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Actual situation of lipoprotein apheresis in Saxony in 2013

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Abstract

Background: Lipoprotein apheresis (LA) is an officially accepted therapeutic approach in Germany. Reliable population-based data on the patients are scarce. It is of special interest to learn what are the main indications for this extracorporeal treatment and how many new patients started over the last years.

Methods: This paper is a summary of the situation of the treatment of high-risk patients via LA in the federal state of Saxony, Germany. The documentation of all patients who agreed to be included into this study have been evaluated. Patients were treated at the University Hospital Dresden (UHD) and in private practices of nephrologists. This evaluation aimed at the characterization of patients treated with LA in Saxony with respect to age, gender, lipid pattern, to the number of new patients per year and the development of the ratio of patients to the Saxon population between 2010 and 2013. The obtained data were compared with the official statistics published by the National Association of Statutory Health Insurance Physicians for whole Germany.

Results: In 2013, 181 patients, primarily males, were treated in 15 LA centers by 32 doctors. Still, the number of apheresis doctors per 1 million inhabitants is under the average in Germany (Saxony: 7.7/1 million inhabitants, average: 12/1 million inhabitants). The usage of LA is 45 per 1 million inhabitants in Saxony; in comparison to 2010, this is an increase of 16 per 1 million inhabitants. The number of new patients in 2013 with an isolated elevation of Lipoprotein(a) (Lp(a)) is twice as high than it was in 2011. The mean duration of all patients being treated with LA, most on a weekly basis, was 5.75 years (UHD: 6.2 years, range: 1 month to 23.1 years; other centers: 5.3 years, range: 1 month to 19.2 years). About 19.3% of all patients suffered from elevated triglyceride (TG) levels (>5 mmol/L). Non-high- density lipoprotein cholesterol (Non-HDL-C) was calculated, which is also acutely reduced by LA sessions.

The following data were reported for those patients who are treated outside the UHD: risk factors such as hypertension and familial predisposition could be seen in almost every patient, and several others such as type 2 diabetes mellitus, genetic defects and obesity were also present. Almost all patients had suffered from cardiovascular events (CVE) occurring before the start of apheresis treatment. LA therapy led to a reduction in occurrence of CVE during LA therapy. In particular, patients with an isolated increased Lp(a) had the highest reduction when comparing CVE before and during apheresis therapy.

In the official statistics published by the National Association of Statutory Health Insurance Physicians the number of LA patients with homozygous familial hypercholesterolemia (HoFH) is clearly too high. Moreover, these statistics do not include patients who are treated at hospitals like the UHD.

Conclusion: All in all it can be shown that the extracorporeal therapy is performed effectively in Saxony, and that more centers than 2010 (additional 5) were conducting this therapy when lipid-lowering medication was not sufficiently effective. It is certain that the number of patients requiring LA will increase in the future.

Keywords: Cardiovascular diseases; Atherogenic risk; LDL cholesterol; Lipoprotein(a); Lipoprotein apheresis; Saxony (Germany)

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1. Introduction

Lipoprotein apheresis (LA) is an effective therapy for treating patients with a high incidence of cardiovascular events (CVE) and when lipid-lowering drugs are not sufficient enough or not tolerated. LA has been performed in Dresden, the capital of the federal State of Saxony, Germany [1,2] since 1990. At the end of 2013, 14 centers and the Apheresis Center at the University Hospital Dresden (UHD) were authorized to perform LA treatment. There are 3 indications [1,3,4] which have been officially accepted in Germany since 2008: 1. homozygous familial hypercholesterolemia (HoFH), 2. severe hypercholesterolemia, if the maximal documented diet and drug therapy for more than one year failed to lower low-density lipoprotein cholesterol (LDL-C) sufficiently, and 3. elevation of Lipoprotein(a) (Lp(a)) levels ≥600 mg/L and (clinically or by imaging technique) documented progressive cardiovascular diseases (CVD).

This evaluation aimed at the characterization of patients treated with LA in Saxony with respect to age, gender, lipid pattern, to the number of new patients per year and the development of the ratio of patients to the Saxon population between 2010 and 2013. A special focus was given to the effectiveness of LA with regard to reductions of lipid concentrations and of CVE, and to the presence of additional risk factors in those patients treated outside the UHD.

Since an elevated (postprandial) triglyceride (TG) level was seen rather often, we also calculated non-high-density lipoprotein cholesterol (Non-HDL-C) [5] and analyzed the effectiveness of LA therapy on this parameter, because the measurement of Non-HDL-C is especially important in patients with elevated TG levels [5]. In the literature, associations have been described between Non-HDL-C and the occurrence and the prediction of CVD [6–8]. Moreover, we wanted to check the accuracy of the official data concerning LA patients in Saxony published by the National Association of Statutory Health Insurance Physicians (Kassenärztliche Bundesvereinigung (KBV)) [9].

2. Patients and methods

2.1. Patients

Saxon patients were treated at the UHD and at 14 LA centers located in Dresden, Riesa, Weißwasser, Hoyerswerda, Löbau, Zittau, Plauen, Aue, Annaberg-Buchholz, Freiberg, Zwickau and Leipzig. Another center in Saxony has the permission to treat, but treated no patients until the end of 2013. All but four patients provided signed written consent for their data to be used anonymously. The local ethical review committee approved this evaluation (EK206062013).

Data were evaluated until the end of 2013 (UHD and the other centers).

With respect to LDL-C and Lp(a) levels just before the first apheresis treatment, 3 different hyperlipoproteinemia (HLP) – groups were defined. Group 1 included patients with an isolated increase of LDL-C (≥3.4 mmol/L) and normal Lp(a) levels (<600 mg/L). Group 2 included patients with an isolated increase of Lp(a) (LDL-C < 3.4 mmol/L, Lp(a) ≥ 600 mg/L), Group 3 with a combined increase of LDL-C (≥3.4 mmol/L) and Lp(a) (≥600 mg/L).

If data from the first apheresis session was missing (for instance due to patients beginning treatment in other centers), we looked at further measurements as to whether Lp(a) and/or LDL-C was increased and allocated them on the basis of this data in the 3 HLP- Groups. Lp(a) was not detectable in one patient from Group 1. Special attention was paid to those patients whose pre-apheresis TG levels exceeded 5 mmol/L during their LA treatment.

Regarding the duration, the interval of LA sessions, adverse effects during LA therapy, lipid levels, risk factors, drug therapy, CVE before and during apheresis therapy: the focus was on patients being treated outside the UHD.

2.2. Methods

The medical history and drug therapy of each patient just prior to and during LA were evaluated. Risk factors such as hypertension, obesity, type 2 diabetes mellitus, the family history and genetic defects were registered. Hypertension was defined by patients taking antihypertensive drugs, obesity was defined by a Body Mass Index (BMI) ≥30 kg/m^2. Familial predisposition characterized the incidence of CVD in first-degree relatives (male relatives < 55 years, female relatives < 65 years) or the presence of hyperlipidemia in relatives. Genetic defects described an existence of mutations in the LDL-receptor gene (heterozygous, homozygous).

Major cardiovascular events like myocardial infarction (MI), stroke, bypass surgery (coronary artery bypass grafting (CABG), aortobifemoral bypass and femoral popliteal bypass) and percutaneous coronary intervention (PCI) with stent implantation and **minor cardiovascular events** like angina pectoris (AP), intermittent atrial fibrillation (IAF), percutaneous transluminal angioplasty (PTA) in the majority with stent implantation in peripheral arteries or in arterial neck vessels and 1 stent implantation in the abdominal aorta, implantation of pacemakers (PCM) or implantable cardioverter defibrillator (ICD) systems, development of asymptomatic high grade stenosis of the internal carotid artery (ACI-stenosis), asymptomatic occlusion of the internal carotid artery, reocclusions (mostly in stents after PTA, PCI), thromboendarterectomy (TEA), transient ischemic attack (TIA), reanimation, other complications like cardiogenic shock and peripheral artery occlusive disease (PAOD) were recorded.