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Retinopathy as a cause of deteriorated quality of life in diabetic patients

The disabled constitute a significant and constantly increasing percentage of inhabitants worldwide. It is estimated that in the developed European Union countries about 15% of individuals are disabled. According to the national census of 2002 in Poland 14.35% of the whole population is ranked among the disabled.

There are numerous definitions of disability. The WHO definition is worth quoting, according to which the disabled is a person whose efficient functioning in the society is impossible, difficult or limited by severe injuries and impaired function efficiency of the organism. One of the most relevant causes leading to disability is diabetes, which is thought to increase the biological age of the organism by 10 years on average and to impair substantially functioning resulting in many injuries and secondarily in severe disability.

Diabetes is the disease of impaired carbohydrate metabolism. Excessive levels of glucose in blood lead to disturbances in almost all organs and systems of the human body.

EPIDEMIOLOGY

In Europe, the incidence of diabetes diagnosed among patients treated by family doctors is high, e.g. 1.46–1.9 in Great Britain or 3.3% in Sweden. The mean age of patients is estimated at 66 years, while the mean duration of the disease at about 8 years. According to the WHO estimates, in 1995 there were about 135 mln diabetic patients worldwide; in 2025 this number will increase to about 300 mln (1). In Poland it is estimated that in 2025 the number of diabetic patients will be 1,425,000 and the prevalence will increase from 3.9% to 4.7% (1).

The increasing diabetes morbidity rate results in higher outlays connected with the fight with the disease. These costs are directly and indirectly related to the disease and result from consequences of a rapid increase in the incidence of diabetes. The costs affect patients as well as the national budget whose diabetes-related expenses are increasingly high.

Diabetes leads to many complications, the essential of which is diabetic retinopathy. Due to this complication many diabetic patients become blind. It is estimated that in the developed countries about 8% of all blindness cases are caused by diabetes.

RETINOPATHY

Moreover, retinopathy is the most common eye disease in diabetic patients and affects 97% of patients with type 1 diabetes (insulin-dependent) and 80% of those with type 2 diabetes (insulin-

independent). On average, after 15 years of diabetes retinopathy develops in 90% of patients with type 1 diabetes and in 25% of those with type 2 diabetes (2). It is estimated that diabetes is the cause of 30% of blindness cases in the European population (2).

In the Fabian et al. study carried out in one of the Szczecin primary care centres retinopathy was found in 24.8% of patients with type 2 diabetes and in 15.6% of patients with type 1 diabetes (3). The incidence of retinopathy in type 2 diabetes is similar to that reported in Swedish studies. Lundman and colleagues demonstrated retinopathy in 27% of patients above the age of 18 years (4), similar incidence was observed in another Swedish study conducted in 2004 (5).

The course of diabetic retinopathy is worsened significantly by smoking and coexisting arterial hypertension (2). Another relevant risk factor is age. In this context some paradox is visible – thanks to advances in the treatment of diabetes the patients' life is prolonged; at the same time retinopathy consequences rank first among the causes of irreversible blindness.

Classification of Diabetic Retinopathy (WHO, 1994):

- 1. Non-proliferative retinopathy without maculopathy.
- 2. Non-proliferative retinopathy with maculopathy.
- 3. Pre-proliferative retinopathy (Intraretinal microvascular abnormalities -- IRMA).
- 4. Proliferative retinopathy.
- 5. Proliferative retinopathy with complications.

Non-proliferative retinopathy occurs in 90–95% of long-term diabetic patients. In its course the vascular wall weakens and becomes permeable to plasma or full blood, which leads to swellings and exudates. The changed vessels do not fulfil their nourishing function. Microaneurysms develop on the retinal arterioles, veins thicken forming the so-called pearl necklace. In this form of retinopathy the vision is not significantly impaired.

The proliferative form of retinopathy is more severe. The blood vessels obliterate, as a result numerous new capillaries develop over the retina and even grow into the vitreous humour. The new "young" vessels have extremely thin walls which the blood easily penetrates. This leads to haemorrhages. Together with vessels the connective tissue develops, which by shrinking and scarring may "affect" the retina. In the advanced stage of retinopathy the retinal detachment occurs, glaucoma is also common. This process leads to impaired vision, diabetic maculopathy, oedema of the retinal macula, retinal haemorrhages; left untreated even to blindness (2, 6).

International Clinical Classification of Diabetic Retinopathy (ICCDR):

- · Mild nonproliferative diabetic retinopathy: microaneurysms only,
- Moderate nonproliferative diabetic retinopathy: more than microancurysms, but less than severe nonproliferative diabetic retinopathy;
- Severe nonproliferative diabetic retinopathy, which may include any of the following: more than 20 intraretinal hemorrhages in each of four quadrants; definite venous beading in two or more quadrants; prominent IRMA (intraretinal microvascular abnormalities) in one or more quadrants,
- Proliferative diabetic retinopathy, which is diagnosed when one or both of the following is present: neovascularization; vitreal or preretinal hemorrhage.

RESEARCH REVIEW

The consequences of advanced stages of diabetic retinopathy may be prevented by screening, diabetes control and monitoring of possible disturbances in microcirculation (6).

Diabetes Control and Complications Trial (DCCT) study revealed essential correlation between hyperglycaemia and the development of type 1 diabetic retinopathy. A group of 1.441 type 1 diabetic patients was investigated including patients with no retinopathy traits and with the minimal changes in the eye ground. The observation period was 4–9 years. The treatment applied in patients was subsequently: according to the conventional or intensive insulin therapy outline (three or more insulin injections in twenty-four hours). The researchers revealed that the intensive diabetes treatment decreased the frequency of retinopathy by 27% and its progress by 34-76% in comparison to the conventional therapy. It was proved that lowering of the HbA₁C level decreased the risk of retinopathy progress in people treated intensively. It seems that no definite threshold value of glucose level exists, below which the risk of diabetic retinopathy development can be completely eliminated. Insulin therapy applied conventionally is related to the increase of risk of retinopathy development, whereas insulin intensive treatment maintains retinopathy progress on the stable level (6–8).

The UKPDS (United Kingdom Prospective Diabetes Study) investigations were conducted in Great Britain in the group of type 2 diabetic patients. It was one of the largest investigations and included 5,102 type 2 diabetic patients. The mean observation period was 10.5 years. Various methods of diabetes treatment were evaluated (diet, sulphonylurea derivatives, metformin, insulin) as well as the arterial hypertension (treated with ACE inhibitors and beta-blockers) on the occurrence of microand macro-angiopathy. It was revealed that the improvement of diabetes control evaluated by means of the measurement of HbA₁C value is closely connected with the decrease in the frequency of the micro-angiopathy type complications occurrence (e.g. retinopathy). The decrease of the HbA₁C level from 7.9 to 7% was accompanied by the statistically essential reduction in the frequency of this type of complications by 25%. Each decrease in the glycated haemoglobin by 1% results in the decrease of risk of retinopathy development by 35%. Unfortunately neither the glycaemia level nor the type of anti-diabetic treatment were proved to have influence on the development of macro-angiopathy. It was underlined that other factors are also crucial in the treatment of the diabetic micro-angiopathy, e.g. the control of the arterial pressure (9, 10).

The WESDR (Wisconsin Epidemiological Study of Diabetic Retinopathy) investigation included 1.210 diabetic patients diagnosed in young age and 1,780 diabetic patients diagnosed in older age. In this investigation an essential relation was stated between the length of diabetes duration and the occurrence of retinopathy. Patients with type 1 diabetes revealed greater frequency of complications in the form of retinopathy in relation to people with diabetes diagnosed in older age (after the 30 years of age). The more serious changes were observed at the beginning of the observation period, frequently the more considerable progress of retinopathy was stated. After four years in patients with type 2 diabetes and with no diabetic changes in the eye ground the progression of retinopathy was rare (7).

The aim of the study conducted by Gaede and assoc. in Stene Diabetes Centre in Denmark was to define the efficiency of the multifactorial therapeutic intervention in patients with type 2 diabetes who had microalbuminuria stated – being the crucial risk factor in vascular complications. The study included two groups of 80 patients in each one (mean age – 55). The first group was treated conventionally: the other was treated by means of multifactorial intensive therapy. The observation period was almost 8 years. After finishing of the study it was stated that multifactorial intensive therapy caused considerable decrease of risk of retinopathy development in 58% (11).

Both forms of diabetic retinopathy are treated by the laser coagulation of the retina; in advanced diabetic maculopathy cases vitrectomy is often required (2, 6).

PREGNANCY DIABETES

Diabetes affects 2–11% pregnant women. It is definitely the most frequently diabetes that occurred in pregnancy or it was detected for the first time in pregnancy. The percentage of women with diabetes before pregnancy is 0.2–0.3%. It is estimated that in Poland the number of deliveries in diabetic women ranges around 1,000 a year. In the physiological pregnancy temporary vasodilatation in the retina is observed which is dependent on gestagens influence.

Pregnancy influence on retinopathy varies. In the pregnant with diabetes complicated by simple retinopathy progression of changes in the eye ground – present before pregnancy – can be

observed. In the majority of patients changes retreat after the delivery. In pregnant women with untreated proliferative retinopathy, especially with additional burden of arterial hypertension, proliferative changes in the retina may considerably progress and lead to the loss of vision. Frequent ophthalmological examinations allow early detection of changes and the laser therapy started early enough decreases the risk of the loss of vision (12). It is generally assumed that considerably advanced proliferative retinopathy resistant to photocoagulation is pregnancy contraindication. Advanced vascular changes in the eye ground are indication to termination of pregnancy with caesarean section. The progression of vascular changes can be prevented by proper diabetes control before pregnancy and a thorough ophthalmological examination before pregnancy, as well as in its duration.

NEW METHODS OF TREATMENT

A new method of diabetes treatment is an individual insulin pump administering insulin from the outside. Soon (2008) a new, disposable insulin injector – Solostar will appear in Poland. The injector is already available in Europe. Solostar is intended to administer insulin analogue, resembles elegant ball pen, thanks to which making injection in a public place may not be even noticed. Insulin in aerosol is already available. The hormone is administered to patients in the same way as in the asthmatic patients.

A constant study is being conducted on the invention of insulin in tablets. So far the creation of the capsule containing insulin failed because stomach acids and digestive enzymes destroy it and prevent from its passage to the circulation. Researchers from Great Britain created a coated tablet resistant to gastric juices. Insulin enclosed inside is released and is absorbed in the intestines. For the time being there are trials of insulin tablets being conducted.

Islet cell transplantation is an attractive alternative therapy to conventional and tradictional insulin treatment or whole vascularized pancreas transplantation for type 1 diabetic patients. It can rebuild endogenous insulin secretion, achieve insulin independence, and reduce risk of recurrent hypoglycaemia and of diabetic complications.

From the public health point of view, the costs of treatment of diabetic complications, including retinopathy, are a great burden to the health protection budget. The lack or markedly limited working abilities, premature disability, increased mortality are dramatic both for the patients and the society reducing its productivity and increasing the insurance costs, which are permanently insufficient (13). The diabetes-related treatment costs are constantly growing, particularly those connected with the treatment of diabetes complications.

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SUMMARY

Diabetes is a relevant health problem worldwide. The morbidity and mortality due to this disease is increasingly high. The complications of long-term and poorly controlled diabetes lead to deterioration of the quality of life of diabetic patients and eventually to disability. In Europe the incidence of diabetes diagnosed amongst patients treated by general practitioners is high, e.g. 1.46–1.9% in Great Britain or 3.3% in Sweden. The mean age of patients is estimated at 66 years while the mean duration of the disease at about 8 years. According to WHO estimates, in 1995 about 135 mln individuals had diabetes; this number will be increased to about 300 mln in 2025. Retinopathy is the most common eye disease of diabetic patients and affects 97% of patients with type 1 diabetes (insulin-independent) and 80% of those with type 2 diabetes (insulin-independent). On average, retinopathy develops in 90% of patients with type 1 diabetes and in 25% of those with type 2 diabetes after the 15-year duration of diabetes. There are two main types of diabetic retinopathy: simple (non-proliferative) and proliferative retinopathy. The measures to prevent the development of advanced diabetic retinopathy include: screening, diabetes control and monitoring of possible microcirculation disturbances. From the public health point of view, costs of treatment of diabetic complications, including retinopathy, are an enormous burden to the health protection budget.

Retinopatia jako przyczyna pogorszenia jakości życia pacjentów z cukrzycą

Cukrzyca stanowi istotny problem zdrowotny na całym świecie. Chorobowość i umieralność z jej powodu mają stałą tendencję wzrostową. Powikłania długotrwałej i niewłaściwie wyrównanej cukrzycy prowadzą do pogorszenia jakości życia chorych i w następstwie do niepelnosprawności. W Europie częstość występowania cukrzycy rozpoznanej wśród osób pozostających pod opiekę lekarzy rodzinnych jest duża i wynosi np. 1,46–1,9% w Anglii czy 3,3% w Szwecji. Średni wiek chorych oceniany jest na 66 lat, natomiast średni czas trwania schorzenia na ok. 8 lat. Według szacunków WHO w 1995 r. na świecie było ok. 135 mln ludzi chorych na cukrzycę, natomiast liczba ta ma wzrosnąć do ok. 300 mln do roku 2025. Retinopatia jest najczęstszą chorobą oka chorych z cukrzycą i dotyka 97% osób z cukrzycą typu 1 (insulinozależna) oraz 80% osób z typem 2 cukrzycy (insulinoniczałeżna). Średnio po 15 latach trwania cukrzycy retinopatia występuje u 90% chorych na cukrzycę typu 1 oraz u 25% chorych na cukrzycę typu 2. Istnieją dwa główne rodzaje retinopatii cukrzycowej: retinopatia prosta (nieproliferacyjna) oraz proliferacyjna. W zapobieganiu następstwom rozwoju zaawansowanej postaci retinopatii cukrzycowej istotne są badania przesiewowe, kontrola przebiegu cukrzycy oraz kontrola wystąpienia ewentualnych zaburzeń w mikrokrążeniu. Z punktu widzenia zdrowia publicznego koszty leczenia powikłań cukrzycy, w tym także retinopatii, stanowią ogromne obciążenie dla budżetu ochrony zdrowia.