicoside overdosage may result in a summing of the antagonist effect of the two drugs on sympathetic nervous system. Drugs with similar effects can produce addictive effects.

Therefore, Thiocolchiside may increases effects of Beta-blockers that act as beta receptor antagonists on the sympathetic nervous system of the heart, and slow down the heart beat, decrease the force of the contractions of the heart muscles, and reduce blood vessel volume. Overdosage of Thiocolchicoside, in particular, may cause blood hypotension, cardiac arrhythmia, increased QT and PR intervals, non-specific ST and T-wave changes, myocardial depression.

In our patient we did not highlight a lengthening of PQ at the ECG after 15 days from the end of therapy. However, the reported symptoms were suggestive of episodic and

temporary depression of sinus node function and disorders of atrioventricular conduction.

The myocardial side effects began after about 7 days. This latency is related to the pharmacodynamic index, i.e the duration and intensity of pharmacological effect of the drug-drug interactions. The age-related changes are an important factor in our patient; in particular the increased cardiac sensitivity to drugs and the decreased metabolic clearance of thiocolchicoside. Repeated administrations of Thiocolchicoside may cause a slight accumulation of the drug, probably due to changes in non-renal clearance or to increased availability enterohepatic recycling[7]. This is more likely in Polypharmacy, which is the use of four or more medications by a patient, generally over 65 years old. The polypharmacy may include increased side effects of drugs.

Conclusion

Thiocolchicoside is a very effective drug for the treatment of symptomatic muscular contractures in rheumatic and neurologic disorders.

In this case, the patient's referred symptoms had disappeared at time of medical control. There is no objective evidence that they were related to medication interaction. However, the suggestion that the patient's referred palpitations could be related to ectopy and that the patient's chest pain could be related to decreased myocardial perfusion, are probably correct pathophysiological and pharmacological hypothesis. Anyway, to avoid possible side effects, it is necessary to observe the dosage recommended and consider the risk related to patient age, comorbidities conditions, and ongoing treatment, paying particular attention to possible interactions with other drugs acting on the autonomic nervous system. The most common medications associated with side effects in the elderly are cardiovascular agents and musculoskeletal agents [8].

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