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INHIBITORS OF NITRIC OXIDE SYNTHASES AND EXOGENOUS IRRITANT-INDUCED BRONCHIAL HYPERREACTIVITY

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Abstract

Nitric oxide (NO) is a messenger molecule involved in many biological functions in both physiological and pathological conditions, such as bronchial hyperreactivity. NO is produced by various cell types including epithelial cells, airways nerves, inflammatory cells and vascular endothelial cells in the respiratory system. In the present study we followed the relationship between nitric oxide production and the bronchial hyperreactivity.

The study was divided into two phases. In the first phase, male guinea pigs (250-350 g b.w.) were administered the selective inhibitor of nitric oxide synthase (aminoguanidine – subst. Sigma) or nonselective inhibitor of nitric oxide synthase (L-NAME – methylester Nω-nitro-L-arginine – subst. Sigma). The agents were administered during 3 days or 17 days. The animals were subsequently exposed to the toluene vapours in in vivo conditions. Animals were killed and small tissue strips from trachea and bronchi were placed to the organ bath with Krebs-Henseleit solution in second phase. The samples were contracted by histamine and acetylcholine in cumulative doses (10^{-8} – 10^{-3} mol/l) after 60 minutes of incubation. The responses of strips were recorded, analyzed and evaluated by Student t-test.

The administration of nitric oxide synthases inhibitors caused significant decrease of responses to mediators of bronchoconstriction. Some differences in the time dependence on inhibitors administration have been observed. More significant decrease of bronchial hyperreactivity has been evoked by short-term administration of both inhibitors in experimental animals in all cases. We observed the more significant effect after the administration of nonselective inhibitor – L-NAME.

The inhibitors of NO synthases decreased hyperreactivity of the bronchial and tracheal smooth muscle evoked by toluene. The decrease was dependent on the duration of their application. These results showed possible participation of constitutive forms of NO-synthases in the bronchial hyperreactivity.

Key words: nitric oxide, inhibitors of nitric oxide synthase, airway hyperreactivity, guinea pigs

INTRODUCTION

Endogenous nitric oxide (NO) plays an important role in several biological systems. This molecule is the mediator in many physiological processes such as vasodilatation, bronchodilation, neurotransmission, tumor surveillance, antimicrobial defense, regulation of inflammatory–immune processes and also in pathophysiological processes as shock, cytotoxicity or inflammatory diseases (1, 2, 3).

NO is produced by various cell types including epithelial cells, airway nerves, inflammatory cells (macrophages, neutrophils, eosinophils, mast cells) and vascular endothelial cells in the respiratory tract (4). Nitric oxide acts as a neurotransmitter of the inhibitory nonadrenergic noncholinergic neurotransmission and it participates in the control of airways tone, ciliary motility, mucus secretion and plasma exudation. NO is generated from semi-essential amino acid L-arginine through the action of the enzyme NO synthases (NOS) in these cells. There are three isoforms of NOS. Two constitutive isoforms – neuronal (nNOS or NOS I) is expressed predominantly in neurons and endothelial (eNOS or NOS III) expressed in endothelial cells. The third isoform - inducible isoform (iNOS or NOS II) is situated in macrophages and in many other cell types (5). The constitutive isoforms are calcium-calmoduline dependent and release NO in small (picomolar) amount several seconds or minutes after activation.

It is hypothetized that NO released by these constitutive isoforms of NOS are involved in the regulation of physiological processes. Inducible NOS is induced by many stimuli including proinflammatory cytokines, lipopolysacharides, some environmental pollutants, allergen and

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release NO (nanomolar amounts) over several hours and continues for days after exposure to the activating stimulus (5). These high levels of NO participate mostly in pathophysiological processes associated with some inflammatory diseases (6). This demonstrates the significant positive correlation between some respiratory diseases and exhaled nitric oxide concentration (7). The increase in the exhaled NO is typical for asthma, bronchitis, infection of upper respiratory tract, etc. The decrease in the exhaled NO is typical for adult respiratory distress syndrome (ARDS), cystic fibrosis but in smokers too (8). The bronchial hyperreactivity (BHR) is one of the symptoms of the above-mentioned diseases. This hallmark is defined as an increase of the degree of airways narrowing in response to the bronchoconstrictor stimuli. Several reports have showed the ability of endogenous NO to modulate airways reactivity to the different mediators (4).

We were interested in the relationship of NO to bronchial hyperreactivity. The measurement of bronchial responsiveness is widely used for the diagnosis and monitoring of respiratory diseases. The changes of NO levels in the organism are one of factors that contribute to the changes of smooth muscle tone and determine the hyperreactivity (9, 10). We followed the relationship of nitric oxide level changes to the exogenous irritant-induced bronchial hyperreactivity. We are interested in substances decreasing the production of NO in organism.

MATERIAL AND METHODS

Male guinea pigs 250-350 g of body weight were used in these experiments. Animals were administered the selective inhibitor of inducible nitric oxide synthase aminoguanidine – subst. Sigma in a dose of 50 mg/kg b.w. intraperitoneally (n=8) or nonselective inhibitor of nitric oxide synthase L-NAME (methylester Nω-nitro-L-arginine) – subst. Sigma in a dose 40 mg/kg b.w. intraperitoneally (n=8). The agents were administered during 17 days (long-term administration) or 3 days (short-term administration). Animals were subsequently exposed to the toluene vapors in *in vivo* conditions two hours in each of three consecutive days. Authors used the method of exposition described by Strapková et al. (11).

Animals were killed and strips from trachea and lung tissue were placed to organ bath with Krebs-Henseleit solution containing 110.0 M NaCl, 4.8 M KCl, 2.35 M $CaCl_2$, 1.20 M $MgSO_4$, 1.20 M $KHPO_4$, 25.0 M $NaHCO_3$ and glucose in glass-distilled water, pH 7.5 ± 0.1 at 36 ± 0.5°C and continuously aerated with mixture 95% O_2 and 5% CO_2. The strips were initially set to 4 g of tension (30 minutes – loading phase) and then the tension was reduced to 2 g (30 minutes - adaptation phase). The strips were contracted by histamine and acetylcholine in the cumulative doses 10^{-8}–10^{-3} log M after 60 minutes of incubation. Krebs-Henseleit solution was renewed every 10 minutes. The responses of strips were recorded on a polygraph. Data (the amplitude of strips contraction in mN from trachea and lung tissue) were processed statistically by the unpaired Student t-test. Differences were considered statistically significant when p-value was below 0.05. All results were expressed as mean ± SEM.

RESULTS

We compared changes in bronchial hyperreactivity evoked by toluene exposure after short-term and long-term administration of NOS inhibitors with a group of animals without treatment with NOS inhibitors. The level of significance set as $p < 0.05$ one *, $p < 0.01$ two**, $p < 0.001$ three***.

The effect of L-NAME on tracheal responsiveness to histamine. We recorded the decrease of tracheal smooth muscle reactivity after administration of nonselective inhibitor L-NAME. The amplitude of contraction was reduced to the concentration 10^{-5} log M of histamine. We revealed the more expressive decrease after long-term administration of L-NAME (Fig. 1).

The effect of aminoguanidine on tracheal responsiveness to histamine. There are some differences in comparison with effect of L-NAME. We did not evoke significant changes in the tracheal smooth muscle reactivity after short-term administration of aminoguanidine. The long-term administration of this inhibitor reduced reactivity in the concentration 10^{-5} log M of histamine (Fig. 2).

Long-term administration of both inhibitors evoked significant decrease of tracheal smooth

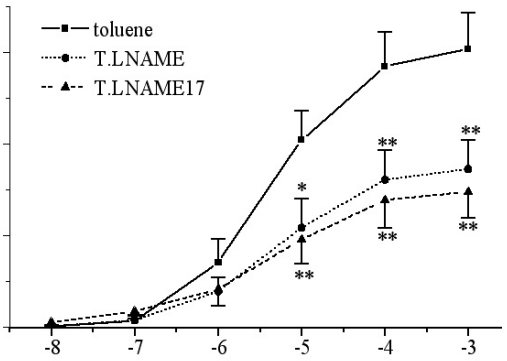

Fig.1 The effect of the pretreatment with L-NAME intraperitoneally during short-term (T.LNAME) and long-term (T.LNAME17) administration on the tracheal strip smooth muscle reactivity to histamine after exposure to the toluene vapours compared with toluene group – without pretreatment (toluene). The lines represent mean contraction amplitudes with standard error of the mean (+ S.E.M.). Axis x – the concentration of histamine in log M and axis y – the amplitude of contraction in mN.
Significance * – p < 0.05, ** - p < 0.01, ***- p < 0.001.

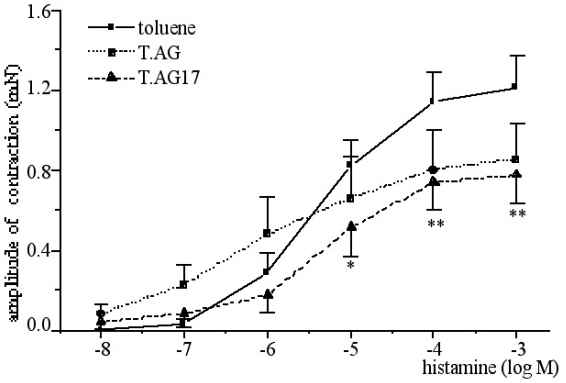

Fig. 2 The effect of the pretreatment with aminoguanidine (AG) intraperitoneally during short- term (T.AG) and long-term (T.AG17) administration on the tracheal strip smooth muscle reactivity to histamine after exposure to the toluene vapours compared with toluene group- without pretreatment (toluene). The lines represent mean contraction amplitudes with standard error of the mean (- S.E.M.). Axis x – the concentration of histamine in log M and axis y – the amplitude of contraction in mN.
Significance ** - p < 0.01.

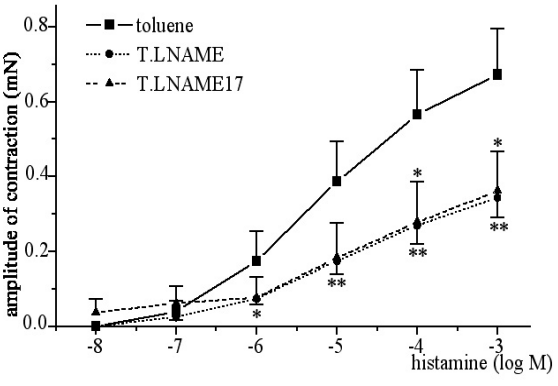

Fig. 3 The effect of the pretreatment with L-NAME intraperitoneally during short-term (T.LNAME) and long-term (T.LNAME17) administration on the lung strip smooth muscle reactivity to histamine after exposure to the toluene vapours compared with toluene group – without petreatment (toluene). Significance * - p < 0.05, ** - p < 0.01.

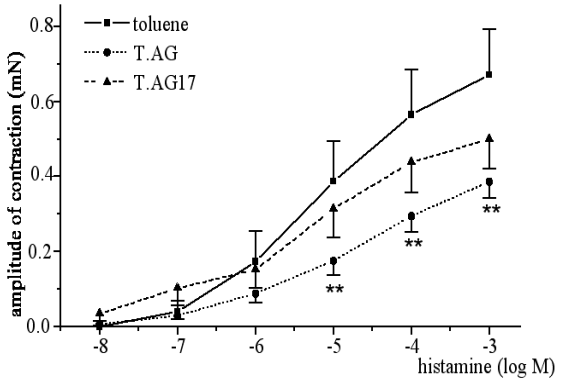

Fig. 4 The effect of the pretreatment with aminoguanidine (AG) intraperitoneally during short-term (T.AG) and long-term (T.AG17) administration on the lung tissue reactivity to histamine after exposure to the toluene vapours compared with toluene group without pretreatment (toluene). Significance ** - p < 0.01.

muscle hyperreactivity in experimental animals. More significant effect was observed after the administration of nonselective NOS inhibitor – L-NAME.

The effect of L-NAME on lung tissue responsiveness to histamine. The smooth muscle of lung tissue showed significant decrease of the amplitude of contraction to histamine also. This decrease was almost identical after a short-term and long-term administration of L-NAME but the short-term administration provoked the fall of amplitude contraction in the concentration 10^{-6} log M of histamine and this decrease was statistically more expressive (Fig. 3).

The effect of aminoguanidine on lung tissue responsiveness to histamine. This effect on the lung tissue smooth muscle was equal to the effect of L-NAME. The effect of inhibitor was significant after

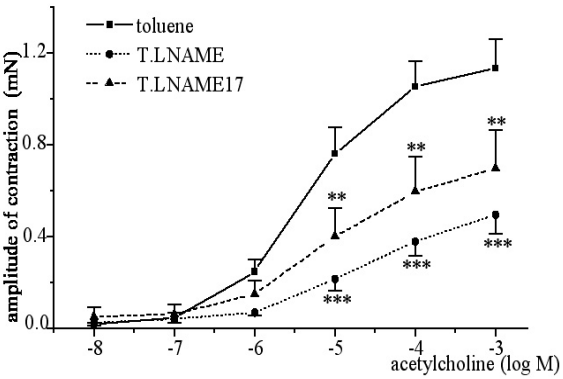

Fig. 5 The effect of the pretreatment with L-NAME intraperitoneally during short-term (T.LNAME) and long-term (T.LNAME17) administration on the tracheal strip smooth muscle reactivity to acetylcholine after exposure to the toluene vapours compared with toluene group without pretreatment (toluene).
Significance *** - $p < 0.001$, * - $p < 0.01$.

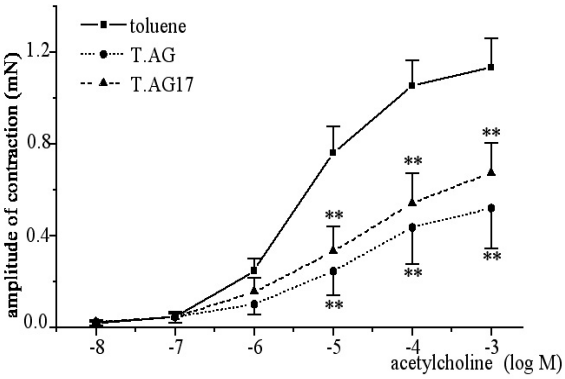

Fig. 6 The effect of the pretreatment with aminoguanidine (AG) intraperitoneally during short-term (T.AG) and long-term (T.AG17) administration on the tracheal strip smooth muscle reactivity to acetylcholine after exposure to the toluene vapours compared with toluene group without pretreatment (toluene). Significance ** - $p < 0.01$.

short-term administration. Long-term administration evoked decrease of reactivity but this was not statistically significant (Fig. 4).

In this case contraction amplitude fall was more expressive after short application both of inhibitors – aminoguanidine and L-NAME, but more significant effect was obvious after administration of L-NAME.

The effect of L-NAME on tracheal responsiveness to acetylcholine. The tendency of smooth muscle responses to acetylcholine was similar to the changes caused by histamine. Decrease of the contraction amplitude was again more significant after short-term administration L-NAME, even at the concentration 10^{-5} of acetylcholine (Fig. 5).

The effect of aminoguanidine on tracheal responsiveness to acetylcholine. The response on acetylcholine after administration of the selective inhibitor NOS was similar to the response after administration of L-NAME (Fig. 6).

The effect of L-NAME and aminoguanidine on bronchial responsiveness to acetylcholine was not significant.

DISCUSSION

We have shown that NO has an important role in the development of bronchial hyperreactivity (BHR) in our conditions. We used the model of hyperreactivity evoked by toluene vapours exposure. Toluene provoked the increase of airways reactivity in our previous studies and we consider this model to be suitable for our experiments (12). The mechanism of this hyperreactivity can be connected with the production of reactive oxygen and nitrogen species. Our aim was to show participation of several isoforms in generation of BHR by using various inhibitors of NOS (L-NAME, aminoguanidine). It is known that a high level of NO produced mainly by iNOS is responsible for development of many respiratory system diseases and their symptoms including bronchial hyperreactivity. Nitric oxide is detectable in the exhaled air of humans and experimental animals with BHR. The increase in exhaled NO can be normalized after administration of oral glucocorticosteroid or after inhalation of the selective iNOS inhibitor – aminoguanidine indicating that high exhaled NO concentrations may determine the enhance of iNOS expression (13).

Various studies have shown that iNOS-derived NO exhibits both beneficial and detrimental effect on bronchial hyperreactivity. Therefore, views on the NO effect in these conditions are currently vary-

ing (4). The enhanced expression and activity of iNOS isoform is currently the mainl goal of experimental studies. Using aminoguanidine Schuiling (1998) revealed dual effect of iNOS-derived NO on ovalbumin-induced airways hyperreactivity. The administration of this iNOS inhibitor in low doses in the acute condition potentiated airways hyperreactivity. High doses of this agent used in the prophylaxis inhibited airways hyperresponsivenes (14). It is interesting that the inhalation of aminoguanidine potentiated BHR measured in sensitized guinea pigs after the late asthmatic reaction to allergen challenge but the inhalation of this inhibitor before development of the late asthmatic reaction reduced BHR and decreased the number of inflammatory cells (7, 13). Thus NO derived by iNOS appears to exert both beneficial (modulating airway smooth muscle tone) and detrimental (deepening airway inflammation) effect on BHR (7). This effect was not described in some works or the inhibition of NOS do not eliminate the effect of NO (15, 16). There are various effects dependent on the time of administration, doses of inhibitors and way of administration. In our study the effect of iNOS inhibitor aminoguanidine was predominantly beneficial.

It is assumed that to this symptom can contribute the deficiency of NO released by constitutive NOS isoforms also (10) but the share of NOS isoforms in this process has not yet been precisely certified. It is proposed that, according to various authors eNOS releasing NO plays the role in the control of the smooth muscle tone (17). Lee et al. (2000) have found that the distribution of the genotype of eNOS was significantly higher in the asthma group than in the control population suggesting the possible involvement of the eNOS in this condition. Other authors think that in BHR nNOS-released NO is important and it plays a role of antagonist of the excitatory cholinergic neurotransmission. Normal function both of constitutive isoforms – eNOS and nNOS in bronchial hyperreactivity was recorded in other papers (19, 20) when expression and activity of iNOS was enhanced.

Different responses are in case of inhibitor of constitutive NOS isoforms L-NAME in various experimental works. L-NAME inhibits all types of NOS with subsequent inhibition of the release of NO by various cells including airway smooth muscle cells. The administration of this nonselective inhibitor induce an increase in the baseline tissue resistance that has been inhibited by NO donors or by addition of inhaled NO (21). eNOS probably modulates primarily the increase in resistance induced by a cholinergic agonist (21, 22). Metha et al. (1997) revealed an increase in the response after inhibiting NO-production with L-NAME during histamine-induced bronchoconstriction in guinea pigs. They reported that L-NAME enhanced bronchial reactivity to histamine in control group but not in antigen-challenged guinea pigs, suggesting a defect in NO bronchodilator activity in the challenged animals. This defect probably did not arise from decreased NO-production because exhaled concentration was the same in control and challenged animals (7). It is possible that effect of L-NAME is dependent on the doses or on the other mechanism of action than NOS inhibition (24).

So, can NOS inhibitors exacerbate airway hyperreactivity or have protective effect? The amplitude of contraction was decreased mainly after the administration of the nonselective inhibitor L-NAME in our conditions. We can assume the participation of constitutive isoforms more in our model of the bronchial hyperreactivity. Our results are consistent with literary data suggesting that NO released by constitutive NOS isoforms play physiological role in the control of smooth muscle tone (10). Various experimental conditions in provocation of hyperreactivity must be taken into account (environmental irritants, allergen-induced BHR), type of animals, doses of used inhibitors, way of rating the changes (in vitro, in vivo) etc. It is possible to envisage about different NO effect in acute and serious clinical state where it manifests mainly deleterious effect contrary to the distinct from NO effect in stable conditions when NO has mainly beneficial effect (3,19).

We found that any of the three isoforms of NOS may play a certain role in BHR. In the present study we show that NO inhibitors (L-NAME, aminoguanidine) have beneficial effect. The administration of these inhibitors prevented from BHR in the guinea pigs in conditions of toluene-induced hyperreactivity. These inhibitors decreased the reactivity of strips from trachea and lung tissue to both bronchoconstrictor mediators – histamine and acetylcholine in our conditions. Some differences in the response of tissue in different airway levels can be connected with various substitution of single NOS isoforms in upper and lower airway. Short-term administration of both inhibitors is more effective in comparison to long-term administration on all cases in our work. Literary data in this field are still poor. We suppose that this observation can result from adaptation of the mecha-

nisms controlling airway reactivity or it is connected with desensitization of the guanylylcyclase. To understand these processes and confirm this hypothesis further studies will be needed. It is necessary to continue the research of the NO role in the respiratory system. This reasearch may bring new therapeutical chances in the treatment of many respiratory diseases with bronchial hyperreactivity.

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ARTERIAL HYPERTENSION, ENDOTHELIAL DYSFUNCTION AND DEFECTS OF HAEMOSTASIS

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Abstract

Arterial hypertension (AH) is a classical risk factor of arteriosclerosis (ATS) and ischemic heart disease (IHD). AH as a part of the metabolic syndrome (MS) is connected with a higher incidence of total and central obesity, dyslipidaemia and impaired glucose tolerance (IGT) or diabetes mellitus type 2 (DM2). But the phenotypic expression of MS is, except of these factors, influenced by some other such as neuroendocrine changes, low grade inflammatory reaction, endothelial dysfunction and hypercoagulable and hypofibrinolytic states. The aim of our study was to assess the influence of some selected components of MS on the leptin and ghrelin levels, hormones involved in the control of energetic homeostasis and on the levels of endothelial markers, such as von Willebrand factor (vWF) and thrombomodulin (TM), in patients with AH.

We examined the blood plasma levels of leptin and ghrelin in a group of 62 patients with AH, who were divided according to the rate of their Body Mass Index (BMI) into 3 groups with BMI above 30, between 25 and 30 and below 25. Each group was divided into 2 subgroups according to the presence of IGT or DM2. Leptin levels were significantly higher in obese patients with IGT/DM2 compared to non-obese controls. We proved a trend to lower ghrelin levels in patients with IGT/DM2 regardless their BMI, which speaks for the fact that ghrelin levels depend rather on hyperinsulinaemia than obesity. In the second part of our study we examined the serum blood levels of vWF (a marker of endothelial activation) and TM (a marker of acute endothelial damage) in a group of 26 patients with 1st stage of AH, according to WHO. The patients were divided into 2 groups, each of them including 13 members, according to the presence of IGT/DM2. There was no relevant difference between the values of vWF in both groups, but the levels of TM were significantly higher in patients with IGT/DM2. We suppose that in our patients with early stage of AH endothelial dysfunction was only connected with the presence of hyperglycemia. We concluded that the changes of neuroendocrine parameters and the endothelial dysfunction are rather influenced by other components of MS than by AH itself.

Key words: arterial hypertension, metabolic syndrome, ghrelin, leptin, endothelial dysfunction.

INTRODUCTION

Arterial hypertension (AH) is considered to be one of the classical risk factors of arteriosclerosis (ATS) and ischemic heart disease (IHD). Arterial hypertension is an important part of the metabolic syndrome (MS), where it is connected with a higher incidence of total and central obesity, dyslipidaemia with typical increasing of triglyceride levels and decreasing of high density lipoprotein levels and impaired glucose tolerance (IGT) or diabetes mellitus type 2 (DM2). The until recently accepted patophysiological concept of 2 primary factors – insulin resistance (IR) with compensatory hyperinsulinaemia (HI) and total and central obesity, which cause the rise of 3 secondary components – IGT, dyslipidaemia and AH, has not fully explained all abnormalities associated with MS. Its phenotypic expression is also influenced by some other factors caused by obesity and IR/HI, such as neuroendocrine changes, low grade inflammatory reaction, endothelial dysfunction and hypercoagulable and hypofibrinolytic states (1).

Neuroendocrine changes in MS include an alterated production of several adipokines and hormones of the energetic metabolism (1). Leptin, an adipokine produced in white adipose tissue (2,3), and ghrelin, secreted mainly from stomach neuroendocrine cells (4,5,6,7), are some of these substances. Leptin inhibits food intake and supports lipid utilization in peripheral tissues (2,3). On the contrary, ghrelin stimulates food intake (4,5,6,7) and increases insulin secretion from pancreas (4). The aim of the 1st part of our study was to investigate the influence of IR/HI and obesity as the primary factors of MS on the levels of these two hormones in patients with AH.

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Endothelial dysfunction can be divided into endothelial activation, which is characterized by the decreased vasodilatatory response mediated by NO (nitric oxide), deteriorated antithrombotic effect of the endothelium, increased capillary permeability and leukocyte extravasation, and into direct endothelial damage(8). The, so called, endothelial markers are used for the diagnostics of endothelial dysfunction. These markers are proteins produced by endothelial cells, such as von Willebrand factor (vWF), a marker of endothelial activation (8), and thrombomodulin (TM), a marker of acute endothelial damage (8). In the 2nd part of our study we focused on the influence of IGT/DM2 on the levels of these endothelial markers in patients with 1st stage of AH (according to WHO).

METHODS

Neuroendocrine hormones: In the 1st part of our study, which deals with the hormones of the energetic metabolism, we examined 62 patients (41 males) with an average age of 56.1 years and with a present AH. In each patient we stated the presence or absence of a saccharide metabolism disorder (IGT/DM2) according to his/her medical documentation. The adiposity rate was assessed with the help of the Body Mass Index (BMI), calculated from the pacient's height and weight. In all patients blood pressure was also measured and the concentrations of triglycerides, cholesterol, leptin and ghrelin in blood plasma were assessed from fasting blood samples. For the assessment of leptin and ghrelin we used standard RIA kits. According to BMI values the patients were divided into 3 groups – with BMI above 30, between 25 and 30 and under 25. Each group was then divided into 2 subgroups according to the presence of saccharide metabolism disorder. In each subgroup mean values with standard deviation of leptin and ghrelin were calculated.

Endothelial dysfunction markers: Into the 2nd part of our study, which focuses on the endothelial dysfunction markers, we included another 26 patients with 1st stage of AH. In 13 of them (7 males) with an average age of 55.8 years IGT or DM2 was stated, according to anamnesis and medical documentation. In the remaining 13 (7 males) with an average age of 50.4 years no such disorder was present. In each patient the levels of vWF and TM in blood serum were assessed and results were done as their mean values with standard deviation.

For statistical analyses we used Student T-test for comparison of the differences between 2 groups and the computer program ANOVA in case of comparing the differences among more than 2 groups.

RESULTS

Neuroendocrine hormones: Mean values of systolic and diastolic blood pressure, cholesterol, triglycerides, leptin and ghrelin in each subgroup are listed in Table 1. In patients with AH we proved a trend to lower ghrelin levels in the presence of saccharide metabolism disorder (IGT, DM2) (Figure 1), but, due to a small number of patients and a large scale of measured values in the subgroups, this trend was not statistically significant. The mean leptin level in obese patients (BMI>30) with IGT/DM2 was 8.50 +/- 6.65 ng/ml and it was significantly higher ($p<0.02$) compared to the level in lean patients (BMI<25) with IGT/DM2, which was 2.20 +/- 0.63 ng/ml. We did not confirm any statistical differences between other subgroups, what may have also been caused by small numbers of patients and a large dispersion of measured values (Figure 2).

Endothelial dysfunction markers: The mean value of von Willebrand factor in patients with 1st stage of AH and a present IGT/DM2 reached the level of 1.57 +/- 0.63 IU/ml compared to 1.47 +/- 0.49 IU/ml in patients without IGT/DM2. This increase was not statistically significant. On the contrary, the level of thrombomodulin in the group with present IGT/DM2 was significantly higher than in patients without IGT/DM2 – 70 (2-135) ng/ml vs. 36 (10-94) ng/ml with $p<0.02$ (Table 2, Figure 3, Figure 4).

Table 1 Mean values of measured parameters in each subgroup of patients in the neuroendocrine hormones study. DM – diabetes mellitus; BMI – Body Mass Index.

BMI > 30						
without DM						
Number [n]	Cholesterol [mmol/l]	Triglycerides [mmol/l]	Blood pressure syst. [Torr]	Blood pressure diast. [Torr]	Ghrelin [pg/ml]	Leptin [ng/ml]
9	5.39 +/-2.12	2.19 +/- 1.32	153.33 +/- 22.91	96.11 +/- 12.69	836.09+/-1503.3	6.25 +/- 6.547
with DM						
Number [n]	Cholesterol [mmol/l]	Triglycerides [mmol/l]	Blood pressure syst. [Torr]	Blood pressure diast. [Torr]	Ghrelin [pg/ml]	Leptin [ng/ml]
6	5.51 +/-2.46	2.59 +/-1.599	145.83 +/- 26.16	89.17 +/- 18.55	267.93 +/147.38	8.50 +/- 6.649
25 < BMI < 30						
without DM						
Number [n]	Cholesterol [mmol/l]	Triglycerides [mmol/l]	Blood pressure syst. [Torr]	Blood pressure diast. [Torr]	Ghrelin [pg/ml]	Leptin [ng/ml]
23	5.36 +/- 1.10	2.28 +/- 1.12	139.91 +/- 19.33	87.61 +/- 9.33	550.55 +/- 852.64	5.14 +/- 6.06
with DM						
Number [n]	Cholesterol [mmol/l]	Triglycerides [mmol/l]	Blood pressure syst. [Torr]	Blood pressure diast. [Torr]	Ghrelin [pg/ml]	Leptin [ng/ml]
8	4.99 +/- 1.15	1.89 +/- 0.45	138.13 +/- 13.16	83.13 +/- 8.84	343.56 +/- 641.51	13.02 +/- 20.31
BMI < 25						
without DM						
Number [n]	Cholesterol [mmol/l]	Triglycerides [mmol/l]	Blood pressure syst. [Torr]	Blood pressure diast. [Torr]	Ghrelin [pg/ml]	Leptin [ng/ml]
14	5.41 +/- 0.80	1.40 +/- 0.43	143.57 +/- 39.15	84.64 +/- 21.80	855.74 +/- 969.48	6.71 +/- 13.92
with DM						
Number [n]	Cholesterol [mmol/l]	Triglycerides [mmol/l]	Blood pressure syst. [Torr]	Blood pressure diast. [Torr]	Ghrelin [pg/ml]	Leptin [ng/ml]
2	4.99 +/- 1.10	2.59 +/- 1.53	135 +/- 7.07	85 +/- 7.07	226.85 +/- 122.68	2.195 +/- 0.63

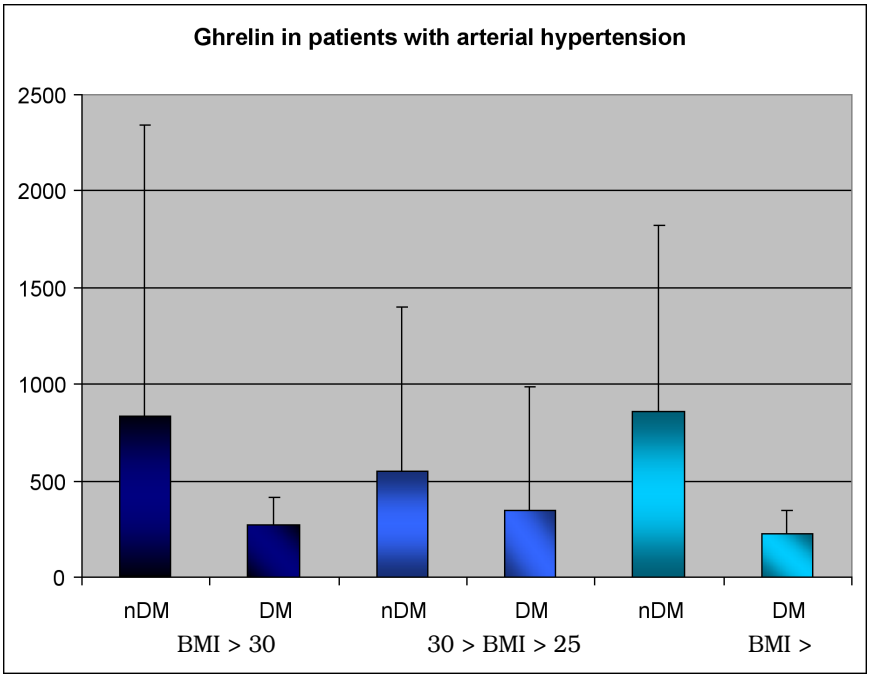

Figure 1 Ghrelin in patients with arterial hypertension. Ghrelin levels are done as mean values in pg/ml with standard deviation. DM – diabetes mellitus; nDM – without diabetes mellitus; BMI – Body Mass Index.

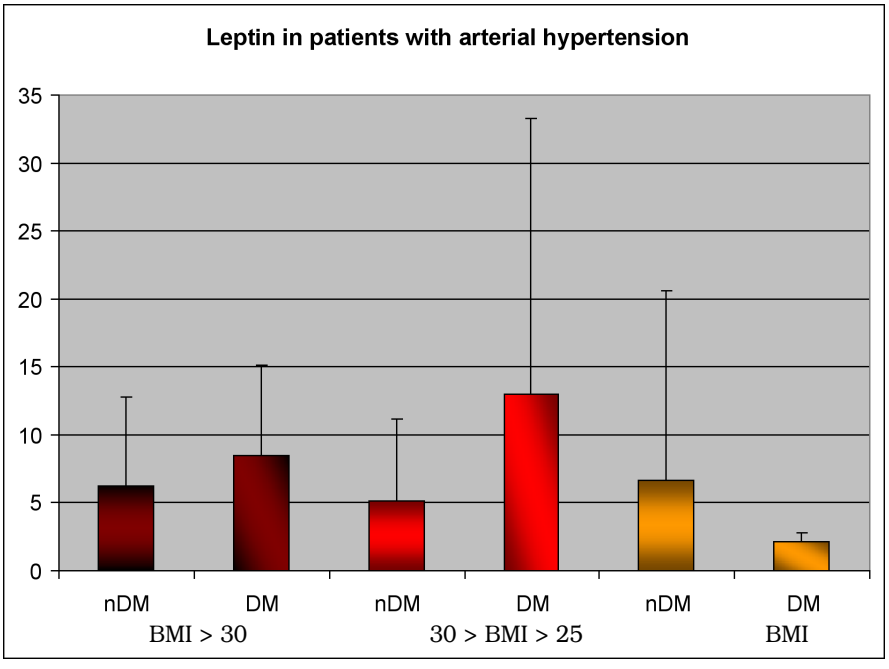

Figure 2 Leptin in patients with arterial hypertension. Leptin levels are done as mean values in ng/ml with standard deviation. DM – diabetes mellitus; nDM – without diabetes mellitus; BMI – Body Mass Index.

Table 2 Mean values and statistical significance of von Willebrand factor and thrombomodulin in both groups of patients involved in the endothelial markers study. DM – diabetes mellitus, IGT – impaired glucose tolerance.

Group	Number (n)	Average age	Women	Men	von Willebrand factor (IU/ml)	Thrombomodulin (ng/ml)
Hypertension (1st stage of AH, WHO)	13	50.4 +/- 12.3	6	7	1.47 +/- 0.49	36 (10-94)
Hypertension (1st stage of AH, WHO) DM type 2, IGT	13	55.8 +/- 9.7	6	7	1.57 +/- 0.63	70 (2-135)
Statistical significance					non-significant	p<0.02

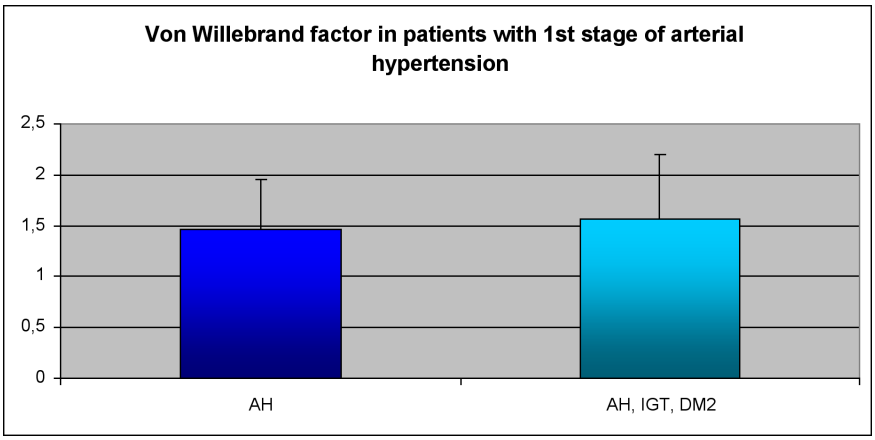

Figure 3 Von Willebrand factor in patients with 1st stage of arterial hypertension. Von Willebrand factor levels are done as mean values in IU/ml with standard deviation. AH – arterial hypertension; IGT – impaired glucose tolerance; DM2 – diabetes mellitus type 2.

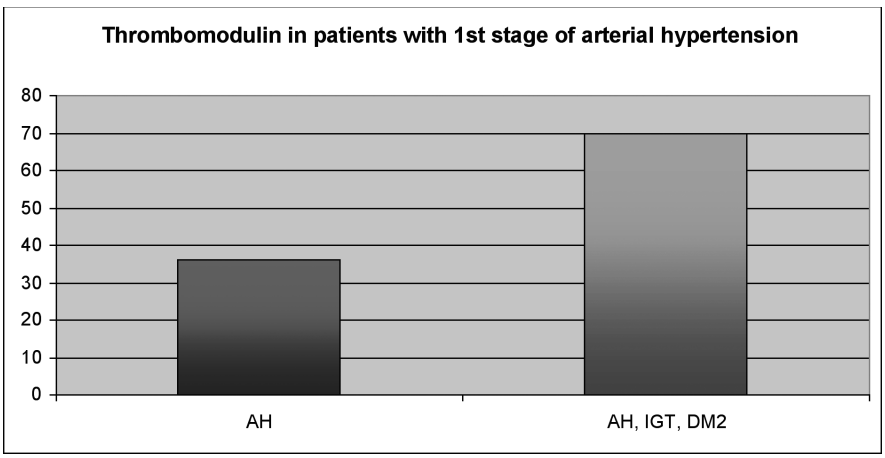

Figure 4 Thrombomodulin in patients with 1st stage of arterial hypertension. Thrombomodulin levels are done as mean values in ng/ml. AH – arterial hypertension; IGT – impaired glucose tolerance; DM2 – diabetes mellitus type 2.

DISCUSSION

In patients with metabolic syndrome changes in production and secretion of several hormones involved in the regulation of energetic homeostasis take place (1). In our pilot study we researched on 2 of these substances – ghrelin and leptin. Leptin is an adipokine secreted from the white adipose tissue. It inhibits food intake by stimulating the production of anorexigenic and inhibiting the production of orexigenic peptides in hypothalamus (2,3). In peripheral tissues it enhances the utilization of intracellular lipids and so increases their sensitivity to insulin (3). High levels of this protein were, paradoxically, observed in obese patients and, according to this fact, these patients are considered to have a leptin resistance (2,3).Thus the significant increase in leptin levels in our obese patients with IGT/DM2 compared to non-obese controls is in conformity with the data in medical literature (2, 3). Ghrelin is a gastrointestinal hormone produced mainly in stomach neuroendocrine cells (4,5,6,7). Its effects are in a large extent antagonistic to the effects of leptin. This peptide stimulates food intake by increasing the production of orexigenic peptides in hypothalamus (4,5,6,7), and, in the periphery, it increases insulin secretion from pancreas and decreases its effects in hepatocytes (4). Ghrelin also stimulates the secretion of growth hormone from the pituitary (4,5,6,7) and exerts vasodilatatory effects on peripheral blood vessels (5,6). Our preliminary results speak for the fact that ghrelin levels depend rather on the presence of hyperinsulinaemia than on obesity. The small number of patients and large dispersion of measured values in some subgroups, which impeded statistical evaluation of the results, was caused by the fact that this was a pilot study focusing on these problems. Into the future we plan to increase the number of patients involved in the study and to expand the number of examined parameters of the metabolic syndrome.

Von Willebrand factor is a glycoprotein, which participates in the adhesion and early activation of platelets. It is produced and stored in the Weibel-Palade bodies in the endothelium. It is secreted by spontaneous exocytosis or by induction with various factors that increase the intracellular calcium (Ca_i) and cAMP. Experimental and clinical studies have confirmed that increased secretion of vWF is caused not only by a direct endothelial damage, but also by its activation with various impulses, e.g. inflammatory cytokines. That is why vWF is nowadays considered to be a marker of the chronic and systemic activation of the endothelium (8). Thrombomodulin is a transmembranic glycoprotein on the surface of the endothelium that binds thrombin and converts its procoagulable effect into the anticoagulable one by the activation of protein C and inhibition of the proteolytic effect of thrombin on factors V and VIII. During the damage of the endothelium caused by the products of activated neutrophiles, such as elastase, cathepsin G and free oxygen radicals, thrombomodulin is split from its surface and its increased levels in blood are considered to be a marker of acute endothelial damage (8). In our study we could not prove any significant difference in the levels of vWF between the group with IGT/DM2 and the control group with no saccharide metabolism disorder, but the levels of thrombomodulin in the group with present IGT/DM2 were significantly higher than in patients without IGT/DM2. Thus we concluded that in our patients with 1st stage of AH endothelial dysfunction was only connected with the presence of hyperglycemia and was not dependent on AH itself.

In the end we can state that the changes in the levels of the observed neuroendocrine parameters and the endothelial dysfunction are rather influenced by other components of MS than by AH itself.

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GENOTOXICITY MONITORING IN SLOVAK SHOW CAVE WORKERS EXPOSED TO RADON

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A b s t r a c t

Radon (Rn) belongs to noble gases group and it is the heaviest of them. Rn is a radioactive gas produced by the decay of radium (Ra), and emits radioactive alpha particles. The most stable isotopic form is radon-222 with half-life of 3.823 days. Natural radon concentration in Earth's atmosphere is very low. Radon is a carcinogenic gas and exposition to it presents some health hazards. The decay products (daughter isotopes) collect on dust in the air and lining of the passageways leading into the lungs.

The aim of our work was genotoxic risk assessment of the Slovak show cave employees of the workers Slovak Caves Administration in Liptovsky Mikulas. They are guides or administrators of the six Slovak show caves.

We evaluated the chromosomal aberrations occurrence by means of cytogenetic analysis of peripheral blood lymphocytes of workers in six Slovak show caves: Vazecka, Demanovska, Bystrianska, Harmanecka, Ochtinska aragonitova and Domica.

Altogether 53 investigations were performed. In 15 cases (i.e. 28.30 %) we found out increase or high exposure to genotoxic agents. The highest number of aberrant cells (Ab.c.) was detected in workers of caves Vazecka (2.57 % Ab.c) and Bystrianska (2.00 % Ab.c.).

Key words: radon, cave, cytogenetic analysis, chromosomal aberrations

INTRODUCTION

Radon is a chemical element in the periodic table that has the symbol Rn and atomic number 86. It is a radioactive noble gas that is formed by the disintegration of radium.

Radon was discovered in 1900 by Friedrich Ernst Dorn, who called it radium emanation. In 1908 William Ramsay and Robert Whytlaw-Gray, who named it niton

(Latin *nitens* meaning „shining"), isolated it, determined its density and it was the heaviest known gas. It has been called radon since 1923 (1, 2).

There are twenty known isotopes of radon. The most stable isotope is radon-222 which is a decay product (daughter isotope) of radium-226, has a half-life of 3.823 days and emits radioactive alpha particles. Radon-220 is a natural product of thorium (Th) and is called thoron. It has a half-life of 55.6 seconds and also emits alpha rays. Radon-219 is derived from actinium (Ac), is called actinon, is also alpha emitter and has a half-life of 3.96 seconds.

Essentially inert, radon is the heaviest noble gas and one of the heaviest gases at room temperature. (The heaviest is tungsten hexafluoride, WF6). At standard temperature and pressure it is a colorless gas but when it is cooled below its freezing-point is has a brilliant phosphorescence which turns yellow as the temperature is lowered and orange red as the temperature air liquefies (3, 4).

Radon is sometimes produced by a few hospitals for therapeutic use by pumping its gas from a radium source and storing it in very small tubes which are called seeds or needles. This practice is being abandoned as hospitals get seeds from suppliers who make them with desired activity levels (5).

Because of its rapid loss to air, radon is used in hydrologic research that studies the interaction between ground water, stream and rivers. Any significant concentration of radon in stream or river is a good indicator that there are local inputs of ground water (6).

Radon is a carcinogenic gas, i.e. radioactive material and must be handled with care at all times. It is hazardous to inhale this element since it emits alpha particles. Also its solid decay

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products, and their respective products, tend to form a fine dust which can easily enter the airways and become permanently stuck in lung tissue, producing heavy localized exposure (7, 8, 9). Rooms where radium, actinium, or thorium are stored should be well-ventilated in order to prevent build-up in the air. The build-up of radon is a potential health hazard in uranium and some lead mines. Build-up of radon in homes has also been a more recent health concern and many lung cancer cases are attributed to radon exposure each year (10, 11).

In literature we found no monitoring of chromosomal aberrations in cave workers. In miners of uranium and ore mines was explained the higher incidence of bronchogenic carcinoma.

MATERIAL AND METHODS

Radon can cumulate in underground areas that are not sufficiently ventilated, i.e. mining shafts, tunnels, but caves. Therefore we perform genotoxicity monitoring of Slovak show cave workers employed by the Slovak Cave Administration in Liptovsky Mikulas. They are guides, or administrators in six Slovak caves: Vazecka, Demanovska, Bystrianska, Harmanecka, Ochtinska aragonitova and Domica.

We evaluated the aberrant cells (Ab.c) occurrence by means of cytogenetic analysis of peripheral blood lymphocytes in this group of workers and also a control group for assessment of genotoxic risk (12). This method is established on short time cultivation (48-52 hours) and cytogenetic analysis of cells. The cells with chromatid or chromosome break as well as chromatid or chromosome exchange are aberrant cells (Ab.c). The number of Ab.c. from 2.0 % to 4.0 % form increased exposition and more than 4.0 % form high exposition to genotoxic agents. The data concerning the numbers of Ab.c. were evaluated by Student's t-test.

RESULTS

We examined 53 workers exposed to radon, with average age 35.92 years ± 6.82 (SD) and average exposition time 9.91 years ± 6.19 (SD). They are 44 men (i.e. 83.02 %) and 9 women (i.e. 16.98 %). The control group consisted of 32 healthy workers from Faculty Hospital in Martin. The workers were not exposed to any genotoxic agents. The average age is 31.84 years ± 5.84(SD).

From every subject we evaluated 100 mitosis, i.e. 5300 mitosis from exposed workers and 3200 mitosis from control subjects.

In exposed group we found in 111 cells chromosomal aberrations, this present 2.09 % Ab.c. ± 0.19 (SEM), and in control group 1.53 % ± 0.16(SEM). There are 106 breaks (95.50%), and 5 exchanges (4.50%) on chromosomes. The chromatide breaks formed 60.36%, chromosome breaks 35.14%, chromatide exchange 0.90% and chromosome exchange 3.60%.

Table 1. Numbers of Ab.c. in show caves

Caves	Mitosis number	Number of Ab.c.	% Ab.c. ± SEM
Demanovska	1800	32	1.78 ± 0.17
Vazecka	2300	59	2.57 ± 0.33*
Bystrianska	700	14	2.00 ± 0.43
Harmanecka	300	4	1.33
Ochtinska aragonitova	100	0	0
Domica	100	1	1.00
Summary	**5300**	**111**	**2.09 ± 0.19**
Control group	**3200**	**49**	**1.53 ± 0.16**

*P < 0.05

Table 2 Numbers of workers with increased or high exposure to genotoxic agents

Exposure to genotoxic agents	Number of workers	% of workers
Increased (2.01- 4.00%)	12	22.64
High (>4.01%)	3	5.66
Summary	**15**	**28.30**

Table 3 Numbers of Ab.c. according to sex

Sex	Mitosis number	Number of Ab.c.	% Ab.c. ± SEM
M	4400	92	2.09 Ī 0.18
F	900	19	2.11 Ī 0.21

The highest number of Ab.c. we detected in workers of Vazecka (2.57 % Ab.c) and Bystrianska (2.00 % Ab.c.) caves. There is a significant increase ($P < 0.05$) in the mean number of Ab.c. in workers of cave Vazecka as compared to control. The numbers of Ab.c. single caves are expressed in Table 1.

In 15 cases (i.e. 28.30 %) we found increase or high exposure to genotoxic agents (Table 2), we found no difference between sex (Table 3), and we found no dependence of the number of Ab.c. on age and time of exposure.

DISCUSSION

Because the radon is one of the heaviest gases, it can cumulate in underground areas, if they are not sufficiently ventilated, i.e. mining shafts, tunnels, but also caves (4). Caves are known for having elevated radon levels. Cave air was first looked at from this point of view in the 1970s and the National Park Service and various states started limiting time underground for tour guides (13). Radon availability is related mainly to the concentration in the spaces in rock fractures and soil pores and to the permeability of the ground to gases. There are these rock types, granites, phosphatic rocks, marine, shales, and some recrystallized limestones and dolomites (14). The measured values of radiation in the caves and mines exceeded the permissible limits and Regional Hygienist of the Central Slovakia declared in 1981 the risk zones and, at the same time, the monitoring of working atmosphere was iniciated. The higher incidence of bronchogenic carcinoma was explained mainly in miners (15). In cave workers we registered no case of carcinoma.

Our evaluations referred to certain exposition of this carcinogen in cave workers too. In summary we found 2.09 % Ab.c. There is not a significant increase as compared to control, but in 28.30 % of exposed workers we found increased or high exposure to genotoxic agents. The essence of prevention is based in the lowering of ionizing radiation and improvement of the sanitary-technical component of prevention. The guides, or administrators in Slovak caves need due medical care.

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SPECIFIC FEATURES OF THE CARE OF ELDERLY

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Abstract

This work was focused on assessing various aspects of quality of life in bio – psycho – social area in elderly in institutionalized community care. Study sample consisted of 46 subjects, 22 of which lived in a hostel for retired and 24 lived in a home for retired. There were 23 women and 23 men in the group.

The quality of life of the elderly is influenced by bio-psycho-social problems. Physical problems are connected with health evaluation. Dependence on self-care interferes with disablement of work performance.

Quality of life, subjective health evaluation, overall satisfaction are lower in residents of home for retired than in those living in the hostel of retired. Disablement in social functioning, dependence on self-care are higher in residents of the home for retired than in those living in the hostel for retired. Disablement in family and home is significantly higher in men than in women. Differences in quality of life, disablement of social functioning, dependence on self-care and health evaluation we can use as a starting-point for planning and realization of changes in health and social care of elderly in community care.

Key words: quality of life, social functioning, health, elderly, community care

INTRODUCTION

Aging of population and rising number of senior citizens is the basic factor that nowadays makes all the societies think about finding and developing a new way and organization of medical, nursing and social care of aged people. There are two substantial aspects for rapid changes in demographic structure of population in developed countries:

– composition of age groups of population has been changing in favour of aged people,

– structure of individual's lifetime has been changing in favour of later life period.

Demographic data have been indicating a permanently rising ratio of population over 60 years. In the Slovak Republic the ratio of population over 60 years in 2002 rose to 15.4 %. The arised model of contemporaneity or urgency of solving problems in society (appears especially in localities where the ratio of aged people comes up to 8-10%) requires new types of social, medical, educational and other services. These trends are influenced not only by such determinants like the ratio of older and aged people and prolongation of senior period, but also by changing expectations of seniors from the life in retirement, effort for quality and dignity of life in old age, searching for social status of elders, democratization of society and searching for new models of life in senior period.

Specific care of elderly is based on objective medical criteria and on subjective needs and satisfaction. Subjective comprehensive condition as a dynamic process of changes can be expressed by dimension of quality of life.

Quality of life has only recently been recognized as the central purpose of health care. There is still insufficient agreement about the definition of quality of life, about its measurement and about the manner in which the results of assessing quality of life can best be used (1).

Health-related quality of life can be usefully measured in relation to the PCASEE model developed by Bech (1996). The PCASEE model provides a comprehensive assessment of a person's subjective perception of his/her well-being. The PCASEE model of quality of life consists of six dimensions: P – physical indicators, C – cognitive indicators, A – affective indicators, S – social indicators, E-1 – economic-social stressors, E-2 – ego functions. This model has been used to measure clinical improvement during treatment and nursing care (2).

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Social functioning as a important aspect of the quality of life can be assesed by WHO Disablement Scale. This scale consists of four components: A – self-care, B – working performance, C – family and home, D – acting on broader social context (3).

Aim: Our work was focused on assessing the specific aspects of quality of life in bio-psycho-social area with seniors in institutionalized community care. This care is provided in a home and in a hostel for retired. Residents of the home for retired require combined health and social care. Residents living in a hostel for retired require mainly social care. The aim of the work was to compare the quality of life, subjective health evaluation, overall satisfaction with stay in the institution, disablement of social functioning, self – care (independence of performing various acts of daily living) relating to gender and type of care required by residents of a home for retired and a hostel for retired. At the same time we evaluated correlations among the above items.

METHODS

Characteristics of the group

Study sample consisted of 46 subjects, 22 of which lived in a hostel for retired and 24 lived in a home for retired. There were 23 women and 23 men in the group. The mean age of those living in a hostel for retired was 72.3 ± 5.7 (x ± SD), those living in home for retired was 75.9 ± 5.5. The mean age of women was 74.4 ± 5.8 and of men was 73.9 ± 5.9. The mean length of stay at the hostel for retired was 3.7 ± 3.9 ys. and for those in the home for retired was 5.3 ± 3.8 years; for women 4.7 ± 3.9 ys. and men 4.3 ± 3.9 ys.

The inclusion criteria were:
– age 65 or higher
– willingness to participate
– informed consent
– ability to understand instructions related to the research methods

The exclusion criteria were:
– hearing disability
– inability or difficulty to communicate
– acute or chronic mental disorder
– acute somatic disease.

To find out empirical data, the **Bech's PCASEE Scale for Measuring Quality of Life** was used with P for physical problems, C for cognitive problems, A for affective problems, S for social dysfunctions, E1 for economic problems and E2 for ego problems. In each group there are five items which are marked by respondents with a number, from 0 – bad, until 5 – good. The summary of single items with the highest mark is 150 (2).

We also used the **WHO Disablement Scale**. On the scale of 0 – no disablement until 5 – severe disablement, the respondents rated four topics: DS - A: self-care – daily activities, DS - B: work – various activities, care of own home, DS - C: family and home – contacts with a spouse, children, relatives, DS - D: acting on broad social context, participation in social events, leisure time (3).

The dependence on self–care activities of daily life was assessed by **Barthel index** (ADL), where higher value means higher independence of the individual on scale from 0 to 100 (4).

We also assessed **subjective negative health evaluation** (HE) and **overall** (global) **satisfaction with the stay in the institution of the community care** (GS) by using self–rating scales with value from 0 to 5. When using subjective negative health evaluation the 0 value represented excellent (that is 100 %) health of the subject and the value of 5 represented very poor (or 0 %) health of the subject. Regarding overall satisfaction with the stay in the institution, the 0 value represented dissatisfaction (or 0 % satisfaction) with the stay, and the value of 5 represented complete satisfaction or 100 % satisfaction.

Statistical analyses. Data analysis was based on a two-step process:

1. The Mann-Whitney test was used to assess the significance of changes in the values of

items. Probability of less than 5 % was taken as indicative of statistical significance.

2. The relationships between assessed items were analysed by Spearman correlations.

RESULTS

The physical problems, cognitive problems, social dysfunctions and ego/personality problems were significantly lower in residents of the hostel for retired than in those living in the home for retired. There were no significant differences in affective problems and economic problems between our study groups. The global quality of life was significantly higher in the hostel group than in the home for retired group (Table 1).

The disablement in self-care – daily activities, work – various activities, care of own home, acting on broad social context, participation in social events, leisure time and dependence on activities of daily life were significantly lower in hostel group than in retired home group. Overall satisfaction with stay in the institution and subjective health evaluation were significantly higher in the hostel group than in the retired home group (Table 2).

Differences in quality of life between men and women were not significant (Table 3).

Disablement in family and home – contacts with a spouse, children, relatives was significantly higher in men than in women. There were no differences in disablement of self-care, work performance, acting on broad social context, independence between men and women. Differences in subjective health evaluation and overall satisfaction with stay in the institution between men and women were not significant (Table 4).

Significant correlations ($-0.5 \geq r \geq +0.5$; $r^2 \geq 0.5$) between physical problems, cognitive problems, affective problems, social dysfunctions, ego/personality problems, subjective health evaluation and global quality of life were found. Significant correlations between subjective health evaluation and physical problems, physical and cognitive problems were found. Correlations between disablement in work performance and dependence in self-care was found (Table 5).

Table 1 Significance of comparisons

a 22, b 24	x	SD	U	P
Pa Pb	14.82 10.96	4.16 3.96	8.74	< 0.01
Ca Cb	17.32 13.96	2.83 3.39	11.05	< 0.001
Aa Ab	16.41 14.42	3.36 4.40	2.89	NS
Sa Sb	14.14 12.00	3.09 3.73	3.86	< 0.05
E1a E1b	14.23 14.08	5.22 4.96	0.04	NS
E2a E2b	16.23 13.67	3.13 4.04	5.81	< 0.05
PCASEEa PCASEEb	93.14 79.33	13.19 18.49	7.51	< 0.01

a – residents of the hostel for retired
b – residents of the home for retired
x – average, SD – standard deviation, NS – not significant

Table 2 Significance of comparisons

a 22, b 24	X	SD	U	P
DS-Aa DS-Ab	0.41 1.25	0.59 1.33	4.67	< 0.05
DS-Ba DS-Bb	1.09 2.13	0.87 1.39	7.36	< 0.01
DS-Ca DS-Cb	1.45 1.83	0.96 1.31	0.98	NS
DS-Da DS-Db	1.14 2.17	0.89 1.24	7.91	< 0.01
ADLa ADLb	97.05 82.50	3.67 12.68	18.65	< 0.001
HEa Heb	2.32 3.42	0.95 0.78	3.90	< 0.001
GSa GSb	4.00 2.83	0.76 0.96	14.38	< 0.001

Table 3 Significance of comparisons

m 23, w 23	X	SD	U	P
Pm Pw	12.30 13.30	4.16 3.94	0.96	NS
Cm Cw	15.78 13.35	2.83 3.39	0.19	NS
Am Aw	15.70 15.04	3.36 4.40	0.47	NS
Sm Sw	12.83 13.22	3.09 3.73	0.24	NS
E1m E1w	14.74 13.57	5.22 4.96	0.70	NS
E2m E2w	15.43 14.35	3.13 4.04	0.72	NS
PCASEEm PCASEEw	86.78 85.09	13.19 18.49	0.04	NS

m – men, w - women

Table 4 Significance of comparisons

m 23, w 23	x	SD	U	P
DS-Am DS-Aw	1.09 0.61	0.59 1.33	3.07	NS
DS-Bm DS-Bw	1.87 1.39	0.87 1.39	1.38	NS
DS-Cm DS-Cw	2.00 1.30	0.96 1.31	5.6	< 0.05
DS-Dm DS-Dw	1.70 1.65	0.89 1.24	0.06	NS
ADLm ADLw	89.13 89.78	3.67 12.68	0.05	NS
HEm Hew	3.04 2.74	0.95 0.78	0.33	NS
GSm GSw	3.39 3.39	0.76 0.96	0.0001	NS

Table 5 Correlations

N 46	r	r^2
P – PCASEE	0.81	0.66
C – PCASEE	0.82	0.67
A – PCASEE	0.71	0.50
S – PCASEE	0.78	0.60
E2 – PCASEE	0.75	0.57
HE – PCASEE	-0.71	0.50
HE – P	-0.71	0.51
ADL – DSB	-0.82	0.67
P - C	0.74	0.55

r – correlation coefficient, r^2 - determination coefficient

DISCUSSION

Aged people are a heterogenous group of population requiring variable level of care, assistance and support. The importance of care is connected with increasing proportion of aged people in population which makes higher demands on health care. The common way of nursing care is usually provided in centres – in the case of acute conditions in hospitals, in the case of exacerbation of chronic diseases in sanatoria for long-term patients (5). The reform of health care opened also the problem of so-called social beds, some sanatoria for long-term patients had been closed and there are many problems with accepting seniors to the homes for retired or homes of social care. The approach to the medical services offered to aged, lonely and long-term patients has become worse. These services before often covered social problems (6). Health care and care of aged person's family is determined also by culture. It has substantial influence on the interaction of aged people with the society including the ability to search for and use medical service.

Peck, who developed Ericson's theory, states facts influencing also occurring the problems in our group.

1. Status-making and self-esteem through work: a lot of employees, especially men, had made their own status and self-esteem through their work. When retiring, an individual loses his or her status and it is very important to find something that compensates the dignity resulting from his or her work appointment.

2. Health and physical condition are getting worse: the process of aging is generally intercepted like worse health and condition. Content aging means also the ability to overcome these obstacles and compensate them, to find pleasure in activities where the physical performance has no meaning.

3. Awareness of mortality: to accept the idea of own mortality which can be helped by focusing on family, relatives and friends and constant tries to create conditions to satisfy others.

Varying conditions for providing nursing care (law on the professions of nurse and midwife) make opportunities for new ways of providing nursing service in various community centres such as centre of daily care, nursing house, health centres, home-care agencies, and so on. Intervention should focus on keeping and support of quality of life, especially in identified spheres of our research. The problems we have specified in the senior community require interdisciplinary approach providing complex problem solution accepting change dynamics in the monitored group (7).

Quality of life by the WHO is defined as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It consists of six broad domains: 1. physical, 2. psychological, 3. levels of independence, 4. social relationships, 5. environment, 6. spiritual. It focused upon the individual's perceived quality of life (8).

The quality of life of elderly in institutionalized community care depends on their bio-psychosocial problems. Physical problems of seniors are connected with their subjective health evaluation. Dependence on self-care is closely associated with disablement of work performance, various activities, care of own home. Quality of life, subjective health evaluation, overall satisfaction with stay in the institution are lower in residents of the home for retired than in those living in hostels for retired. Disablement in social functioning, dependence on self-care are higher in residents of the home for retired than in the hostel groups. Disablement in family and home – contacts with a spouse, children, relatives is significantly higher in men than in women. Differences in quality of life, disablement of social functioning, dependence in self-care and health evaluation we can use as a starting-point for planning and realization of changes in health and social care of seniors in community care (9).

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THE POSITION OF HYGIENE AND EPIDEMIOLOGY IN PUBLIC HEALTH

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Abstract

Hygiene and epidemiology belong to preventive branches commonly with social hygiene and social medicine. These branches are the basis of public health. Public health is influenced by the individuals, communities and all facts of population. Healthy life conditions are influenced by determinants of health (physical, chemical, biological, social, cultural and spiritual factors). Among the essential roles of public health belong the identification, monitoring, prevention, surveillance and evaluation of the determinants of health. An important place in public health belongs to science and research, the results of which should be implemented in preventive intervention strategies. Public health surveillance is the ongoing systematic collection, analysis, and interpretation of outcome-specific data for use in the planning, implementation, and evaluation of public health practice. Surveillance makes summing-up of great many pieces of information that can be of use to general public.

Key words: hygiene, epidemiology, public health, determinants of health, public health surveillance.

INTRODUCTION

Hygiene and epidemiology belong to preventive medical branches since long ago. The basic hygienic rules were involved already in old Jewish and Arabic religious scriptures. The relations between health and environment, as well as the impact of social problems on human health, were defined also in the 5th century B.C. by Hippocrates. He, at the same had significantly influenced also the progress in epidemiological thinking by the use of epidemiological methods. From ancient Rome have been preserved the hygienic-technical archaeology as e.g. aqueducts and the private and public baths. Unfavourable form the development of hygiene was the period of the Middle Ages. Low sanitary standard was behind a multitude of outbreaks of communicable diseases as e.g. plague, smallpox and cholera. Only at the end of the 18th and in the courses of the 19th century hygiene and epidemiology were constituted as scientific medical branches (1).

Simultaneously with the progress of medicine and health science also hygiene and social medicine started to develop. Health in its broad social relations, and unequal social conditions and problems anchored in them were pointed at also as early as in ancient times by Hippocrates, Aristotle and Avicenna. Important changes in health services, and thus also in securing of hygienic and epidemic measures in Slovakia took place only in the era of ruling of Maria Therese and her son Joseph II, in the second part of the 18th cent. (2).

HEALTH POLICY

Environmental and social factors, but also the level of health services are constantly influencing the health of individuals, and vice versa, human activities have an important impact on the environment which can be the key to the better life and positive impact on the health of individuals and thus of the whole society. Negative environmental and social factors have detrimen-

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tal effect on human health. The regional or national health policy can be defined as the sum of rules and regulations leading to the implementation of the defined aims of improving and maintaining of public health. Public health influences particular fields including the health services – Fig.1 (3,4).

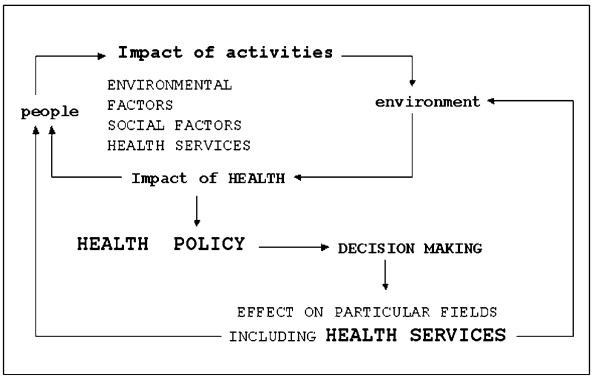

Fig. 1 Health and the health policy

Populations consist of individuals living within certain family and community environment which is a part of environment including all communities. The policy influencing the health of an individual and the community can be defined as health strategy influencing the entire environment – the environmental policy. If we understand health as a component of the environment in which we live, we have to consider the impacts of human activities as the impact on the individual, family, public and environmental health.

Public health is influenced by individuals with their approaches to their lives and health. The impact of family on community is considerable (e.g. nutrition, life style, etc.) and it impacts thinking and attitudes of individuals forming them.

Healthy life conditions are influenced and modified by factors often overestimated, among which belong physical, chemical and biological ones, but also underestimated e.g. social, cultural and economic ones (Tab.1). The resulting effect of their action is a complex effect on the

Tab.1 Factors influencing the health of an individual and of population

Determinants of health	**CATEGORY**	
Age, gender, immunity, nutritional status, invalidity	Physiological	Individual, Family, Community
Education, occupation, perception of risk	Behavioural	
Poverty, unemployment	Socio-economic	
Atmosphere, water, soil, energy, environmental pollution, foodstuff	Physical Chemical Biological	Environmental
Family, society, culture	Social	
Employment, investments	Financial	
Primary care, specialised services	Health services	Institutional
Self-government, government	Other institution	
Laws	Policy	

health of people who by their activities influence the health of people who by their activities influence the healthy life conditions (5,6).

PUBLIC HEALTH AND PUBLIC HEALTH CARE

At the end of 1940s WHO defined health of an individual. Physical, mental and social well-being are obtainable only in case when the means for it are available to the public and the protection of the healthy living and working environment can be maintained. The state of the highest possible level of health and the least hampering of health of the given community, influenced by the socio-economic level and the quality of health care, can be defined as public health care. Its aim is to protect, promote and maintain the public health in a complex, consistent, complete and effective way. Its component is also the effort for supporting, developing and protecting health, including prevention of diseases (7,8).

Public health in EU, under the auspices of WHO, is oriented to the implementation of political documents, programmes and health projects. Securing of the high level of health protection is possible only through its maintaining on population level, prevention of civilization diseases and elimination of health–threatening factors. The starting point of the proposed concept of public health in Slovakia is the document of the European Parliament and European Council No.1786 issued on 23 September 2002, on the programme and activities in the field of public health for the years 2003-2008, in the frame of WHO, and the basis of its recommendations (9,10).

Among the essential roles of public health belong the identification, monitoring, prevention, surveillance, and control of the above mentioned determinants of health. In the field of individual, family, community and public health indispensable are information, education and individual health promotion. Desirable is mobilization of partnerships in communities, which significantly influences planning of health policy, however, with adequate legislative support. Provision of health services cannot do without good, effective management, supplemented by evaluation of their effectivity, accessibility and quality. An irreplaceable place in public health belongs also to science and research, the results of which should be implemented in preventive strategies oriented on the improvement of health of the whole society.

Health care does not equal the public health and vice versa. Promotion of health status of the population not only in the sense of the absence of the disease or infirmity, but also in the sense of the life-span in good life quality – those are the primary goals of public health of today. The efforts of health workers and of the entire society should be the lengthening of the productive age of the population, protection and promotion of physical and mental health. Prevention of the diseases and injuries is possible only in cooperation with the general public. Their collaboration can be achieved through their better information and knowledge on the possible ways of protection and promotion of their individual health. At the same time their ability to react adequately to health-threatening situations can be improved and their interest in following and evaluating the determinants influencing their individual health can be attained. Therefore, the protection, promotion and maintenance of health are the roles of public health. Early identification of health-threatening situations and risks necessitates the use of objectivization of the relations and wide knowledge of public health proved in practice, but also empirically and scientifically. Here an important role is played not only by quantification but by quality evaluation of the existing and emerging relations. Such obtained background data, supported by adequate legislation, become an integral part of the health-promoting programmes and of the health policy of the government.

SURVEILLANCE AND PUBLIC HEALTH

Surveillance (the complex and sustained collection of all accessible information) in public health consists of systematic collection of data, their summing up, analysis and interpretation. The processed data are dispersed and employed in planning, formulation, and implementation

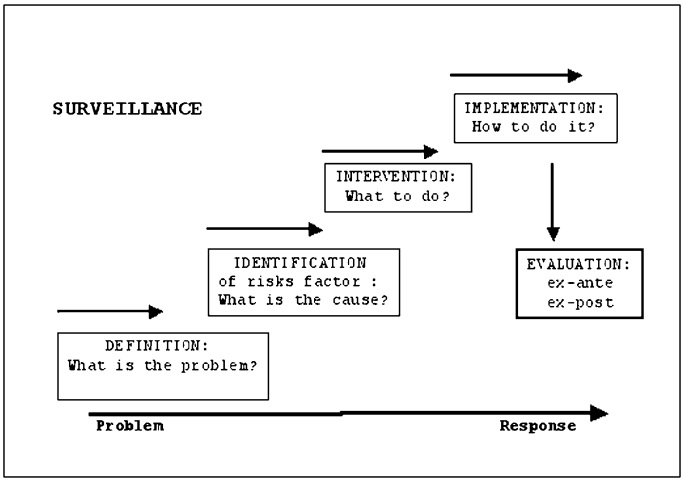

Fig. 2 The public health approach in hygiene and epidemiology

of health promoting programmes and projects in the frame of public health. The public health approach in hygiene and epidemiology rests on identification of the problem, and the search for adequate response – the schematic procedure is illustrated in Fig. 2 (8).

After elucidation of the problem the risk factor should be identified, and the cause found out. "What to do?" is defined in intervention, and "How to do it?" is a part of implementation into health measures, programmes and community projects. Eventually, the effectiveness of the implemented measures should be evaluated (ex-post evaluation), if on the basis of empirical experience, we have not tried to evaluate the preventive strategy already before its implementation (ex-ante evaluation) (11). Thus, surveillance helps to estimate importance of the given problem. It facilitates evaluation of geographic distribution, processing of case-history data of the diseases and predisposing factors. It facilitates defining of the problem, stating of hypotheses, and stimulates the research in the field of hygiene and epidemiology, which are parts of public health. Consequently, it facilitates monitoring of the changes (of particular diseases and infirmities, but also changes in health strategies), and planning in all the fields also outside health services.

Surveillance makes summing-up of great many pieces of information that can be of use not only to health-providers but also to politicians, and in adequate form also to the general public – Fig. 3 (6).

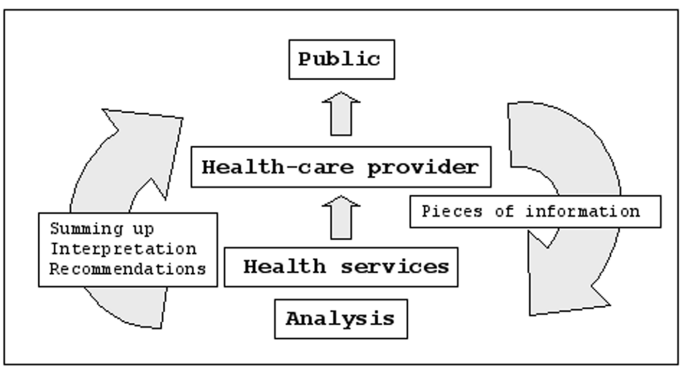

Fig. 3 Circulation of information in public health

CONCLUSION

The health of the society is influenced by the health of individuals, communities, and consequently by all facets of population (6,12). The position of health services in forming of health policy, however their impact on its orientation, securing, acceptance and implementation is of the first rate importance. The ultimate goal of public health: healthy people in healthy communities. This goal remains still unobtainable. The key to better life in healthy environment is prevention that, for long, occupies a dominant place in hygiene and epidemiology.

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