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The role of plasmapheresis in the treatment of thyrotoxicosis: Case series and review of the literature

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Abstract

Background: The place of plasmapheresis in the treatment of thyrotoxicosis has not been established, and the available data on its effectiveness and safety are divergent. Objectives: The aim of this study was to evaluate the use of plasmapheresis as a preparation for radical treatment – surgery or radioiodine ablation in the treatment of thyrotoxicosis. Methods: The group described comprised 6 patients: 4 patients with amiodarone-induced hyperthyroidism and 2 patients with thyrotoxicosis in the course of Graves' disease with significant cardiac co-morbidity, hospitalized between 2010-2015 in the Department of Endocrinology at the 4th Military Hospital in Wroclaw, Poland. The indications for plasmapheresis were lack of response to treatment (5 patients) and intolerance to treatment (1 patient).

Results: With the help of plasmapheresis in a short time we achieved normal thyroid function in all patients as a preparation for definitive treatment: thyroidectomy or radioactive iodine ablation. Definitive treatment was performed with good results in 5 patients. One patient died due to myocardial infarction as a complication of severe stenosis of the aortic valve, waiting for the scheduled surgery. There were no adverse effects of treatment with plasmapheresis.

Conclusions: Plasmapheresis seems to be an effective and safe treatment of thyrotoxicosis in the course of amiodarone and Graves' disease in selected patients, preparing them for a definitive treatment. The treatment is underutilized. Further research with larger studies is needed to answer the role of plasmapheresis in the treatment of hyperthyroidism.

Keywords

plasmapheresis; thyrotoxicosis; hyperthyroidism; Graves' disease

Introduction

There are no specific epidemiological data on the incidence of amiodarone-induced thyrotoxicosis (AIT) in Europe. The available data show large differences in the percentage of people who develop thyroid dysfunction (both AIT and hypothyroidism) when using amiodarone, in the range 3.7-18% [1,2]. There are two known aetiological mechanisms for amiodarone-induced thyrotoxicosis: oversupply of iodine as a substrate for the production of thyroid hormones, which usually occurs in

patients with underlying thyroid pathology, such as Graves' disease or nodular goitre – type I AIT (iodine of 37.3% by weight of particles of amiodarone; one 200 mg tablet of amiodarone contains 75 mg of iodine); and the result of a direct toxic effect of amiodarone itself leading to destructive thyroiditis – type II AIT – usually occurring in normal thyroid glands. The differences between type I and type II AIT are presented in Table 1. Because of the half-life of amiodarone (approx. 50 days) the discontinuation of therapy and the use of antithyroid drugs is often ineffective, and it requires a treatment dependent on the type of AIT and the patient's condition (Table 1) [3]. Often patients who used amiodarone had, in line with its indications, heart disease; they had not only the supraventricular and ventricular tachyarrhythmia commonly treated by amiodarone, but also the underlying structural heart disease.

The pro-arrhythmic and ionotropic effect of thyrotoxicosis are deleterious in patients with structural heart disease leading to a worse prognosis in this patient group.

Differences and therapeutic management of three types of amiodarone-induced thyrotoxicosis (reserved for stable cardiac patients), adopted [4, 5] are shown in Table 1.

Graves' disease (GD) is currently the most common cause of hyperthyroidism in developed countries with a sufficient supply of iodine. It affects approximately 3% of women and 0.5% of men during their lifetime [6]. It is an autoimmune disease in which the role of the autoantigen is as a receptor for thyroid-stimulating hormone (TSH). GD, although it remains the most common cause of thyrotoxicosis in Poland, is rarely as severe as the described amiodarone-induced thyrotoxicosis for two reasons: the response to treatment is generally better (due to the pathophysiology of both diseases), and much less frequently in the group there coexists a structural heart disease. However plasmapheresis is an option in GD patients who cannot either tolerate or are not responding to standard anti-thyroid treatment. Therefore, in extreme cases, sometimes the use of plasmapheresis is necessary, as a life-saving method.

In the treatment of thyrotoxicosis, plasmapheresis is used very rarely: when despite the use of available treatment we cannot achieve euthyroidism, in cases of failure to improve the patient's condition by the use of standard therapy in unstable patients with severe disease or the existence of contraindications to standard treatment [7].

In dysfunction of the thyroid gland, plasmapheresis is used as a method for rapid control of thyrotoxicosis by removing the excess of thyroid hormones circulating in the serum [8].

Case Series

The patients described in the article are patients with thyrotoxicosis, in a severe general condition resulting from heart disease, in whom, despite the standard thyrostatic treatment administered we observed no improvement, but in most cases, progressive deterioration of their condition, both in the clinical state and the results of laboratory tests, or who because of complications of this treatment could not continue it. They were all patients consecutively hospitalized in the Department of Endocrinology of the 4th Military Hospital in Wroclaw, Poland, in the years 2010-1015.

A 52-year-old man (initials GL) with a coronary heart disease, after cardiac arrest due to ventricular tachyarrhythmia two years ago, with atrial hypertension and thyroid goitre. For 27 months due to severe cardiac rhythm abnormalities he had been treated with amiodarone in average dose

(100 mg per day with good tolerance). About three or six months before the hospitalisation at the Department of Endocrinology amiodarone had been withdrawn by the patient's cardiologist. The patient wasn't sure about the withdrawal time, there was no medical record. The patient was brought to hospital by ambulance after fainting on the street. On admission the patient was with a very severe condition. The physical examination by the doctor receiving the patient demonstrated destruction, dehydration features, hypotension (90/60 mm Hg), irregular heart rate approx. 130/min (a Burch-Wartofsky score of 10 points), tachypnea (> 20/min), decompensated heart failure (a Burch-Wartofsky score of 10 points), disturbance of consciousness (a Burch-Wartofsky score of 20 points), oxygen saturation was 79% and the temperature was 39.0 degrees C (a Burch-Wartofsky score of 10 points).

The ECG showed atrial fibrillation, the heart ultrasound (ejection fraction) - EF 40%, the thyroid ultrasound showed multinodular goitre - normo/hypoechogenic nodules with a diameter of less than 1 cm, and laboratory tests showed features of acute renal failure and the significantly increased concentration of free thyroid hormones (Fig. 1 and 2). Based on the clinical picture and laboratory tests, and a Burch-Wartofsky score of 60 points, the patient with nodular goitre (AITI) was diagnosed with the thyroid crisis induced by amiodarone. Two weeks before the admission to hospital because of cardiac arrhythmias, the patient had received an increased dose of beta blocker (sotalol 2x80mg a day), he also had received at that time antithyroid drug (thiamazole) of increasing doses ranging from 3x20 mg to 3x40 mg and hydrocortisone at a dose of 80 mg day (4x20 mg), without clinical effect, on the contrary: with the deteriorating clinical status of the patient and with an ever-increasing concentrations of free thyroid hormones. During hospitalization, the patient was treated with following drugs: antithyroid drug (thiamazole 2×40 mg iv); glucocorticosteroids (GKS) (hydrocortisone 4×50 mg iv) and in the symptomatic treatment: fresh frozen plasma, dopamine in continuous intravenous infusion, a beta-blocker (metopolol 10 mg in fractionated intravenous doses), low-molecular-weight heparin subcutaneously, intravenous fluids and oxygen therapy. There was obtained no reduction in the concentration of free thyroid hormones and no improvement of the clinical status of the patient, quite the contrary. Without waiting any longer there were applied 3 plasmapheresis treatments every other day. After the second plasmapheresis (the first one was with no clinical effect), there was a spectacular improvement of clinical signs and the normalization of concentration of free thyroid hormones. That enabled performing a surgery. The patient was transferred to the Surgical Ward where he was operated on day 4 after the last plasmapheresis treatment – the whole symptomatic treatment lasted a total of 10 days. The indication to plasmapheresis treatment was the patient's poor response to conventional therapy and his serious condition, threatening death from cardiac causes. No complications in the thyroidectomy procedure were observed. The patient on the third day after the surgery was transferred back to the Department of Endocrinology.

A 74-year-old man (initials SC) diagnosed with a tight stenosis of the aortic valve, with the implantable cardioverter-defibrillator for secondary prevention, thyroid nodular goiter, and atrial fibrillation treated with amiodarone in the standard dose (100 mg / day) over the past 18 months, was brought by ambulance to hospital because of a difficult contact with the patient, identified by his family. On admission, the patient was in a serious condition, unconscious (a Burch-Wartofsky score of 30 points), dehydrated, with hypotension (60/40 mmHg), temperature of 38.8 degrees C (a Burch-Wartofsky score of 10 points), tachycardia 105/min (a Burch-Wartofsky score of 5 points), features of heart failure in the

form of leg edema (a Burch-Wartofsky score of 5 points). The ejection fraction in heart ultrasound was assessed at 40-45%. A month earlier, the patient had been diagnosed with hyperthyroidism and while continuing treatment with amiodarone, the patient had been prescribed the antithyroid drug (thiamazole) at a dose of 3x20 mg, which two weeks later was changed to 4x20 mg, also glucocorticosteroid was added in a daily dose of 60 mg, the dose of the previously used beta blocker was increased up to 60 mg (sotalol 40 mg in the morning, 20 mg in the evening). In view of the deteriorating condition of the patient, deteriorating contact with him and the constantly growing, despite treatment, concentration of free thyroid hormones, the family doctor referred the patient to hospital. A Burch-Wartofsky score of 50 points – the patient was diagnosed with thyroid crisis induced by amiodarone in a patient with nodular goiter (AIT I). During hospitalization amiodarone was discontinued, the antithyroid drug was administered intravenously (thiamazole 2×40 mg IV); glucocorticosteroids (GKS) (4×hydrocortisone 50 mg IV) and in the symptomatic treatment: fresh frozen plasma, digoxin 0.5 mg/ml in fractionated intravenous doses, low-molecular-weight heparin subcutaneously and oxygen therapy. There was obtained no decrease in the concentration of free thyroid hormones and no improvement of the clinical status of the patient, on the contrary, additionally there appeared diarrhea. Despite the cardiovascular risks, the patient underwent 3 plasmapheresis treatments within 5 days, which resulted in improvement of the patient's condition. The patient in the following 4 days was transferred to the Department of Surgery, where he underwent surgery. There were no complications observed in the procedure, on the 3rd day after the surgery the patient was transferred back in a good general condition to the Department of Endocrinology.

A 66-year-old man (initials BS), overweight, with type 2 diabetes, chronic heart failure, a history of three myocardial infarctions, treated with PCI (twice) and CABG two years before, due to atrial fibrillation treated with amiodarone in the standard dose (100 mg/day) for 36 months, the treatment had been discontinued two months before. Admitted on an emergency basis to the Department of Endocrinology because of the difficult to control hyperthyroidism. On admission, the patient was in an overall serious condition, conscious, with a logical contact, high blood pressure (180/90 mm Hg), irregularities in heart rate approx. 130/min (a Burch-Wartofsky score of 20 points), tachypnea (> 20/min) , cardiac decompensation (a Burch-Wartofsky score of 10 points) with a reduced saturation to 95%, high temperature of 39.2 degrees C (a Burch-Wartofsky score of 15 points). The ECG showed numerous supraventricular arrhythmias, the cardiac ultrasound showed EF 35%, the ultrasound of the thyroid without any irregularities, and laboratory tests showed significantly increased concentration of free thyroid hormones (Fig.1 and 2). Based on the clinical and laboratory tests, a Burch-Wartofsky score of 55 points, the patient was diagnosed with thyroid crisis induced by amiodarone in a patient without thyroid pathology (AITII). Ten days before the admission to hospital because of heart rhythm disorders and the diagnosis of hyperthyroidism, the patient had received the antithyroid drug (thiamazole) of an increasing doses ranging from 3x20 mg to 4x20 mg, he had also received an increased dose of beta blocker (sotalol 80 mg in the morning, 40 mg in the evening), to the treatment there had been added glucocorticoid at a dose of 80 mg per day; without clinical effect, with ever-increasing concentrations of free thyroid hormones. During hospitalization, the patient was treated with the following drugs: antithyroid drug (thiamazole 2×40 mg IV); glucocorticosteroids (GKS) (4×hydrocortisone 50 mg IV) and in the symptomatic treatment: fresh frozen plasma, intravenous beta-blocker (metoprolol 10 mg in

fractionated doses), nitroglycerin infusion, low-molecular-weight heparin and oxygen therapy. The treatment of hypertension was modified. There was obtained no reduction in the concentration of free thyroid hormones and no improvement of the clinical status of the patient, quite the contrary. It was therefore decided to treat the patient with plasmapheresis. Four plasmapheresis treatments were applied every other day, after the third plasmapheresis there was a spectacular improvement of clinical picture (the first two were without clinical effect and there was no significant reduction of free thyroid hormones). This enabled performing surgery, the patient was transferred to the Surgical Ward, where he was operated on day 3 after the last plasmapheresis – the whole symptomatic treatment lasted a total of 11 days. The indication to the plasmapheresis treatment was no effect of the typical oral and intravenous treatment and the rapid deteriorating severe condition of the patient. No complications in the thyroidectomy procedure were observed. The patient on the third day after surgery was transferred back to the Department of Endocrinology.

The fourth patient, a 65- year-old man (initials IS), diagnosed with a tight stenosis of the aortic valve, with supraventricular arrhythmias, heart failure, the cardiac ultrasound showed the ejection fraction of 35%, was admitted in a serious condition to the Department of Endocrinology because of outpatient diagnosis of hyperthyroidism. He had been treated for atrial fibrillation with amiodarone in the standard dose (100 mg daily) for 20 months. Hyperthyroidism had been diagnosed about a week before, treated with a daily dose of the antithyroid drug 120 mg (thiamazole 3x40 mg), glucocorticosteroids 60 mg, and the beta blocker (unchanged dose) sotalol 60 mg/day. On admission to the ward the patient awake, periodically disorientated and illogical, agitated (a Burch-Wartofsky score of 10 points, high temperature (38.6 degrees C, a Burch-Wartofsky score of 10 points), tachycardia approx. 135/min (a Burch-Wartofsky score of 20 points), low blood pressure 100/60 mmHg, the features of heart failure in the form of pulmonary edema (a Burch-Wartofsky score of 15 points.) The patient was diagnosed with a thyroid crisis with a normal thyroid function (AITII). The amiodarone was discontinued. There was implemented an intravenous treatment, like in patient SC, however, it failed to stabilize the patient's condition, the concentration of free thyroid hormones was above the limit of quantification of the analytical method. After the first and only plasmapheresis performed in the patient, there was no effect in improving the patient's condition or noticeable reduction in the concentration of free thyroid hormones. The following day there was a cardiac arrest and despite the resuscitation the patient was declared dead.

Two patients diagnosed with Graves' disease, a 40-year-old man (PM), the first instance of hyperthyroidism of eight weeks, the other man, a 38-year-old one (AW), diagnosed 3 months before with the relapse of hyperthyroidism, before that the remission had lasted 10 years. Both patients without comorbidities. On admission, both patients in serious condition. The 40-year-old patient (PM) diagnosed with a severe hyperthyroidism (a Burch-Wartofsky score of 50 points), high temperature of 38.8 degrees C (10 points), mild psychomotor agitation (10 points), on abdominal symptoms: nausea, periodically loose bowel motions (10 points), tachycardia up to 140/min (20 points). He was admitted to the Department of Endocrinology because of the deepening hyperthyroidism in the field of hormonal tests and clinical picture, despite the treatment the patient had been applied regularly for 8 weeks: antithyroid drug (thiamazole 60 mg: 3x20 mg and beta blocker in a daily dose of 160 Mg - propranolol 4x40 mg). In view of the deteriorating condition of the patient despite the implementation of antithyroid intravenous

treatment (thiamazole 2×40 mg IV), GKS (3x100 mg hydrocortisone IV) and no effect of the current, standard treatment, the patient was administered 3 plasmapheresis treatments within 5 days. In this case the indication was a thyroid crisis with inadequate response to conventional therapy. After obtaining almost complete euthyreosis, the patient was treated with 13 mCi radioiodine, J 131, with good results. The patient remains under observation - currently the hypothyroidism is well controlled with drugs.

On admission, the 38-year-old patient (AW), basing on clinical symptoms, was diagnosed with a threatening thyroid crisis (a Burch-Wartofsky score of 40 points): the patient was agitated (10 points), suffering abdominal pain (10 points) and tachycardia up to approx. 130/min (10 points), without circulatory decompensation. He had been treated for 12 weeks with antithyroid (3x20 mg), due to burdensome palpitations he had received a beta-blocker (160 mg / 24h). On admission, the patient complained about persistent itchy papular rash covering the torso, which began soon after the antithyroid drug had been administered, the patient could not remember such a reaction while having being treated with the antithyroid drug for the first time, there was no medical record of that period. The patient was treated with antithyroid intravenously (2x40 mg), GKS intravenously (3x Hydrocortisone 100 mg), the treatment with a beta-blocker was continued. Laboratory tests showed the three-digit results in liver transaminases, with no other apparent reason apart from the reaction to the antithyroid drug. The patient was prepared for plasmapheresis treatment - 3 plasmapheresis treatments were administered within 5 days. The indications for plasmapheresis in that case were intolerance of the current treatment with an antithyroid drug (hepatotoxicity and skin lesions) and strongly expressed symptoms of thyrotoxicosis. After achieving the euthyreosis, the patient was treated with radioiodine 13 mCi, J 131, with good results. The patient remains under observation - currently the hypothyroidism is well controlled with drugs.

Figures 1 and 2 show the lack of effectiveness of standard treatment, expressed by high levels of free thyroid hormones, and the decrease of free thyroid hormone concentration in all the cases in the course of plasmapheresis: to normal range values (4 cases) or suboptimal ones (1 patient) in a short time. One patient died while waiting for planned surgery for acute coronary syndrome in the Cardiology Department (the patient underwent only one course of plasmapheresis – the data are not included in the figures).

In five people the definitive treatment of thyrotoxicosis was successful, and the patients are under the observation of the Endocrinology Outpatient Clinic.

Discussion

Plasmapheresis is an effective method of quick correction of the thyroid hormone levels in patients with heart disease and with thyrotoxicosis, in whom other methods of treatment have failed or could not be continued. In most patients, after 3 sessions of plasmapheresis during 5 consecutive days we achieved euthyroidism and readiness for definitive treatment. Plasmapheresis is not used as the only method of treatment, but as a preparation for the definitive one (surgery or radioiodine ablation).

Plasmapheresis in thyrotoxicosis is reserved for specific patients only, which is associated with the significant cost of the procedure in Poland (1 session of plasmapheresis costs approx. 500 euro), with low availability of the procedure in our country and relatively rare intolerance or ineffectiveness of

commonly used medicines.

All the cases presented in the article are clinical situations in which the standard algorithms of treatment proved ineffective and were associated with poor prognosis. Plasmapheresis has proved to be the most effective method of rapid normalization of thyroid hormone levels, thereby stabilizing the clinical condition of patients. Furthermore, we did not observe significant complications of the procedure in any of the patients.

- Plasmapheresis removes the excess thyroid hormones by several mechanisms: [7]
- removal of thyroxine-binding globulin (TBG) or T3 and T4 bound to albumin and increased elimination of total T4
- redistribution or dilution of free thyroid hormones (fTH)
- plasma as replacement fluid has the advantage of increasing the concentration of thyroglobulin to bind free thyroid hormones (fTH)
- removal of 5'-monodeiodinase from blood serum.

lasmapheresis procedures are carried out in daily cycles, every two or every three days. [9] It is continued until euthyroidism is achieved or the condition of the patient is stabilized.

The indications for the use of plasmapheresis in patients with hyperthyroidism are the following: [9]

- ineffectiveness of standard therapeutic methods
- contraindications to standard therapies
- rapid deterioration of the clinical state associated with thyrotoxicosis
- necessity to stabilize the condition of a patient with hyperthyroidism before definitive treatment
- thyroid storm.

Furthermore, plasmapheresis, to a small extent, also removes amiodarone from plasma. [10]

Because of the exchanged solution, plasmapheresis is divided into that of albumin and that of plasma. Plasmapheresis with the plasma exchange method is more effective due to the removal of TBG, which binds much more thyroid hormone (TH) (80%) in comparison with albumin (10-20%). In practice, significantly more albumin plasmapheresis is used because of the much less frequent and less severe complications. Also in our centre we use plasmapheresis of albumin. A comparison of these two types of plasmapheresis, with their advantages and disadvantages, is presented in Table 2.

The search strategy for the literature review included the key words alone and mixed: plasmapheresis, treatment, poor treatment with thyrotoxicosis, Graves' disease, amiodarone- induced thyrototoxicosis, amiodarone, goiter in Pubmed database.

The results described in the present publication are consistent with Dutch studies. There are many documented cases where plasmapheresis was a life-saving procedure. In the largest case review, which describes 11 patients, the indications for plasmapheresis were poor response to standard treatment (7 patients), agranulocytosis as a complication of thyrostatic treatment (3 patients), thyrotoxicosis induced by iodine (Jod-Basedow syndrome in 1 patient), and the need for rapid

preparation for orthopaedic surgery (1 patient). The same source described the procedure as safe – no major complications of therapy were observed [7].

There are also articles in which plasmapheresis is described as a controversial method of thyrotoxicosis treatment. In the authors' opinion, in haemodynamically unstable patients, this method of treatment is of a high risk and burden, and is associated with poor prognosis, with the worsening of heart failure. The study cited one case of the Department of Endocrinology in Cracow, Poland – a patient with severe AIT who underwent plasmapheresis treatment and died of respiratory failure [10]. In our experience, before taking a decision about plasmapheresis treatment, first of all it must be considered what would be a greater burden for the patient: the plasmapheresis treatment or thyrotoxicosis, which is the cause of progressive haemodynamic disturbances, especially in view of the use of other methods of treatment or for its delayed effects. In our group of patients, all of them (6) were undergoing plasmapheresis precisely because of the ineffectiveness of standard therapy – before and during hospitalization – and the need for rapid correction of thyroid function, in the absence of other available and fast methods of treatment. In 5 cases euthyroidism was obtained, followed by definitive treatment without complications. One patient died of a heart attack which was a complication of stenosis of the aortic valve.

In the patients discussed in this article we carried out treatment of hyperthyroidism in the form of withdrawal of amiodarone, the use of high doses of antithyroid drugs and glucocorticoids (during hospitalisation – mostly in the form of intravenously administered agents), with no use of sodium perchlorate or Lugol's iodine treatment, which are also in force in the treatment standards in Poland. Because of the suspicion of destructive type of amiodarone-induced thyrotoxicosis occurring in patients with AIT due to the accumulation of iodine in the thyroid gland during amiodarone treatment, use of a drug blocking the sodium iodine symporter (potassium perchlorate) did not appear to have a pathophysiological justification. What is more, potassium perchlorate is unavailable in our clinic. In a multicentre randomized study in the Netherlands it was found that perchlorate alone, or in combination with corticosteroids, was ineffective in the treatment for patients with AIT type 2 [11,12]. In patients with Graves' disease it was decided to treat patients definitively with radioactive iodine J131 (due to the lack of patients' consent for surgery), which prevented the use of Lugol's iodine in the treatment of these patients. Moreover, due to the severity of thyrotoxicosis, the use of Lugol's solution was associated with a significant risk of the escape phenomenon and further excessive release of fT [13].

It should be emphasized that an important element of the treatment process in the difficult patients described above is interdisciplinary collaboration. Apart from the Endocrinology Department, the Intensive Care Unit and the Surgery Ward with the surgical team and the Nuclear Medicine Department are involved. Time and synchronization of the procedures are of particular importance, due to the rapid rise in concentrations of TH and the need for thyroidectomy soon after achieving the euthyroid state.

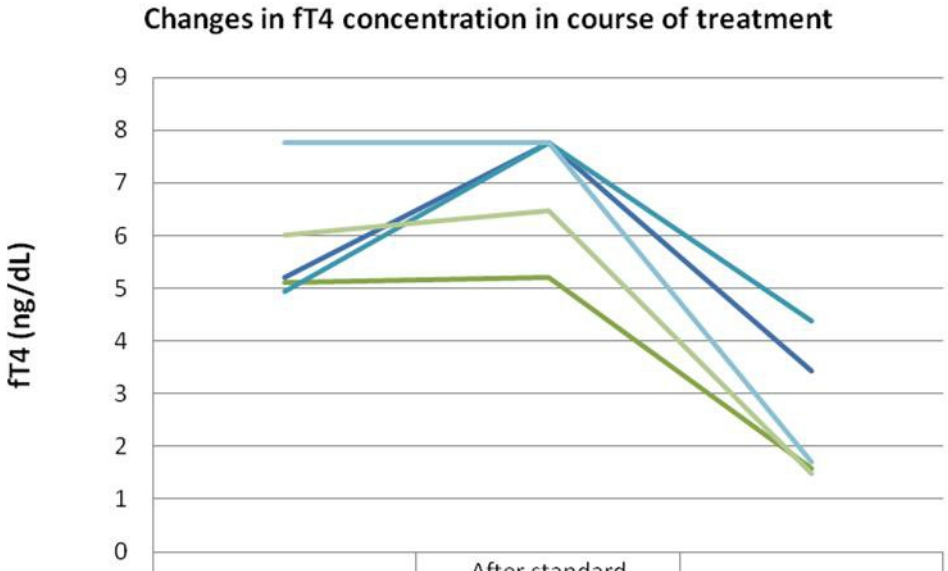
Conclusion

Plasmapheresis may be a very effective and useful alternative to standard treatment of rapid normalization of the thyroid hormone level and thus stabilizing the clinical status of patients with amiodarone-induced thyrotoxicosis in both types of AIT and GD in patients with heart disease and with

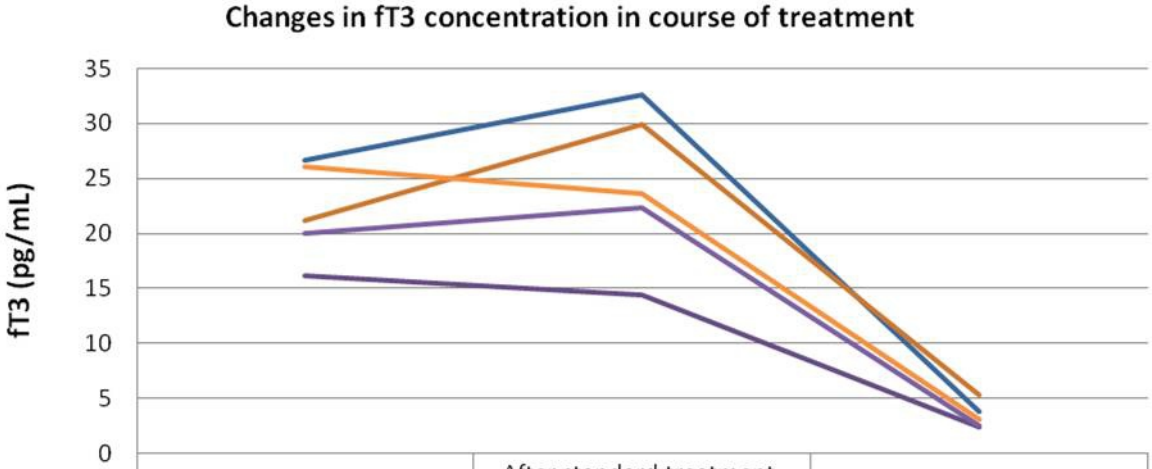
lack of effectiveness of or existence of contraindications to standard therapy.

Treatment of patients with heart disease and thyrotoxicosis requires a multidisciplinary approach to the treatment and the cooperation of many centres.

Figures



	Before treatment	After standard treatment, bofore plasmapheresis	After plasmapheresis
1 fT4	5,22	7,77	3,44
2 fT4	5,11	5,21	1,59
3 fT4	4,94	7,77	4,39
5 fT4	6,01	6,48	1,49
6 fT4	7,77	7,77	1,7



	Before treatment	After standard treatment, bofore plasmapheresis	After plasmapheresis
1 fT3	26,64	32,55	3,84
2 fT3	16,21	14,44	2,43
3 fT3	21,15	29,94	5,32
5 fT3	19,99	22,3	2,58
6 fT3	26,11	23,59	3,13

Figure 1&2: Changes of the fT3 and fT4 concentration before and in the course of plasmapheresis treatment.

Tables

Table 1: Differences and therapeutic management of three types of amiodarone-induced thyrotoxicosis (reserved for stable cardiac patients), adopted [4,5].

	Type I AIT	Type II AIT	Mixed type AIT
Underlying, previous thyroid abnormality	Yes	No	Yes/No
Pathomechanism	Excessive hormone synthesis due to iodine excess	Excessive release of preformed hormones due to thyroid destruction	Excessive hormone synthesis due to iodine excess and excessive release of preformed hormones due to thyroiddestruction
Thyromegaly	Multi nodular or diffuse thyromegaly normally present	Occasionally small, diffuse, firm, sometimes tender	Changes in thyroid morphology usually present
Thyroidalradio iodine uptake	Normal/raised (can also be lowdue to dilutingeffects of excessiodine)	Low/absent	Differentpatterns
Serum interleukin-6 concentration	Normal/slightly raised	Profoundly raised	Usually raised
Thyroid ultrasound	Nodular, hypoechogenic, increased volume, mild to markedly increased color flow Doppler signal (usually hypervascularity)	In a range of norm, absentvascularity	Usually increased volume
Therapeutic management	If possible, withdraw amiodarone	If possible, withdraw amiodarone	If possible, withdraw amiodarone
	Carbimazole (ormethimazole), 30–60 mg/day.	Prednisolone 40–60 mg/day for 2–3 months	Carbimazole (ormethimazole) 30–60 mg/day with prednisolone 40–60 mg Rapid response suggests type II AIT, hence consider stopping carbimazole (ormethimazole)
	Definitive treatment after restoration of euthyroidism is either by radioiodine or thyroidectomy		Poor response may indicate type I AIT: taper steroids and continuecarbimazole (ormethimazole). Consider reducing

Table 2: Comparison of plasmapheresis of albumin and of plasma [9].

Exchanged solution	Albumin	Plasma
Advantages	No risk of exposure to viral infections Mild reactions of anaphylaxis, if any	More effective Less costly
Disadvantages	Decrease level of blood coagulation factors and immunoglobulins	Risk of exposure to viral infections Acute reactions of anaphylaxis
Clinical usefulness	Most of cases	Mostly used in haemolytic-uraemic syndrome, thrombotic thrombocytopenic purpura, thrombotic microangiopathies

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