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THE PROTECTIVE EFFECT OF LOW DOSES OF ALCOHOL ON CARDIOVASCULAR DISEASES

Štefan Kujaník
Department of Physiology, Medical Faculty, P. J. Šafárik University, Košice, Slovak Republic

Abstract

The main cause of cardiac arrhythmias and other cardiovascular complications is usually coronary heart disease and/or atherosclerosis. Alcohol is one of the most widespread and harmful addictive drugs. It kills the brain cells, decreases the effects of antihypertensive pharmacological therapy, is associated with cardiomyopathy, increased coronary artery calcium content, altered pulmonary function, liver diseases, sleep disorders, immunodeficiency, disorders of the epithelium in the intestine, increased serum interleukin-6 concentration, decrease in dendritic branching of the cerebral cortex, and triggers alcohol-associated cancers. On the other hand, the first studies on experimental animals or „the French Paradox“ in humans have shown several beneficial effects of lower doses of alcohol on some cardiovascular diseases. The possible mechanisms of these beneficial effects are vasodilation, A1-adenosine, alpha1-adrenoceptors, the epsilon isoform of protein kinase C, and KATP channel receptor stimulation, blockage of endothelial dysfunction and platelet aggregation, antiinflammatory action, activation of cardioprotective proteins, antioxidatory action of some polyphenols in wine, elevation of HDL- and decrease in LDL-cholesterol, presence of alcohol dehydrogenase type ADH3. However, the beneficial effects are mostly present in lower doses of alcohol only (1-2 drinks per day or three times a week). Higher doses are usually harmful.

Key words: alcohol, cardiovascular diseases, cardioprotection, vasodilation, inflammation, platelet aggregation

INTRODUCTION

Alcohol is one of the most widespread and harmful addictive drugs. Alcohol supplies energy to our organism, thus supports also obesity development during normal nutrition. In a small amount it acts as vasodilator, in larger amounts it has a direct vasopressoric effect (1). Alcohol kills the brain cells, decreases the effects of antihypertensive pharmacological therapy, is associated with cardiomyopathy, occasional ventricular tachyarrhythmias, altered pulmonary function, liver diseases, sleep disorders, immunodeficiency, disorders of the epithelium in the intestine, increased serum IL-6 concentration, decrease in dendritic branching of the cerebral cortex, triggers alcohol-associated cancers, etc. In small amounts it produces vasodilation, in larger amounts directly the vasopressoric effect (1). Recently it has been concluded that wine drinking is connected with lower risk than beer or spirits because of lower risk of cardiovascular diseases (2). If it is caused by some compounds included in wine, by the way of drinking or by further factors remains unclear.

However, in some recent investigations on animals predominantly (3, 4) it has been shown that a moderate alcohol administration can produce several health benefits. Given acutely to non-alcoholic animals, ethanol may even have anti-arrhythmic properties whereas chronic administration clearly increases the animals’ susceptibility to cardiac arrhythmias and blocking influence on the development of cardiovascular diseases (CVDs). The aim of this review article is to show some mechanisms of possible beneficial effects of lower alcohol doses on cardiovascular diseases in the field of endothelial function, platelet aggregation, inflammation and cardioprotection which can support the mechanisms of CVDs.

CARDIOPROTECTIVE EFFECTS OF LOWER DOSES OF ALCOHOL

Cardioprotection is an important factor in the development of CVDs acting against their rise. Several prospective studies have demonstrated a consistent, strong, dose-response relation bet-
ween increasing alcohol consumption and decreasing incidence of coronary heart disease (CHD). The data are similar for men and women in a number of different geographic and ethnic groups. Consumption of one or two drinks per day is associated with a reduction in risk and recommended (5). Studies of coronary narrowings defined by cardiac catheterization or autopsy show a reduction in atherosclerosis in persons who consume moderate amounts of alcohol. The inverse association is independent of potential confounders, such as diet and cigarette smoking. Concerns that the association could be an artifact due to cessation of alcohol consumption in persons who already have CHD have largely been disproved (6). No clinical trials have been performed to test the alcohol-CHD relation. However, the large numbers of observational studies support a protective effect of moderate consumption of alcohol (7).

Recent studies in animal models indicate that transient alcohol exposure can indeed reduce myocardial infarct size and exert a preconditioning-like protective effect. Moreover, the mechanism of alcohol-induced cardioprotection in part resembles the signalling cascade triggered by ischemic preconditioning, with adenosine receptors, protein kinase C, protein tyrosine kinases, and mitochondrial K\textsubscript{ATP} channels all being implicated as key components. The primary protective effect of alcohol use is probably in the chronic setting where alcohol exposure causes a second window type of protection that persists for many days thereafter. Regular moderate drinking should keep the heart in a second window state indefinitely (3).

Studies conducted in a variety of animal models in vitro and in vivo have indicated that chronic ethanol consumption improves functional recovery after global ischemia, reduces biochemical markers of ischemic injury, and decreases myocardial infarct size. Many of these beneficial actions appear to occur independent of alterations in systemic and coronary hemodynamics and transmural myocardial perfusion. Adenosine A\textsubscript{1}-receptors, alpha\textsubscript{1}-adrenoceptors, the epsilon isoform of protein kinase C, and K\textsubscript{ATP} channels have been shown to mediate cardioprotection associated with chronic ethanol ingestion. These data suggest another mechanism by which chronic, intermittent consumption of ethanol may reduce overall cardiovascular mortality, decrease the incidence of coronary artery disease, and improve survival after myocardial infarction in many humans (8).

Endothelial nitric oxide synthase (ENOS) is a key regulator of vascular homeostasis and myocardial functions through the controlled production of nitric oxide (NO). These studies were conducted to determine if the apparent alcohol-associated cardioprotection is mediated, in part, through modulation of the ENOS protein and activity in the cardiovascular system. Moderate alcohol intake improved postischemic myocardial systolic and diastolic function and attenuated the postischemic reduction in coronary vascular resistance in rats. Moderate alcohol also enhanced maximum vascular relaxation and increased plasma NO production concomitant with increase in ENOS protein. Higher levels of alcohol impaired maximum vascular relaxation. These results suggest that moderate alcohol improves postischemic myocardial functions and increases NO production by vascular endothelium. An increase in NO may explain, at least in part, the cardioprotective benefits of moderate alcohol consumption (9).

Excessive alcohol consumption has long been associated with CVDs, including cardiomyopathy, hypertension, coronary artery disease, and stroke. However, according to some recent evidence, the moderate alcohol intake can actually provide a measure of cardioprotection, particularly against coronary heart disease and ischemia-reperfusion injury. Additional studies in future are needed to determine the role of genes and the environment in assessing mechanisms underlying the benefits of alcohol use and cardiovascular disease risk, define the biological mechanisms underlying alcohol-induced peripheral vascular damage, clarify the role of genetic variation in alcohol-metabolizing enzymes, genetic susceptibility, and pharmacogenomics in determining cardiovascular disease risk and effective treatment, determine common mechanisms underlying alcohol-induced cardiovascular disease, such as oxidative stress and inflammation, assess the role of insulin resistance, blood clotting, protein kinase C isoforms, and signal transduction mechanisms mediating alcohol’s beneficial effects, and explore the potential of stem cells in myocardial regeneration and repair in hearts damaged by alcohol (10).
Ethanol feeding in mice doubled expression of activated protein kinase C epsilon (PKCE), whereas PKC inhibition blocked protection during ischemia-reperfusion. Ethanol feeding also increased expression of protein kinase B (Akt), whereas PKC inhibition prevented increases in Akt kinase activity. The authors conclude that signalling pathways involving PKCE are critical for sustained ethanol-mediated cardioprotection and that Akt may be a downstream effector of resistance to myocardial reperfusion injury (11).

The lysophospholipids sphingosine 1-phosphate (S1P) and lysophosphatidic acid (LPA) reduce mortality in hypoxic cardiac myocytes. S1P is also cardioprotective in both mouse and rat models of cardiac ischemia/reperfusion (I/R) injury. Although these results are consistent with prior work in other cell types, it is not known what signalling events are critical to cardioprotection, particularly with respect to ceramide and the preservation of mitochondrial function, which is essential for cardiac cell survival. Neither receptor regulation nor signalling has been studied during I/R in the heart with or without the application of S1P or LPA. The role of sphingosine kinase in I/R and in ischemic preconditioning (IPC) has not been defined, nor has the fate or function of S1P generated by this enzyme, particularly during preconditioning or I/R, been elucidated. Whether S1P infused systemically in animal models of myocardial infarction in which survival is an end-point will be hemodynamically tolerated has not been determined. If not, the substitution of agents such as the monosialoganglioside GM-1, which activates sphingosine kinase, or the development of alternative ligands for S1P receptors will be necessary (12).

While the cardioprotective effects of wine have been attributed to the polyphenolic antioxidants present in the wines, the mechanisms of cardioprotection afforded by alcohol consumption remain speculative. Some studies demonstrate an induction of the expression of several cardioprotective proteins in the heart after low dose alcohol consumption. Alcohol consumption also improves post-ischemic ventricular function and reduces myocardial infarct size and cardiomyocyte apoptosis. Thus, cardioprotection produced by lower doses of alcohol is able to block the development of CVDs.

**BENEFICIAL INFLUENCE OF ALCOHOL ON ENDOTHELIAL DYSFUNCTION**

The vascular endothelium is an important factor in control of the regional haemodynamics influencing the development or blockage of some cardiovascular pathologies. Healthy endothelial cells secrete nitric oxide (NO), which serves in several useful functions. It inhibits platelets and other white blood cells from adhering to the vascular wall. The released NO also diffuses to the vascular smooth muscle cells and relaxes them. In addition, normal amounts of NO can inhibit the division and migration of vascular smooth muscle cells toward the lumen. When the endothelial cells are sick or dysfunctional, or when they have sloughed off the underlying basement membrane, they do not make enough NO to inhibit platelet adhesion and aggregation.

Platelets are able to release the platelet-derived growth factors, which stimulate vascular smooth muscle cells to divide. The platelets also release chemotactic factors, which draw the dividing vascular smooth muscle cells down toward the lumen. This produces intimal thickening, which results in a stenosed lumen.

The low density lipoproteins (LDL) are known to enter the arterial wall and contribute to the development of foam cells and fatty streaks. If LDL becomes oxidized by oxidants or free radicals released from endothelial cells, vascular smooth muscle or other cells, it becomes modified LDL. Modified LDL can stimulate endothelial cells to release cellular adhesion molecules, which attract monocytes and T lymphocytes to attach to the arterial wall. Modified LDL can also stimulate the production of the monocyte chemotactic protein, which draws monocytes into the intimal space. Then these monocytes can differentiate into macrophages, scavenger cells. The macrophages take up modified LDL in an unregulated fashion and become engorged with yellow cholesterol and become foam cells (13). Thus, lower doses of alcohol can block endothelial dysfunction and development of CVDs.
THE INFLUENCE OF ALCOHOL ON PLATELET AGGREGATION

Increased blood clotting and platelet aggregation is also able to support the development of several cardiovascular diseases (CVDs). Cardiovascular mortality is especially low for example in southwest France (the French Paradox connected with special dietary customs and low alcohol doses in that region). Several epidemiological studies have shown that moderate intake of alcohol is associated with a lower risk of CVDs but the mechanism of this effect is not fully elucidated. One of the proposed mechanisms is its beneficial effect on hemostasis (platelet aggregation and activation, coagulation factors including von Willebrand factor, and the fibrinolytic system). Platelet aggregation is an important process which contributes to the atherosclerosis. Alcohol intake has been associated with lower platelet activity but the relationship of it with measures of platelet activation has not been studied. A cross-sectional analysis of adults free of cardiovascular disease had been enrolled in the Framingham Offspring Study (14). Alcohol consumption had been assessed usually with a standardized questionnaire. Alcohol consumption in that study had been inversely associated with both platelet activation and aggregation, particularly in men.

With regard to the effect of alcohol on platelet function, evidence in the literature suggests (15) both platelet activation and platelet inhibition by ethanol. A unifying hypothesis is that platelets are partially activated by ethanol, with partial degranulation allowing for continued circulation of platelets with impaired function. Evidence also exists showing that ethanol intake decreases fibrinogen, factor VII, and von Willebrand factor levels. In addition, alcohol intake has been found to increase fibrinolysis by increasing tissue plasminogen activator activity. The effect of ethanol on platelets, coagulation factors, and the fibrinolytic system is likely to contribute to protection against cardiovascular diseases. Chronic heavy ethanol consumption in whole blood of the rats has shown (16) reduced ADP-induced mean maximal aggregation in the alcoholic group compared to the control group at dose of 5 microM and decreased platelet aggregation responses to collagen in the alcoholic group. Therefore, increased mortality from coronary artery disease in chronic alcoholism may be explained by other factors such as dietary imbalances and coexisting conditions, which include hypertension and depression.

On the other hand, drinking large amounts in a short period (binge drinking) is associated with increased cardiovascular morbidity and mortality. Acute alcohol intake significantly increases platelet aggregation in suspension when stimulated with low concentrations of ADP (0.1 and 0.5 microg/ml). This effect was not observed when consuming red wine. In contrast, adhesion to fibrinogen was significantly inhibited by alcohol but not red wine at high shear rate after several drinks. The inhibition was accompanied by a reduction in aggregate size at 90 and 180 min after the beginning of this experiment. Adhesion to collagen was not altered by either alcohol or red wine (17). That means, rapid intake of alcohol increases platelet aggregation, which might contribute to increased mortality associated with binge drinking. Red wine does not show increased platelet aggregation, which might support reduction of cardiovascular disease in red wine consumers. Lower doses of alcohol are able to block platelet activation, aggregation and development of CVDs.

INFLUENCE OF ALCOHOL ON INFLAMMATION

Inflammation is also able to stimulate the development of CVDs. Moderate alcohol consumption is associated with substantially lower risk of CVDs caused by inflammatory processes. Atherosclerosis, the leading cause of death in western countries, is a multifactorial condition in which a local and low-grade inflammatory response plays an important role. Increase in markers of inflammation prospectively defines risk of atherosclerotic complications and predicts all-cause mortality. Alcohol consumption has been related with all-cause mortality and cardiovascular risk with a J-shaped relationship, suggesting that alcohol consumption might have an antiinflammatory effect. Several publications suggest the immunomodulatory and antiinflammatory effect of moderate alcohol consumption (18).
The relationship between alcohol intake and inflammatory markers can partially explain the beneficial effect of alcohol. Moderate alcohol consumption and levels of some inflammatory markers had been recently studied in 959 healthy men and 473 women with reported alcohol intake in the U.S.A. (19). Markers of inflammation were soluble tumor necrosis factor-alpha receptors 1 and 2 (sTNF-R1 and sTNF-R2), C-reactive protein (CRP), and interleukin-6 (IL-6). Significant inverse linear trends for sTNF-R1 and sTNF-R2 was found with increasing alcohol intake. Moderate intake of alcohol was associated with lower levels of inflammatory markers and made lower risk of CVDs through these mechanisms.

Little is known about association between markers of inflammation and alcohol consumption in Russian population where binge drinking is frequent. Totally 1963 men and 1734 women were studied, alcohol consumption consisted mainly of vodka intake, C-reactive protein was measured. A revealed U-shaped association between CRP and total alcohol intake was due to high CRP levels in ex-drinkers. Ex-drinkers of both sexes were older and reported more diseases than non-abstainers. This U-shaped association became non-significant in both genders after adjustment for age, BMI, smoking status, diabetes mellitus and cardiovascular medication. The authors conclude (20) that the U-shaped association between CRP and weekly alcohol consumption was due to higher CRP levels in ex-drinkers than in non-abstainers. Factors other than the current level of alcohol consumption might be responsible for high CRP levels in ex-drinkers. When abstainers were excluded from analyses, the results indicated a pro-inflammatory effect of binge alcohol consumption in non-abstainers.

Experimental studies show that any severe inflammation and cell death do not occur in acute ethanol intoxication. Moderate alcohol consumption induces sustained cardiac protection by activating the protein kinase C epsilon (PKCε) and protein kinase B (Akt). Thus, moderate alcohol intake is associated with lower levels of inflammatory markers and lower risk of CVDs.

CONCLUSIONS

Alcohol is one of the most widespread harmful addictive drugs. It kills the brain cells, decreases the effects of antihypertensive pharmacological therapy, is associated with cardiomyopathy, increased coronary artery calcium content, altered pulmonary function, liver diseases, sleep disorders, immunodeficiency, disorders of the epithelium in the intestine, increased serum interleukin-6 concentration, decrease in dendritic branching of the cerebral cortex, and alcohol-associated cancers are known, as well. On the other hand, the recent epidemiological studies indicate that moderate alcohol consumption reduces the incidence of the heart and CVDs. More than 100 prospective studies show an inverse association between moderate drinking and risk of heart attack, ischemic (clot-caused) stroke, peripheral vascular disease, sudden cardiac death, and death from all cardiovascular causes (21). The effect is fairly consistent, corresponding to a 25-40% reduction in risk and observed in both men and women. However, it is valid for moderate consumption only. The possible mechanisms of moderate alcohol benefit are raise of the levels of high-density lipoprotein (HDL cholesterol – 22), anti-arrhythmic and anti-ischaemic properties, activation of A1-adenosine and alpha1-adrenoceptors, blockage of endothelial dysfunction and platelet aggregation, antiinflammatory action, activation of cardioprotective proteins, antioxidatory action of some wines, etc. Higher HDL levels are associated with greater protection against heart disease. Moderate alcohol consumption has also been linked with beneficial changes in a variety of factors that influence blood clotting, such as tissue type plasminogen activator, fibrinogen, clotting factor VII, and von Willebrand factor (22). Such changes would tend to prevent the formation of small blood clots that can block arteries in several organs.

There is also some evidence that genes influence how alcohol affects the cardiovascular system. The enzyme alcohol dehydrogenase helps metabolize alcohol. One variant of this enzyme, called alcohol dehydrogenase type 3 (ADH3), exists in two forms. One quickly breaks down alcohol, the other does it more slowly. Moderate drinkers who have two copies of the gene for the slow-acting enzyme are at much lower risk for cardiovascular disease than
moderate drinkers who have two genes for the fast-acting enzyme (23). Thus, moderate alcohol consumption not only maintains a healthy heart, but can also reduce the damage to affected tissue following a heart attack. This benefit is most expressed in men over 40 and women over 50 years of age.

Amount of alcohol in drinks differs in various countries. One drink means 10 g of alcohol in Europe and Australia, 12 g in the U.S.A. and Canada or 21 g in Japan which represents 300 ml of beer, 100-150 ml of wine or 20-40 ml of spirits. The beneficial effects of alcohol require no more than 1 to 2 drinks per day or drinking at least three times a week. Regular alcohol intake is usually defined as consumption more than 5 days per week. Alcohol consuming is a very complicated question and its positive and negative effects must be taken into account for the final result. Consuming of small doses of alcohol only are recommended by the American Heart Association, American College of Cardiology and several cardiological societies in Europe together with the acetylsalicylic acid, blood pressure and blood lipid control in prevention or dietary treatment of CVDs.

Table 1: The mean rate of the alcohol metabolism adapted according to (24). Legends: g – gram, ml – milliliter. However, women, children, young persons and patients treated by several drugs metabolize alcohol more slowly compared to this table.

<table>
<thead>
<tr>
<th>Beer (12-grades) containing 15.4 g of alcohol per 500 ml</th>
<th>Duration of complete metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 ml</td>
<td>2 hours 51 minutes</td>
</tr>
<tr>
<td>1 liter</td>
<td>5 hours 42 minutes</td>
</tr>
<tr>
<td>1.5 liter</td>
<td>8 hours 34 minutes</td>
</tr>
<tr>
<td>2 litres</td>
<td>11 hours 25 minutes</td>
</tr>
<tr>
<td>2.5 litres</td>
<td>14 hours 16 minutes</td>
</tr>
<tr>
<td>3 litres</td>
<td>17 hours 7 minutes</td>
</tr>
<tr>
<td>3.5 litres</td>
<td>19 hours 57 minutes</td>
</tr>
<tr>
<td>4 litres</td>
<td>22 hours 48 minutes</td>
</tr>
<tr>
<td>4.5 litres</td>
<td>25 hours 39 minutes</td>
</tr>
</tbody>
</table>

Wine containing 25.2 g of alcohol per 200 ml

<table>
<thead>
<tr>
<th>Duration of complete metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 ml</td>
</tr>
<tr>
<td>400 ml</td>
</tr>
<tr>
<td>600 ml</td>
</tr>
<tr>
<td>800 ml</td>
</tr>
<tr>
<td>1 liter</td>
</tr>
<tr>
<td>1.2 liter</td>
</tr>
<tr>
<td>1.4 liter</td>
</tr>
</tbody>
</table>

Rum containing 15.8 g of alcohol per 50 ml

<table>
<thead>
<tr>
<th>Duration of complete metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 ml</td>
</tr>
<tr>
<td>100 ml</td>
</tr>
<tr>
<td>150 ml</td>
</tr>
<tr>
<td>200 ml</td>
</tr>
<tr>
<td>250 ml</td>
</tr>
<tr>
<td>300 ml</td>
</tr>
<tr>
<td>350 ml</td>
</tr>
<tr>
<td>400 ml</td>
</tr>
</tbody>
</table>
**Table 3:** Putative biological mechanisms underlying cardioprotection by low–moderate alcohol consumption, adapted according to (26, 27) and some other authors. HDL – high-density lipoprotein, LDL – low-density lipoprotein, CHD – coronary heart disease.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cardioprotective effect of moderate alcohol intake</th>
</tr>
</thead>
</table>
| Lipid and lipoprotein profile | Increases HDL-cholesterol  
Moderately decreases LDL-cholesterol  
Inhibits oxidation of LDL-cholesterol |
| Haemostasis | Reduces platelet aggregation  
Reduces fibrinogen levels  
Increases fibrinolysis  
Decreases blood viscosity |
| Cardiovascular system | Increases coronary blood flow  
Reduces blood pressure (<1–2 drinks per day)  
Decreases the risk of ischemic stroke  
Decreases the risk of CHD  
Decreases inflammation (CRP)  
Reduces the risk of peripheral vascular diseases |
| Central nervous system | Decreases the risk of cognitive decline  
Leads to the formation of new brain cells |
| Hormones | Reduces blood insulin levels  
Increases insulin sensitivity  
Increases oestrogen levels  
Lowers the risk of type 2 diabetes |
| Lifestyle | Reduces stress |
| Other effects | Increases paraoxonase activity  
Decreases plasma homocysteine levels  
Lowers the risk of gallstones |
Table 4. The healthy life style for prevention of cardiac diseases and diabetes according to [27, 28].

1. Avoid obesity (BMI should be < 25)
2. Correct nutrition (high intake of fiber and nonsaturated fat, low intake of saturated fatty acids, low intake of sugar, Mediterranean diet)
3. Regular physical activity (fast walking at least 30 minutes per day)
4. No smoking
5. Consuming 0.5-2 doses of alcohol per day (women not more than 1 dose)

REFERENCES


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POROSITY OF THE BASAL MEMBRANE OF THE EPITHELIUM ABOVE PEYER'S PATCHES - VARIATIONS IN THE COURSE OF THE PIG'S SMALL INTESTINE

KAČERIKA KIKALOVÁ1, ĽUDÉK ČÍŽEK2

1 Institute of Normal Anatomy, Palacký University Olomouc, Faculty of Medicine and Dentistry. 2 Institute of Preventive Medicine, Palacký University Olomouc, Faculty of Medicine and Dentistry, Olomouc, Czech Republic

Abstract

The purpose of this study was to analyze quantitatively the basal membrane porosity in the pig’s small intestine. Materials and methods: Tissues of a pig (Sus scrofa f. domestica) were used. Epithelium was removed by 1% boric acid and the basal membrane was examined by scanning electron microscopy. The size and frequency of the pori were established in areas of 400 µm². Results: The size of the basal membrane of pori on the villi was larger in Payer’s Patches than in the normal mucosa. Their frequency had a downgrade in the course of the small intestine. Conclusions: The villi above Peyer’s Patches were probably distinct from the villi of the normal mucosa both morphologically and functionally.

Key words: aggregated lymphoid nodules, Peyer’s Patches, apertures, basal membrane, intestinal villi, pig

INTRODUCTION

Aggregated lymphoid nodules - Peyer’s Patches are secondary lymphoid organs in the small intestine, which are components of the gut-associated lymphoid tissue. They play an important role in the process of oral antigen stimulation. Their structure and ultrastructure have been well described at different species (1,2). Pigs (Sus Scrofa f. domestica) have, on average, 10 – 15 Peyer’s Patches in their small intestine (3). The major part of the surface of Peyer’s Patches is covered by villi, the specific follicle-associated epithelium (FAE) bears only about 10 % (4). The basal membrane is a thin layer of molecules of the extracellular matrix. There is a porosity in the basal membrane under FAE. It is a morphological adaptation that facilitates interactions among antigens and cells within immune response (5,6). When we investigated the surface of pig’s Peyer’s Patches, we saw a small aperture on the basal membrane of the epithelium of the villi above Peyer’s Patches. We decided to find out if the oral-aboral gradient of the number and size of Peyer’s Patches has an equivalent to the frequency and size of the apertures.

MATERIALS AND METHODS

The small intestine samples were taken from a 6-week-old female pig (Sus scrofa f. domestica), which had been obtained from a slaughterhouse. The animal from industrial breeding had been kept 12 hours without food before killing. We took five samples (5 × 10 mm) from three regions of the small intestine – the first Peyer’s Patch (PP) which was larger than 7 cm, PP from the terminal ileum and normal mucosa from the middle of the small intestine. Every sample was inserted to 1% boric acid and stored in a refrigerator in the temperature of 5° overnight. Subsequently specimens were cleaned in an ultrasonic cleaner TESON 1 (Tesla), fixed by a mixture of 2% glutaraldehyde and 1% formaldehyde in 0.1M phosphate buffer of pH 7.4 for 24 hours and dehydrated in a graded acetone series. Then they were dried by a critical point drier CPD-030 (Bal-tec), coated by a 10 nm layer of gold and palladium in a sputtering device Polaron E 5100 and examined under a Tesla BS 340 scanning electron microscope (SEM). From SEM examination we provided photographs of the basal membrane with distinct pores at magnification 2100x.

Address for correspondence:
Kateřina Kikalová, MD, Institute of Normal Anatomy, Faculty of Medicine and Dentistry, PU, Hněvotínská Str. 3, 779 00, Olomouc
Phone:++420 585632223; e-mail: kikina@tunw.upol.cz
We printed these photos and divided the surface into areas of 400 $\mu m^2$. We calculated the number of apertures of the basal membrane and measured their size in randomly chosen areas. We examined 68 areas for calculating the frequency of the apertures and 100 apertures for a determination of their size in each from those three areas under examination. Data were analyzed using the U test for sizes of the apertures and the $\chi^2$ test for their frequency. We had to divide data into two groups for the $\chi^2$ test, the first group included areas with 0 – 5 apertures, the second one included areas with 6 and more apertures, see Table 3.

We had the hypothesis that there would be no difference between the size and frequency of the apertures in three monitored zones.

$H_0: \text{Size first PP} = \text{Size terminal ileum} = \text{Size normal mucosa}$

$H_0: \text{Frequency first PP} = \text{Frequency terminal ileum} = \text{Frequency normal mucosa}$

We worked with the reliability level 0.95 for testing the hypothesis.

**RESULTS**

Villi above Peyer's Patches are distinctly different from villi of the normal mucosa. (Fig. 1) Pori were well distinctive within all three areas under the examination. (Fig. 2,3) They covered the basal membrane to the crypts and they were distinct in ostia of the crypts, too. The basal membrane above follicle dome looked like a network. (Fig. 4) An average size of the pori is shown in table 1. We established that the average diameter of the pori in the basal membrane of the villi was the widest above Peyer’s Patches and the narrowest in the normal mucosa. A statistical investigation revealed that differences between the size of the pori in both first Peyer’s Patch and the normal mucosa and Peyer’s Patch in the terminal ileum and the normal mucosa were statistically significant.

An average frequency of the pori is shown in table 2. The frequency of the pori in the normal mucosa was surprisingly similar to the frequency of the pori above the first Peyer’s Patch, while it was lower above Peyer’s Patch from the terminal ileum. It seemed that the frequency moderately decreased from the jejunum to the ileum. When we compared data by the test $\chi^2$ we found statistically significant differences between the frequency of the pori in the first Peyer’s Patch and the normal mucosa, furthermore, between the first Peyer’s Patch and Peyer’s Patch from the terminal ileum. The difference between the normal mucosa and Peyer’s Patches from the terminal ileum was not demonstrable.

**Table 1.** Average size of the pori in three areas under examination. (PP - Peyer’s Patch, TI - terminal ileum).

<table>
<thead>
<tr>
<th></th>
<th>average size (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>first PP</td>
<td>13.125</td>
</tr>
<tr>
<td>PP of the TI</td>
<td>11.4875</td>
</tr>
<tr>
<td>normal mucosa</td>
<td>8.975</td>
</tr>
</tbody>
</table>

**Table 2.** Average frequency of the pori in areas 400 $\mu m^2$ on the basal membrane. (PP - Peyer’s Patch, TI - terminal ileum).

<table>
<thead>
<tr>
<th>area</th>
<th>first PP</th>
<th>PP from the TI</th>
<th>normal mucosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>average frequency</td>
<td>6.7</td>
<td>5.1</td>
<td>6.1</td>
</tr>
</tbody>
</table>

**Table 3.** Selected areas according to the frequency of the pori for the test $\chi^2$. (PP - Peyer’s Patch, TI - terminal ileum).

<table>
<thead>
<tr>
<th></th>
<th>&lt;=&lt; 5</th>
<th>=&gt;&gt; 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>first PP</td>
<td>20</td>
<td>48</td>
</tr>
<tr>
<td>PP of the TI</td>
<td>41</td>
<td>27</td>
</tr>
<tr>
<td>normal mucosa</td>
<td>35</td>
<td>33</td>
</tr>
</tbody>
</table>
The hypothesis about the uniform size and frequency of the pori in the basal membrane was not confirmed.

**DISCUSSION**

Intraepithelial lymphocytes (IEL) are the largest compartment of the lymphocytes regarding to the size of the mucosal surface in the body. They are mostly T-lymphocytes, more than 70% of them have CD 8 phenotype (7). Lymphocytes have to go through the basal membrane on their
passage from the blood circulation to the epithelium. Pori of the basal membrane are morphological reflects of this passage and presumably they are temporary (5,6). According to our observations the size of the pori matches dimensions of the lymphocytes (a small lymphocyte: 6 – 8 µm, middle: 10 – 12 µm and large: over 12 µm).

The number of the intraepithelial lymphocytes varies corresponding to the studied species and its age. For example, the number of the intraepithelial lymphocytes in sucking pigs increases from 3.3/100 enterocytes on the first day to 38.9/100 enterocytes on the 31st day of life. In con-

Fig. 3. Scanning electron microscope, pori of the basal membrane of the villi above Peyer’s Patches in terminal ileum.

Fig. 4. Scanning electron microscope, basal membrane above lymphoid follicle after removal of the epithelium.
contrast to IEL in the normal mucosa, IEL in the follicle-associated epithelium have a tendency to accumulate into groups (8).

We didn't confirm the hypothesis about constant both size and frequency of the pori of the basal membrane. Morphological differences between villi of the normal mucosa and villi of the Peyer’s Patches are known (9,4). An evident difference between size of the pori in the normal mucosa and Peyer’s Patches indicates that the villi above Peyer’s Patches are not only morphologically but also functionally distinct from the villi of the normal mucosa. Presumably not only the follicle-associated epithelium but also the epithelium of the villi above Peyer’s Patches is under the influence of the submucosal and mucosal lymphoid tissue.

The frequency of the pori in the area of $20 \times 20 \mu m^2$ was between 5.1 – 6.7 (table 2). We assumed that the findings from the test $\chi^2$ could be influenced by the used distribution of the frequency because average values of the pori in separated areas were not overmuch different. A decreasing trend of the frequency of the pori in the course of the small intestine may be due to enlarging area of the lymphoid tissue in the terminal ileum. The reducing frequency of the pori corresponds with both the decreasing number of the IEL in piglet’s small intestine and the lower frequency of the pori in rat’s large intestine as compared with the small intestine (5). It would be desirable to enlarge our study to obtain more exact evaluation.

REFERENCES


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CARDIOVASCULAR AUTONOMIC REGULATION AFTER NONPHARMACOLOGICAL CHILDHOOD OBESITY TREATMENT

1INGRID TONHAJZEROVA, 1MICHAL JAVORKA, 2OLGA CHROMA, 1ZUZANA TRUNKVALTEROVÁ, 2JANA JAVORKOVA, 1ZUZANA LAZAROVA, 1KAMIL JAVORKA

1Department of Physiology, 2Clinic of Children and Adolescents, Jessenius Faculty of Medicine, Comenius University and Faculty Hospital, Martin, Slovak Republic

Abstract

Obesity is associated with alterations in vagosympathetic activity, but little is known the effect of childhood obesity nonpharmacological treatment (NT) on cardiovascular dysregulation.

Aim: To study NT effect on cardiovascular autonomic regulation in children and adolescents with overweight and obesity.

Method: Ten subjects (7 girls, 3 boys aged 13.5-17.5 yrs) with overweight and obesity were investigated before and after NT. Evaluated parameters: Heart rate variability (HRV): mean R-R interval, rMSSD, pNN50, spectral powers in high and low frequency bands; blood pressure variability (BPV): mean BP, systolic and diastolic BP, spectral powers in low and high frequency bands of systolic BPV. The spectral power in high frequency band of HRV (HF-HRV) was taken as an index of parasympathetic activity and the spectral power in low frequency band of BPV (LF-BPV) was taken as an index of sympathetic control.

Results: The mean R-R interval was significantly prolonged after NT. The HF-HRV was significantly higher and the LF-BPV was significantly lower after NT in the study group.

Conclusions: We found the improvement of cardiovascular autonomic regulation by twelve-week nonpharmacological treatment in children and adolescents with overweight and obesity. It seems that the reversibility of cardiovascular sympathovagal dysfunction can be mediated by complex nonpharmacological treatment effect including dietary regimen associated with weight loss, regular physical activity and relaxation method (autogenic training) effects.

Key words: obesity, children, nonpharmacological treatment, heart rate variability, blood pressure variability

INTRODUCTION

Obesity is a chronic metabolic disorder associated with cardiovascular diseases, and increased morbidity and mortality rates. Although childhood obesity brings a number of additional problems – metabolic, endocrine, cardiovascular, orthopaedic, psychological and others – the greatest health problem is seen in next generation (1).

Obesity can be associated with alterations in vagosympathetic activity, evidence of which has been described already in children and adolescents (2,3,4). An increase in body weight is accompanied with a decline in parasympathetic tone, a rise in mean heart rate, and, conversely, heart rate decreases as a consequence of weight loss (5). However, little is known about the effect of nonpharmacological childhood obesity management with weight reduction on cardiovascular autonomic dysfunction and subsequently, the possible reversibility of autonomic nervous system impairment.

Oscillations of heart rate and blood pressure around their mean value - heart rate and blood pressure variability - provide information on sympathovagal activity in cardiorespiratory regulatory system (6,7). The analyses of the heart rate and blood pressure variability are usually used for the cardiac autonomic neuropathy diagnosis because of their advantages – non-invasivity and high sensitivity. Heart rate variability (HRV) – particularly spectral power in high frequency band – is taken as an index of parasympathetic control (8). On the other side, spectral activity in low frequency band of blood pressure variability (BPV) is considered as a marker of sympath-
thetic vasomotor control. Therefore, the examination of the variabilities and application of new mathematical tools for their analyses can provide complex and important information on the character of regulation/dysregulation and reversibility of the cardiovascular autonomic dysfunction e.g. after nonpharmacological treatment (NT).

The aim was to study the effect of nonpharmacological obesity treatment on cardiovascular autonomic regulation in children and adolescents with overweight and obesity using heart rate (HRV) and blood pressure variability (BPV) analyses.

METHODS

The study was approved by the Ethics Committee of Jesssenius Medical Faculty, Comenius University, and it was done in accordance with the Helsinki Declaration from 1975 as revised on 1983. All subjects and their parents were carefully instructed about the study protocol and they gave informed consent to participate in the study prior to examination.

Subjects

We have examined 34 children and adolescents with overweight and obesity aged 12 – 18 years. Ten subjects (7 girls, 3 boys aged 13.5-17.5 years, mean age ± SEM: 15.5 ± 0.42 years) successfully underwent overall complex nonpharmacological programme of childhood obesity treatment lasting twelve weeks and they were examined before and again after the therapy. All probands were non-smokers, without drugs and substances influencing cardiovascular system (i.e. caffeine, alcohol) and they had no evidence of hypertension, cardiovascular and endocrinologic diseases, diabetes mellitus or other diseases.

The nonpharmacological childhood obesity management based on the principles and recommendations of Task Force Obesity (1) includes the basic goals:

– increasing of the patient’s motivation and their family for long-term general life-style (behaviour modification)
– nutrition education – minimalisation of high-fat products, increasing the quantity of fruits, vegetables, low-fat products
– regular dietary habits
– regular physical activity (once per day physical exercise lasting minimally 10 minutes)
– self-control and the confidence improvement using relaxation methods (autogenic training).

The observation of this programme associated with learning of autogenic training was supervised regularly by child psychologist (OCh) at least once per week.

Protocol

Children and adolescents were examined in quiet room with standard temperature (23°C) and minimal arousal stimuli from 8.30 to 12.00 a.m. The subject has remained in supine position on the bed for 50 min of the continual ECG and blood pressure recording through thoracic belt for heart rate variability (HRV) analysis. Systolic blood pressure (SBP) was monitored beat-to-beat using volume-clamp method (9) by Finapres 2300 (Ohmeda, Louisville, CO, USA). The finger cuff of appropriate size was wrapped around middle phalanx of the third finger of the left hand. The finger was passively maintained at the heart level to avoid blood pressure distortion caused by hydrostatic pressure. Analogue outputs of the Finapres and ECG device CHIRASTAR 60 (Chirana, Slovak Republic) were transferred into PC by analogue-digital convertor PC-711 (Advantech Co., Taipei, Taiwan) with the sampling frequency of 500 Hz.

The analysis of heart rate and blood pressure variability:

R-R intervals and systolic blood pressure values were analyzed in selected interval started 30 min after lying back (the length of the interval was 180 s). Spectral analysis (Fast Fourier Transform) was performed on resampled (2 Hz, cubic spline) and consecutive 256 point time series. Consequently, mean power spectrum of the analysed segment was computed and spectral powers in the low frequency band (LF: 0.04-0.15 Hz) and the high frequency band (HF: 0.15-
0.5 Hz) were obtained by integration. The spectral power in high frequency band of heart rate variability analysis (HF-HRV) was considered as marker of parasympathetic control and spectral power in low frequency band of blood pressure variability analysis (LF-BPV) was taken as an index of sympathetic nervous system control.

In addition, the parameters of HRV \textit{time domain analysis} - the mean R-R interval, the square root of the mean squared difference of the successive R-R intervals (rMSSD) and the proportion of the interval differences of successive R-R intervals >50 ms (pNN50) - as markers of parasympathetic activity, the mean values of systolic and diastolic blood pressure, spectral powers in low frequency band of HRV (LF-HRV) and high frequency band of BPV (HF-BPV) were also evaluated.

\textit{Anthropometric measurements:}

Anthropometric measurements – weight, height (body mass index-BMI: weight/height in m$^2$), circumference of waist and hip (WHR:waist-to-hip ratio) and percentage fat by the method based on Bioelectrical Impedance Analysis (OMRON BF 302, Japan) – were performed after the examination.

\textbf{Statistics}

All data are expressed as mean ± SEM. The non-gaussian distribution of the variables was ascertained using Lilliefors test. Because basal spectral absolute values differ greatly among individuals, the spectral powers of heart rate variability analysis were then logarithmically transformed for statistical testing. Data were statistically evaluated by Wilcoxon test and Student's paired t-test. Significance was accepted as $p<0.05$.

**RESULTS**

\textit{Heart rate and blood pressure variability analysis:}

The mean R-R interval was significantly prolonged after the nonpharmacological treatment (933±29 vs. 848±28 ms, $p=0.013$, Fig. 1) in the studied group. The spectral power in high frequency band of heart rate variability analysis (HF-HRV) was significantly higher ($p=0.038$, Fig. 2) and the spectral power in low frequency band of blood pressure variability (LF-BPV) was significantly lower ($p=0.021$, Fig. 3) after the nonpharmacological treatment. In addition, time domain parameters of HRV analysis expressing mainly parasympathetic activity (rMSSD, pNN50) were higher after the nonpharmacological treatment (86.12±13.68 vs. 71.62±12.14; 0.46±0.06 vs. 0.39±0.07), but this difference was not significant. Significant differences were not in the remaining parameters.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Mean values of the R-R interval before and after nonpharmacological treatment (NT) in children and adolescents with overweight and obesity. Significant difference: *$p=0.013$.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig2.png}
\caption{Mean logarithmic values of spectral power in high frequency band of heart rate variability before and after nonpharmacological treatment (NT) in children and adolescents with overweight and obesity. Significant difference: *$p=0.038$.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig3.png}
\caption{Mean values of spectral power in low frequency band of blood pressure variability before and after nonpharmacological treatment (NT) in children and adolescents with overweight and obesity. Significant difference: *$p=0.021$.}
\end{figure}
All values of anthropometric measurements – BMI, WHR, percentage fat – were significantly lower ($p=0.005$, $p=0.017$, $p=0.005$, Table 1) after the nonpharmacological treatment.

Table 1. The characteristics of children with overweight an obesity before and after nonpharmacological treatment (NT). BMI – body mass index, WHR – waist-to-hip ratio, SBP-systolic blood pressure, DBP-diastolic blood pressure. $p<0.05$ was considered as significant difference.

<table>
<thead>
<tr>
<th></th>
<th>Before the NT (n=10)</th>
<th>After the NT (n=10)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>30.91±0.94</td>
<td>29.34±0.89</td>
<td>$p=0.005$</td>
</tr>
<tr>
<td>WHR</td>
<td>0.82±0.02</td>
<td>0.79±0.02</td>
<td>$p=0.017$</td>
</tr>
<tr>
<td>Percentage fat</td>
<td>34.66±1.49</td>
<td>32.82±1.57</td>
<td>$p=0.005$</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>122±5.51</td>
<td>116±6.44</td>
<td>$p&gt;0.05$</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>61±5.88</td>
<td>56±3.23</td>
<td>$p&gt;0.05$</td>
</tr>
</tbody>
</table>

DISCUSSION

Obesity and autonomic nervous system (ANS) are closely and intrinsically related. The autonomic nervous system is an important regulator of both cardiovascular system and energy expenditure and it is assumed to play a role in the pathophysiology of obesity and its complications. However, another important question is a possibility and mechanism of the cardiovascular system dysregulation improvement by nonpharmacological treatment (NT) of body overweight and obesity.

In this study we assessed the effect of the NT childhood obesity treatment on cardiovascular regulation using short-term analysis of the heart rate and blood pressure variability. It is generally accepted that spectral activity in high frequency band of the heart rate variability analysis is determined mainly by parasympathetic modulation reflecting respiratory sinus arrhythmia (10, 11). The decreased parasympathetic activity is frequent finding of the studies concerning the evaluation of the ANS changes in childhood obesity (3,12). Similarly, in our previous study we found lower parasympathetic activity in children and adolescents with obesity (4). Subsequently, in this work, we observed the improvement of the parasympathetic cardiac regulation, which clinically reflects into lower heart rate, after 12-week lasting NT associated with weight loss. It is consistent with other studies, in which the improvement of autonomic disturbances after weight loss in adult obese patients was observed (13, 14, 15).

Time delay in baroreflex loop and its non-linearity are the main mechanisms responsible for the low frequency sympathetic nerve discharge oscillations. These oscillations are transferred into peripheral vascular resistance changes through $\alpha$-adrenergic receptors of the vascular smooth muscles and the oscillations are reflected in blood pressure changes (16, 17). Therefore, the spectral activity in low frequency band of blood pressure variability is taken as a marker of sympathetic vasomotor control. Contrary to findings of the parasympathetic activity changes in obesity; the conclusions related to sympathetic part are controversial. Several works observed a decrease of sympathetic and parasympathetic activity in obese children (3), other authors found sympathetic overactivity in obese children and adolescents as a possible risk factor of hypertension (18, 19). In our studied group of children and adolescents with overweight and obesity we found a decrease of the sympathetic activity for blood pressure control (expressed by spectral power in low frequency band of BPV) after undergoing of nonpharmacological treatment. Thus, we suppose possible improvement of the sympathetic control dysfunction (which can be related to metabolic changes, i.e. insulin resistance, as well as vascular abnormalities) in childhood overweight and obesity.
In obese children; the information about complex nonpharmacological childhood obesity treatment effect on the cardiac sympathovagal dysbalance is limited. Sedentary life-style associated with physical inactivity is important contributing factor on the development and maintenance of childhood overweight and obesity. Therefore, the role of regular physical activity in nonpharmacological childhood obesity treatment is emphasized (1, 20).

Gutin et al. (21) studied the effect of physical activity on the heart rate variability in obese children. They found that training lasting four months significantly improved autonomic dysfunction – increased the parasympathetic activity expressing by time-domain analysis parameter MSSD. These findings are consistent with studies showing the beneficial effects of regular physical activity on the heart and cardiovascular autonomic regulation (22, 23). The mechanisms of regular physical activity effect on the cardiovascular system are unclear and some authors suppose shifting of the sympathovagal balance toward parasympathetic predominance, change in sinoatrial node activity, reduction of cardiac beta-adrenergic receptors, baroreceptor-low/high pressure sensitivity adjustment and other factors, which should be considered (22, 24). Therefore, we suggest that regular physical activity – as an part of nonpharmacological programme – is very important contributing factor leading to the improvement of cardiac sympathovagal dysregulation in children with overweight and obesity.

Moreover, we also hypothesize that an alterations in cardiac structure and function can be a consequence of excessive adipose tissue accumulation associated with overweight and obesity. In our studied group the nutrition education and diet regimen resulted in weight reduction (average 5% weight loss). Thus, similarly as other authors we suppose that loss of fat causes functional improvement of mechanical effects associated with obesity – direct influence of the nerve fibers compression by fat tissue resulting in restriction of diaphragm and consequent decline of respiratory sinus arrhythmia. Subsequently, the increase in vital capacity simultaneously induces activation of parasympathetic nerves through stimulation of lung stretch receptors (14).

In addition, several authors have demonstrated obesity-related vascular dysfunction (endothelial dysfunction, carotid intima-media thickness and stiffness influencing structural and mechanical properties of the vessels) in children partially reversible by a diet combined with exercise training (25, 26). The improvement of vascular alterations can be one of the mechanisms leading to the sympathetic vasomotor control reversibility.

Moreover, a possible mechanisms of the cardiovascular sympathovagal dysfunction improvement evoked by nonpharmacological treatment include also positive changes in metabolic characteristics associated with overweight and obesity (i.e. insulin resistance, leptin level) as well as the relaxation method impact (a decrease of autonomic hyperexcitability due to application of autogenic training) (27, 28, 29). Besides this aspect, we assume that the reversibility of the impaired cardiac function following weight reduction depends also on the degree and duration of obesity as well as fat distribution.

Concluding, this study demonstrated that cardiovascular autonomic dysregulation associated with overweight and obesity in children and adolescents was improved by a twelve-week lasting childhood obesity nonpharmacological programme concentrated to long-term lifestyle modification. It seems that the reversibility of cardiovascular sympathovagal dysfunction can be mediated by complex nonpharmacological treatment effect including dietary regimen associated with weight loss, regular physical activity and relaxation method (autogenic training) effects.

REFERENCES


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DIAGNOSIS AND SURGERY OF THYROID TUMORS – TEN YEARS EXPERIENCES

CALKOVSKY VLADIMIR, SRNKOVA KATARINA, KAPSOVA JANA, HAJTMAN ANDREJ
Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine, Comenius University and Faculty Hospital, Martin, Slovak Republic

Abstract

Background: In Slovakia about 5% of population suffer from thyroid gland diseases. Their accurate diagnosis and treatment may be a problem. Aim: The aim of the study was to analyse some possibilities of diagnosis and surgical treatment of thyroid gland diseases and their complications. Methods: The authors processed the documentation of 357 patients with malignant tumors of thyroid glands who have been surgically treated at the Clinic of Otorhinolaryngology and Head and Neck Surgery, JFM CU and FH in Martin between 1995 and 2005. They evaluated the family history, the effectiveness of diagnostic methods, the type of the tumor, the extent of the surgical intervention, and some complications resulting from the injury of recurrent laryngeal nerve and parathyroid gland, and postoperative bleeding. Results: The highest preoperative diagnostic sensitivity in determination of the biological nature of changes in the thyroid gland tissue had puncture aspiration biopsy. Most of the patients (n=270; 76%) had papillary carcinoma or follicular type of papillary carcinoma, respectively. Most frequent type of surgical treatment was total thyroidectomy (TTE), primarily performed in 173 patients (48.6%). Completed thyroidectomy after partial one was done in 70 patients (19%). In 114 patients (32.4%) surgery on lymphatic system with or without TTE was performed. Forty-nine patients (13.7%) complained of the paresthesia; in 11 cases (3.1%) the hypoparathyroidism was confirmed by laboratory finding of hypocalcemia. Physiological function of glottis was proved in 95.8% of surgically treated patients. The permanent injury of recurrent laryngeal nerve on one side was found in 13 patients (3.6%) and on both sides in 2 patients (0.6%). Conclusion: Nowadays, thyroid tumors belong to those malignant diseases that can be treated very effectively. Team cooperation is a basic presumption of early and high-quality diagnosis and treatment of patient with malignant goiter.

Key words: thyroid gland, goiter, malignant, thyroidectomy, larynx, paresis, hypoparathyroidism

INTRODUCTION

The thyroid gland diseases are very heterogeneous and relatively frequent. Their prevalence in Slovakia is about 5% of population. The choice of the right treatment may be difficult (1,2). Since there is a growing body of information on these diseases the treatment becomes more efficient, and surgical therapy can be done also at some ENT clinics. The therapy of the patients with the thyroid gland disease is based on interdisciplinary team work. The surgical treatment is always indicated by endocrinologist. Less often, patients from other surgical departments are being sent to the specialized ENT clinics for reoperation. The possibility of primary and definite surgical solution of the thyroid gland disease consists of the accurate diagnosis and adequate surgical strategy.

The aim of the study was to analyse the group of the hospitalized and surgically treated patients at the Clinic of Otorhinolaryngology and Head and Neck Surgery, JFM CU and FH in Martin during 1995-2005 with malignant thyroid tumors, to evaluate the possibilities for diagnosis, indications for surgery, its radicality and possible postoperative complications.

METHODS

In a retrospective study 357 (65 males, 292 females) patients with malignant goiter surgically treated between 1995-2005 were analysed. The family history of thyreopathy was positive in 77 patients (21.6%). Age interval was 17-76 years, average 43.6±8.

Address for correspondence:
Calkovsky Vladimir, MD, PhD
Clinic of Otorhinolaryngology and Head and Neck Surgery
JFM CU and MFH
Kollarova 2
036 59 MARTIN
Slovakia

Phone: 00421-43-4203282
E-mail: Calkovsky@jfmed.uniba.sk
RESULTS

The most frequent sign of the thyroid gland tumor in the study group was the quick enlargement and nodular change. Ultrasonic examination revealed nodular change in 271 patients (75.9 %), diffuse change in 51 (14.3 %) and combined nodular-diffuse change in 35 patients (9.8 %) (Table 1).

Tab.1 The type of the changes of thyroid gland based on ultrasonic investigation; n = number of patients

<table>
<thead>
<tr>
<th>Type of the change</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular</td>
<td>271</td>
<td>75.9</td>
</tr>
<tr>
<td>Diffuse</td>
<td>51</td>
<td>14.3</td>
</tr>
<tr>
<td>Combined nodular and diffuse</td>
<td>35</td>
<td>9.8</td>
</tr>
<tr>
<td>All</td>
<td>357</td>
<td>100</td>
</tr>
</tbody>
</table>

Percutaneous aspiration biopsy (PAB) was performed in 52 patients (14.6 %) and the diagnosis of malignant diseases obtained by this method was in all cases confirmed by final histologic examination that determined the type of the tumor. Most frequently – in 270 cases (76 %) - it was papillary carcinoma or follicular type of papillary carcinoma, respectively (Table 2).

Tab.2 Type of the tumor based on definitive examination; n = number of patients

<table>
<thead>
<tr>
<th>Tumor</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary</td>
<td>270</td>
<td>76</td>
</tr>
<tr>
<td>Follicular</td>
<td>44</td>
<td>12.1</td>
</tr>
<tr>
<td>Anaplastic</td>
<td>18</td>
<td>5.6</td>
</tr>
<tr>
<td>Medullary</td>
<td>8</td>
<td>1.2</td>
</tr>
<tr>
<td>Sarcoma, lymphoma</td>
<td>17</td>
<td>5.1</td>
</tr>
<tr>
<td>All</td>
<td>357</td>
<td>100</td>
</tr>
</tbody>
</table>

Most frequent type of surgical treatment was total thyroidectomy (TTE), primarily performed in 173 patients (48.6 %). Completed thyroidectomy after partial one was done in 70 patients (19 %). In 114 patients (32.4 %) surgery on lymphatic system with or without TTE was performed (Table 3).

Tab.3 The type of the surgical treatment; n = number of patients

<table>
<thead>
<tr>
<th>Surgical treatment</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total thyroidectomy (TTE)</td>
<td>173</td>
<td>48.6</td>
</tr>
<tr>
<td>Completed TTE</td>
<td>70</td>
<td>19</td>
</tr>
<tr>
<td>Lymphatic system surgery (with/without TTE)</td>
<td>114</td>
<td>32.4</td>
</tr>
<tr>
<td>All</td>
<td>357</td>
<td>100</td>
</tr>
</tbody>
</table>

Calcemia was measured on the day of surgery or on the 1st postoperative day, respectively, and later according to the clinical condition of the patient. Forty-nine patients (13.7 %) complained of paresthesia; in 11 cases (3.1 %) the hypoparathyroidism was confirmed by the laboratory finding of hypocalcemia (Figure 1).
Physiological function of glottis was proved in 95.8 % of surgically treated patients. The permanent injury of recurrent laryngeal nerve on one side was found in 13 patients (3.6 %) and on both sides in 2 patients (0.6 %) (Figure 2).

**DISCUSSION**

At complex interdisciplinary cooperation, the tumors of thyroid gland are one of the best curable malignant diseases. There is frequent discussion on the validity of percutaneous aspiration biopsy (PAB) and to the lower degree also on peroperative histology (POH) (3,4,5,6). The sampling during aspiration biopsy under ultrasonic control can be difficult and the result itself can be influenced by objective and subjective factors. In our study group, PAB was done in 52 (14.6 %) patients. In all cases, the results obtained by PAB were in accordance with those obtained by POH. However, the percentage of the patients with PAB was relatively low. According to the literature, the results obtained by technically correct PAB in comparison with POH have higher validity (3,5,7,8) These new opinions are based on the limited possibility of an accurate diagnosis in follicular carcinoma and follicular type of papillary carcinoma, and the results obtained by POH are doubtful also in medullary carcinoma (8,9). On the other hand, perfectly done and evaluated PAB gives a great chance to an accurate diagnosis in neoplastic processes. Therefore, it seems more suitable to prefer PAB to POH in the diagnosis of the nodular changes of thyroid gland.

There is also frequent discussion on the per- and postoperative complications of the thyroid gland surgery and their management. Bleeding from thyroid gland arteries, from large vessels of the neck and mediastinum, injury of laryngeal recurrent nerve, removal or permanent ischemia of parathyroid glands, esophageal, tracheal and thoracic duct injury, and tracheomalacia could be a result of incidental injury due to anatomical abnormalities, pathological finding of large extent or technical reasons, and they require an immediate solution (10).

Bleeding from the vessels supplying thyroid gland requires to strictly keep the rules of safe hemostasis mainly in the „risky” areas (11). As the main risky areas are considered the branching of \textit{a.thyroidea inferior}, anastomosis between lower and upper thyroid arteries, lower laryngeal artery under Berry’s ligament, branching of \textit{a.thyroidea superior}, „sling” artery from the branching of \textit{a.thyroidea inferior} between medial side of the thyroid gland lobe and the trachea, pretracheal area under the lower margin of the gland due to possible occurrence of \textit{a.thyroidea ima} and branching \textit{plexus thyroideus impar} (12). In these areas we avoid to use electrical coagulation with respect to the possible thermic injury of recurrent laryngeal nerve. Minor diffuse bleeding is treated by fibrin foam, bulky bleeding by ligature.
Large vessels of the neck and mediastinum can be injured because of their atypical course, during the preparation of retrosternal goiters from mediastinum, the resection of cervical lymphatic system, e.g. (13). We did not note any massive bleeding from mediastinum, probably because we use a gentle manual technique to release the retrosternally located goiters. In our opinion, it is much easier to surgically solve the large goiters, even located retrosternally than to remove small ones with fibrotic alteration. Surgery on large retrosternally and retroesophageally located goiters is also connected with the risk of tracheal and esophageal injury, which did not occur in our study group.

As regards the surgical technique itself, we share the opinion with other authors that the nerve should be prepared and visualized already at the beginning of the operation (14,10) to prevent its injury. There are several causes of possible iatrogenic recurrent laryngeal nerve injury done by surgeon. The nerve can be completely or partially cut, contused, ligated or thermically damaged by electrical coagulation.

There is no consensus on the suture of the cut recurrent nerve either among specialists or neurologists (15). Often, even at technically perfect suture of the nerve the physiologic function of the glottis is affected. However, the suture prevents the atrophy of the muscle and improves the quality of the voice (16). In case of the both-side lesion of the recurrent nerve it is necessary to perform an urgent tracheotomy (17). With respect to the possibility of the long-lasting spontaneous nerve recovery all glottis-dilating interventions should be performed at least after 6-12 months.

On the basis of our experiences we agree with the Wang’s way of nerve identification (18), which is relatively simple and conclusive. The identification of the nerve in the complicated operation field may be very difficult, in some cases impossible. In these situations the course of the nerve during thyroidectomy can be only anticipated. Tracheotomy is performed in the case of paresis of both recurrent nerves early after surgical intervention.

If one or more parathyroid glands are removed or become ischemic, autotransplantation into the neck or forearm muscles is done. Parathyroid glands suspicious of tumorous infiltration need to be submitted to peroperative histological examination (19). According to our experiences, at the unintentional removal of one parathyroid gland neither clinically nor laboratory manifested hypoparathyroidism develops.

Complications requiring urgent surgical intervention early after operation are most often caused by airway obstruction (laryngeal edema, hematoma, both-side injury of recurrent laryngeal nerves) (20). In first hours after surgery, laryngeal edema is the most frequent cause of dyspnoe and can be evoked by difficult intubation and extubation, hematoma or complicated preparation. In most patients, the treatment is non-invasive including voice control, air humidification and corticosteroids.

In conclusion, we would like to emphasize the necessity of complex interdisciplinary approach to the patients with thyroid gland diseases. All non-toxic goiters should be investigated by percutaneous aspiration biopsy (PAB) if this is not contraindicated (6). Based on the literature as well as our own experiences PAB is considered to be a method of choice, and to be more reliable than peroperative histology (POH). All auxiliary examinations need to be evaluated as complex that helps to get a general view on the disease (1). Important is also the competence of the centers with perfect service to perform thyroid gland surgery. Is the „attractive” thyroid gland surgery the domain of the general surgeons or is it the contents of the ENT specialists experienced in the head and neck surgery? Even if the answer is not at all clear, the surgery should be done by those who own the suitable equipment and the „know-how”. And, as the life of the patients depends on the experiences and skills of health professionals it is important first of all to provide them care at the highest possible level.

REFERENCES


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SURGICAL TREATMENT OF LESIONS OF NERVUS FACIALIS  
VIKTOR MATEJČIK  
Department of Neurosurgical Clinic, Comenius University, Medical Faculty and Faculty Hospital, Bratislava, Slovak Republic

Abstract

Objective: The study presents the results of reconstruction surgical treatments of lesions of n. facialis with n.hypoglossus and n.accessorius performed in our clinic in 1998 - 2004.

Patients and Methods: 10 patients were treated by anastomosis of n. facialis with n. hypoglossus (HFA), 1 patient by anastomosis of n. facialis with n. accessorius (AFA). All operations were performed under the microscope; HFA and AFA anastomoses were sutured without tension at perineurium. The techique of suturation of facial nerves did not differ from the suturation of peripheral nerves in extremities. For the connection of n.VII-XII was not used plasma pasting. We did not use end-to-side anastomosis or reconstruction of n.VII-VII in pontocerebellar angle, in pyramid or symmetric anastomoses of n.VII-VII in any case. The results were objectivized by the VI-grade scale Brudny’s modification of House-Brackman classification introduced originally for scaling of the outcome of HFA anastomosis. In this study, this classification has been used for the objectivization of AFA anastomosis results.

Results: In all cases of HFA and AFA anastomosis the 3rd grade of facial nerve function was reached. Glossal hemiatrophy or atrophy of m. sternocleidomastoideus and m. trapesius was found in patients treated by cross anastomosis with n. hypoglossus or n. accessorius. In HFA, and even more expressed in AFA anastomosis in excitation or longer lasting oral communication, there were gentle synkineses in the region of labial angle, chin and lower eye lid.Major diskineses were not observed in any of reported treatments. Recovery in older patients up to 60 years was coming more slowly, in one case after 6 months.

Conclusion: When compared AFA with HFA anastomosis, HFA brings better mimic function and more discrete synkineses. We prefer HFA anastomosis also because the discomfort caused by the atrophy of m. trapesius and m. sternocleidomastoideus was apparently more perceived by patient treated by AFA than the negative effects of hemiatrophy reported by patients treated by HFA.

Key words: facial nerve reconstruction surgery

INTRODUCTION

Nervus facialis conducts not only motor fibres to mimic muscles but also parasympathetic efferent fibres and taste-sensing afferent fibres, as well as motor fibres to the ear muscles and masticatory muscles (1).

The nerve is composed of three segments:
1. intracranial
2. pyramidal (canalis facialis)
3. peripheral

Injury in the first two segments causes the paralysis of one half of the face, defects in ear-drum function, in taste perception and in secretion. Injuries in the pyramidal output and foramen stylomastoideum result only in motor defects.

Lesion of facial nerve may be caused by injury. If the nerve is damaged by a sharp object (e.g. glass), it should be treated immediately. In the cases where direct re-connection is impossible, reconstruction surgery is performed by means of neural graft, or by a reconstruction heterotopic cross-innervation which includes another nerve that is completely or partially sacrificed. In the latter case, the function of one nerve is sacrificed for a gravely imperfect function of another nerve. The complete cross anastomosis includes connection of the whole nerve while only a portion of the nerve is used for the partial anastomosis. A lesion of facial nerve is the only indication of cross-reinnervation that has been clinically justified. The pre-conditions for the successful cross-reinnervation are much more complex than the pre-conditions for a direct re-joining of the nerve.
The paresis of damaged and inaccessible proximal end of nervus facialis has been resolved by anastomosis using nervus hypoglossus, nervus accessorius and the distal part of nervus facialis for more than 100 years. The first known successful reconstruction surgery of n. facialis by the use of n. hypoglossus was reported in 1900 (2).

The reliability of this first surgical procedure is unequivocal. Problems that may be present here are linked to tongue hemiatrophy (speech, swallowing) or sometimes to hypertonia, synkinesis and mimic defict. Anastomosis with n. accessorius is accompanied by the atrophy of m. sternocleidomastoideus and m. trapesius.

Facial expressions represent a significant form on unconscious communication. Their absence intensifies the feeling of isolation. In addition to cosmetic defects, lagophthalmus is the major reason for the indication of facial reinnervation. The capability of reinnervation of facial muscles is preserved for a significantly longer time periods than it is in the case of skeletal muscles. Irreversible fibrotic changes may occur within 3 years after the denervation, but the time period up to 20 years has been also observed (3). Successful treatment after 5-21 years have been reported in the literature (4). A complete recovery of the functions of mimic muscles after the injury of nervus facialis is the ideal condition. The attempts to reach this aim last for more than one and half century without full success. Ideal results of facial functional rehabilitation should include:

1. symmetry in the quiescent state
2. symmetry of the conscious movements
3. improvement of the activity of oral, nasal and ocular muscles.

Although surgical reconstruction of the paresis of n. facialis has a major psychological and emotional impact on the patient, it is necessary to let the patient know that the success rate of the treatment is about 90 % and the fine mimics will not be fully reconstituted. Even the optimal performance of the surgery that will restore the gross facial movements will not reconstitute the fine emotional facial movements since the differentiated activity between individual rami is impossible due to aberrant regeneration. Involuntary emotional mimics will never be recovered. The aim of the presented report is to compare the effectiveness of HFA and AFA anastomoses.

**PATIENTS AND METHODS**

In 1998-2004 11 patients were treated by microsurgery at the Neurosurgical Clinic in Bratislava. All the patients showed a complete lesion of n. facialis. The reasons of the paralysis of n. facialis included:

- a tumour of pontocerebral angle (neurinoma n. acustici) in 10 patients
- damage after Jannett surgery indicated by pain in 1 patient.

The group of 11 treated patients consisted of 3 females, between 25 to 77 years, with the average age of 46 years. The average interval from the diagnosis of the damage to the surgery was 7 months. We preferred cross anastomosis with n. hypoglossus – 10 and with n. accessorius – 1, for the treatment of the paresis of nervus facialis. These methods were considered in cases of the absence of the innervation of facial muscles by the proximal part of n. facialis.

In two cases it was possible to join the descendent ramus of n. hypoglossus with the distal part of n. hypoglossus with presumed prevention of the glossal hemiatrophy.

Patients were monitored at least for 12 months after the surgery. Brudny modification of the House-Brackmann scale (5) was used for the evaluation of all surgical interventions (Table 1).

The results of EMG examinations revealed denervation in all patients. Post-treatment EMG examinations were performed repeatedly in all patients. The analysis of the results of post-treatment examinations was performed with respect to the character of the treatment.
Table 1. Brudny's Modification of House-Brackmann Scale for Grading Facial Paralysis for Reanimation With Hypoglossal-Facial Anastomosis.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Normal</th>
<th>II Mild Dysfunction</th>
<th>III Moderate Dysfunction</th>
<th>IV Moderately Severe Dysfunction</th>
<th>V Severe Dysfunction</th>
<th>VI Total Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. At repose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Appearance</td>
<td>N</td>
<td>N</td>
<td>Mild asymmetry</td>
<td>Marked asymmetry</td>
<td>Very marked asymmetry</td>
<td>Disfiguring asymmetry</td>
</tr>
<tr>
<td>2. Tone</td>
<td>N</td>
<td>N</td>
<td>Good</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Increased</td>
</tr>
<tr>
<td>B. Selective volitional motion of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Forehead</td>
<td>N</td>
<td>Some</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>2. Eye closure</td>
<td>N</td>
<td>Full effortless</td>
<td>Full, with effort, or tongue motion</td>
<td>Incomplete, upon tongue motion only</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>3. Blinking</td>
<td>Spontaneous</td>
<td>Violitional</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>4. Upper lip elevation</td>
<td>N</td>
<td>Modest</td>
<td>Modest</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>5. Lower lip depression</td>
<td>N</td>
<td>Modest</td>
<td>Minimal</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>6. Smile</td>
<td>Spontaneous, symmetrical, synchronous</td>
<td>Spontaneous, symmetrical, synchronous</td>
<td>Spontaneous (modest), asymmetrical, synchronous</td>
<td>Upon tongue motion, asymmetrical, asynchronous</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>7. Lips pursing</td>
<td>N</td>
<td>N</td>
<td>Full, with sealing</td>
<td>Incomplete, no sealing</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>C. Synkinesis due to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Tongue movement</td>
<td>No abnormal facial movement</td>
<td>Minimal lower lid and mouth</td>
<td>Moderate lower lid and mouth</td>
<td>Slight lower lid and mouth</td>
<td>Slight mouth</td>
<td>Severe around eye and mouth</td>
</tr>
<tr>
<td>2. Swallowing</td>
<td>No abnormal facial movement</td>
<td>Minimal lower lid</td>
<td>Moderate lid and mouth</td>
<td>Slight lower lid and mouth</td>
<td>No facial movement</td>
<td>Severe around eye and mouth</td>
</tr>
</tbody>
</table>

S/P = status post anastomosis (short ≤ 1 year, long > 1 year); N = normal
RESULTS

The final cosmetic effect did not include a full functional recovery in any case. Grade III of Brudny classification was obtained for all cases of HFA and AFA (Table 2).

Table 2: Classification of patients according to the type of reconstruction surgical treatment of n. facialis.

<table>
<thead>
<tr>
<th>Character of reconstruction surgery</th>
<th>Number of patients</th>
<th>Results according to Brody modification of the House-Brackmann scale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I</td>
</tr>
<tr>
<td>HFA</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>AFA</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>-</td>
</tr>
</tbody>
</table>

The most frequently performed anastomosis was HFA - 10 accompanied by AFA - 1. The first mentioned (HFA) yielded better results.

Facial symmetry was achieved in all patients, defects in swallowing or dysarthria were not observed in any of the treated patients. All patients showed tarsorrhaphy in the initial phase of the paralysis of n. facialis. All patients were able to close eyelid completely (with an effort in the case of AFA anastomosis). Keratitis was not found in any of the cases. All cases showed good results with respect to the recovery of muscle tonus and trophic state. The fine motoric activity was absent, however, patients could close the eyelid well. Our observations indicate that HFA anastomosis results in a good peripheral innervation, recovery of facial tonus and facial movements. Two attempts to prevent the hemiatrophy of the tongue by a connection of descendent ramus of n. hypoglossus with the distal part of n. hypoglossus can be evaluated as unsuccessful in this respect because glossal hemiatrophy could not be prevented here. In the case of HFA and AFA anastomoses minute synkineses were observed in the region of labial angle, chin and lower eye lid. More severe synkineses were observed after the AFA anastomosis, especially in the excited state or after longer speech.

Re-innervation appeared up to 2 – 4 months past the reconstruction surgery in all patients, also up to 7 months in older patients.

Post-treatment EMG was significantly restored except for the superior ramus leading to m. frontalis, however, the functional results were unsatisfactory.

DISCUSSION

Reinnervation of facial muscles after n.VII damage is important for the patient on functional and social reasons. The results of facial muscles reinnervation were unsatisfactory, therefore dealing with this problem remains still important.

Although our study is only a thin survey of the proper operations and results, n.VII is not the only nerve where the cross anastomoses are used. We did not mentioned in our work about cross anostomoses in the treatment of brachial plexus injuries, and reconstructions of n.VII-VII in pontocerebellar angle in pyramid observed in the work M. Samii (1974), by extrapyramidal pathway (N.Dott, 1958), or symmetrical anastomoses of n.VII-VII (Smith et al. 1971), etc.

Restoration of muscle activity in HFA and AFA anastomoses requires not just a perfect peripheral re-innervation but also a complete rebuilding of the central mechanisms of motility analyser based on a complete functional connection of n. hypoglossus or n. accessorius with the motile region of n. facialis. The degree of the recovery of voluntary movements after reconstruction surgery of n. facialis depends not only from the age but also on patient’s motivation. The information about the success of suturation and about the re-innervation of mimic muscles can be obtained from the general EMG. The worst results are usually observed for m. frontalis (6,7). In spite of a weak and incomplete re-innervation of m. frontalis, the innervation of m. zygomaticus...
was very efficient. The ultimate cosmetic effect - a normal functional recovery - has not been obtained in any of the reported cases (8).

In more than the last four decades, several authors appraised hypoglosso-facial anastomoses as a reliable method for the re-innervation of facial muscles (9). We observed insufficiency in fine regional movements independently on other face regions as well as the absence of emotional movements on the paralyzed side. Current priority in constituting anastomoses between n. VII and n. XII is an end-to-side technique, n. XII left partially preserved to prevent glossal atrophy. In our two cases of hypoglosso-facial anastomosis, hemiatrophy of the tongue could not be prevented even by distal re-innervation from n. hypoglossus rami. Hypoglosso-facial anastomosis ensures face symmetry and prevents the atrophy of facial musculature. The group of patients that showed facial symmetry in relaxed state as well as voluntary closing the eyelid did not achieve facial symmetry during the speech.

Comparably to Balance (10), we registered an inferior result for AFA anastomoses. A slight asymmetry of the quiescent face and difficult eye closing represent an unfavourable result observed for the n. facialis – n. accessories anastomosis, however, the joint movements of shoulder and face were not registered. Hypotrophy of m. sternocleidomastoideus and m. trapesius were observed in this case.

Coonley (11) reported good muscular tonus in 95 % of all patients. When the hypoglosso-facial anastomosis could be performed during first two years after the injury, reliable muscular tonus was present in 98 % of patients. We achieved a very good or good result (Grade III of the scale) in all cases of reconstruction surgery. Fine synkineses in an excited emotional state or after a long speech were observed for all reconstruction surgical treatments. These synkineses were most pronounced for AFA anastomosis. Similar result was reported also by authors of other clinical studies (8,9,12,13). The incidence of synkineses is inversely proportional to the quality of re-innervation: the better the re-innervation, the less frequent are the synkineses. No case of spontaneous or severe synkineses has been observed in our patients in this study.

Inferior results in cross anastomosis may be caused by two unfavourable factors:
- incomplete peripheral regeneration
- low probability for a central re-building to a new function.

The result of this treatment will thus be always worse than a direct connection or connection via the neural graft originating from the original nerve.

In spite of all facts mentioned above, we do not regard our results as definitively positive ones. Intentional and unintentional facial movements utilize different pathways, although most often mediated by n. facialis and n. hypoglossus (14,15). The results of central reconstruction (dependent much on the persistence, rehabilitation process and patient’s age) are incomplete (7). All patients showed a good peripheral innervation, recovered tonus of the face and facial movements. Aberrant regeneration excludes differential activity between individual neural rami. Involuntary emotional facial expressions will never recover. Therefore, the suspensory facioplastic surgery is indicated in the cases when re-innervation of n. facialis is impossible or other head nerves are also injured.

REFERENCES


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