Influence of Alternating Extremely Low Frequency ELF Magnetic Field on Structure and Function of Pancreas in Rats

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The aim of this study was to estimate the influence on ultrastructure and function of endocrine and excretoric part of pancreas in rats of extremely low frequency alternating magnetic fields with parameters used in therapy in humans. The animals from the two experimental groups were exposed to a rectangular magnetic field waveform at a frequency of 10 Hz and induction of 1.8–3.8 mT—(group P) or a sinusoidal magnetic field at a frequency of 40 Hz and induction of 1.3–2.7 mT—(group S), respectively. The control rats were subjected to sham exposure. The cycle of 1, 3, 6, 9, and 14 daily exposure sessions lasting 30 min was made in all groups. Some of rats after finishing the cycle of 14 exposures were left in the same conditions except for the magnetic field for 3 or 10 days. In both groups of rats exposed to magnetic field, a distinct tendency to decrease glucose concentration, compared to control group, was observed during the exposure cycle. Serum glucose became normal after the end of exposure sessions. The concentrations of insulin in both groups of rats exposed to magnetic field were significantly higher, compared to the controls, during the exposure cycle. After the end of exposure cycle the concentration of insulin in group S became normal. In contrast, in group P the concentration of insulin decreased significantly on the last day of exposure, with a subsequent increase in the following days. The activity of α-amylase and lipase in the serum of experimental and control rats was not affected. In both groups of exposed rats, reversible changes of ultrastructure of the pancreatic islets, including expansion of the Golgi apparatus, extension of rough endoplasmatic reticulum, mitochondrial swelling, expansion of β-granules and increase in number of empty vesicles in β cells, occurred during the exposure. In acinar cells of exposed animals, a slight extension of rough endoplasmatic reticulum and mitochondrial swelling as transitory changes were observed. The structural and functional changes in pancreas are probably adaptative ones. Bioelectromagnetics 23:49–58, 2002.

Key words: ultrastructure; acinar cell; β-cell; serum glucose; serum insulin

INTRODUCTION

Increasing application of extremely low frequency alternating magnetic fields (ELF–MF) in medicine still requires fundamental research investigating the influence of these fields on the cells, tissues and organs. Changes of concentration of transmitters of autonomous nervous system, activity stimulation of numerous enzymes and hormones, stimulation of oxidation-reduction processes and cellular synthesis suggest a possibility that these fields influence carbohydrate metabolism as well as endocrine and exocrine function of the pancreas [Levy, 1993; Sieroń et al., 2000; Tenforde, 1991].

Data are scarce on the influence of ELF alternating magnetic fields on pancreas activity and structure. Results of research evaluating influence of such fields on levels of particular parameters characterising endocrine and exocrine secretory function of pancreas are not coherent, and it is often difficult to compare the different research methods.

Long term exposure to an alternating magnetic field at frequency 10 Hz, induction 8 mT [Cieślar et al., 1995b] and frequency 50 Hz, induction 20–50 mT [Hefco et al., 1969] led to a decrease in glucose concentration in the serum of experimental animals. A hypoglycemic effect of ELF magnetic field has been confirmed by clinical studies on healthy volunteers and diabetics subjected to a sinusoidal field at a frequency

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of 50 Hz and induction of 3.4 mT [Cassiano et al., 1967]. In other studies, no significant influence was seen on insulin and glucose concentration in serum of experimental animals and healthy volunteers after exposure to an alternating magnetic field at a frequency of 50 Hz and induction of 5–20 mT [Baroncelli et al., 1985]. There are also reports that point to 50 Hz alternating magnetic field activation of glycogenolysis in liver [Tomaszewska and Dumanski, 1981]. Temparary suppression of insulin secretion from β cells of pancreatic islets with secondary increase in glucose concentration was observed in serum of animals exposed to 13.3 Hz alternating magnetic field of 2.7 mT induction [Gorczyńska and Węgrzynowicz, 1991] and 5 Hz magnetic field of 1 mT induction [Jolley et al., 1983].

ELF–MF show high efficacy in the treatment of late organ complications in diabetes, such as diabetic retinopathy [Danilowa and Pieleszczuk, 1986; Sieroń et al., 2000] and also peripheral polyneuropathy and diabetic angiopathy [Cieślar et al., 1995a; Sieroń et al., 2000; Kiriłow et al., 1996; Sadurska et al., 1992] Single observations point to the possibility to applying magnetotherapy to treat chronic pancreatitis [Fiedorow et al., 1990]. The majority of patients treated with magnetic field showed improvement of their clinical state, expressed as disappearance of pains and disturbances of intestinal motor activity and normalisation of laboratory markers of illness (blood amylase and trypsin activity). In spite of the fact that the results of experimental research do not enable conclusive evaluation of the influence of ELF magnetic fields on carbohydrate metabolism, some authors treat juvenile diabetes as a contraindication to application of magnetic fields [Grünner, 1987].

The aim of this work was to evaluate the influence of long term exposure to ELF alternating magnetic fields with parameters used for human therapy on the endocrine and exocrine secretory function of pancreas and the ultrastructure of the pancreas in experimental animals.

MATERIALS AND METHODS

The research material consisted of 105 male rats of the Wistar strain aged 16 weeks (mean body weight 284.4 ± 12.6 g). During the experiment, rats were kept in optimal environmental conditions, a constant temperature of 21–22 °C and constant humidity. The lighting was turned off or on under a 12 h cycle. The rats were fed with standard granulated feed of Murigran type (Motycz, Poland) in accordance with typical dietetic standards and had free access to water.

The animals were randomly divided into three equal groups of 35 rats each; the groups had no significant differences in body weight. The structure of the animal groups is presented in Table 1. Rats in the two experimental groups P and S were exposed to alternating magnetic fields generated in the cylindrical applicator of an Ambit 2000 apparatus for magnetotherapy (Ambit, Poland). Group P (mean body weight 281.6 ± 11.3 g) was exposed to a rectangular waveform magnetic field at a frequency of 10 Hz and induction in the range from 1.8 to 3.8 mT, depending on location of measurement points inside of applicator. Group S (mean body weight 285.4 ± 12.9 g) was exposed to sinusoidal magnetic field at a frequency of 40 Hz and induction in the range from 1.3 to 2.7 mT, depending on location of measurement points inside of applicator. The last group, K (mean body weight 286.2 ± 13.1 g) was the control group, subjected to sham exposure, during which the applicator remained unconnected and, therefore, generated no magnetic field. The whole body of each animals was exposed for 30 min a day, always at the same hour in the morning.

The animals from groups P, S, and K were divided into seven subgroups, each consisting of five rats, with different exposure times. Rats in particular subgroups were subjected to the cycle of 1, 3, 6, 9, and 14 daily exposure sessions, respectively. Rats in the two remaining subgroups completed a cycle of 14 daily exposure sessions and were then kept in same

TABLE 1. Structure of Animal Groups

Group	Parameters of magnetic field	Number of exposures					Number of days of recover	
P N = 35	Rectangular shape f = 10 Hz I = 1.8–3.8 mT	1 n = 5	3 n = 5	6 n = 5	9 n = 5	14 n = 5	3 n = 5	10 n = 5
S N = 35	Sinus-shape f = 40 Hz I = 1.3–2.7 mT	1 n = 5	3 n = 5	6 n = 5	9 n = 5	14 n = 5	3 n = 5	10 n = 5
K N = 35	Sham-exposure	1 n = 5	3 n = 5	6 n = 5	9 n = 5	14 n = 5	3 n = 5	10 n = 5

N-number of animals in experimental groups P and S and in the control group K; n-number of animals in particular subgroups.

conditions as before, except for magnetic field exposures, for 3 and 10 more days, respectively.

After completion of an experimental cycle of a fixed number of exposure sessions, the animals from different subgroups were fasted for 20 h after the last exposure and then exsanguinated in ether narcosis, always at the same time in the morning. The blood (average 5–7 ml) was obtained from the right ventricle of heart and then decanted and centrifuged. The serum was used to determine glucose and insulin concentration, as well as α-amylase and lipase activity. After opening the abdominal cavity, samples of the pancreas body were taken, which after appropriate fixation and preparation were used for ultrastructural examination in electron microscope.

Serum concentration of glucose was determined with the oxidase method, using Glukoza–Oxyreagent manufactured by Pointe Scientific Poland Sp. z o.o. [Tietz, 1976]. Insulin serum concentration was determined with a radio immunological method, using the rat insulin RIA Kit manufactured by Linco Research Inc. [Billestrup and Nielsen, 1991]. α-amylase (E.C.3.2.1.1.) serum activity was determined using the AMYL enzymatic colorimetric test, manufactured by Boehringer Mannheim [Hohenwallner, 1989]. Lipase (E.C.3.1.1.3) serum activity was determined using the turbidimetric test LIP, manufactured by Boehringer Mannheim [Verduin, 1973].

For electron microscopic examination, the pancreatic body was fragmented into blocks with 1 mm edge length and fixed with 3% glutaraldehyde, buffered with Na–cacodylate buffer to pH 7.2 for 2 h. After rinsing in cacodylate buffer, the blocks were postfixed in 1% osmium tetroxide (OsO_4). After next rinsing in cacodyl buffer, the blocks of tissue were dehydrated in a set of increased alcohol concentration and in propylene oxide, then embedded in Epon 812 epoxy resin mixture and polymerised at a temperature of 60 C for 36 h. After polymerisation, the tissue blocks were sectioned with an ultramicrotome (Reichert comp.) into ultrathin sections of about 500 Å (50 nm) thickness, which were then contrasted with solutions of uranyl acetate and lead citrate. Ultrathin sections were examined in a JEM 100C electron microscope (Jeol, Japan). Ultrastructural changes of the endocrine and exocrine part of pancreas were analysed.

The results of serum glucose and insulin concentration, as well as of α-amylase and lipase serum activity in different groups, are presented as mean values ± SD. They were statistically analysed with the ANOVA rank Kruskal–Wallis test, followed by the post hoc nonparametric Mann–Whitney U test. In analysis of correlation between serum insulin and glucose concentration, the correlation coefficient (r) was estimated on the basis of regression lines y = ax+b and then evaluated with statistical test using its equation:

$$t = \frac{r \cdot \sqrt{n-2}}{\sqrt{1-r^2}}$$

according to Spearman [Armitage, 1971].

RESULTS

Measurements of Endocrine Function

The mean values of serum glucose concentration in rats in both groups exposed to magnetic field and in the control group are presented in Figure 1 as a function of exposure time. A single exposure of animals to magnetic field brought no significant changes of glucose concentration in groups P and S as compared to the control group. But after several repeated exposures (from third day to day 14 of exposure cycle) a tendency was observed, in both groups P and S, for glucose concentration to drop in comparison to the control group. However, in both groups only the lowest glucose concentration observed on the last day of exposure cycle was statistically significantly lower than the value in the control group ($P<0.01$). After the end of exposure cycle serum glucose concentration in both groups of experimental animals did not differ significantly from respective values in the control group.

The serum insulin concentration in rats in both groups exposed to magnetic field and in control group is shown in Figure 2 as a function of exposure time.

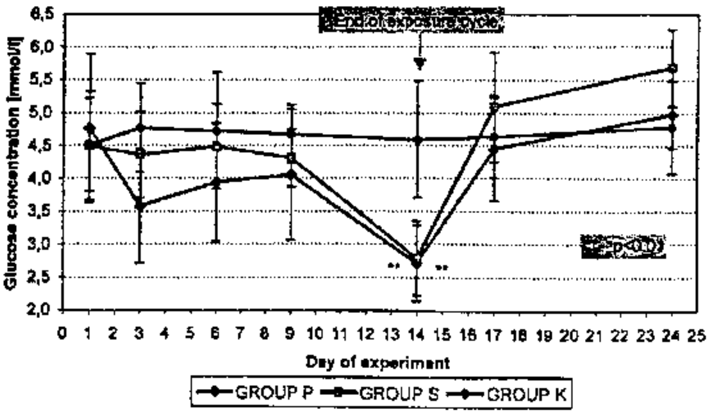

Fig. 1. Glucose concentration (mean value and SD) in serum of rats in groups exposed to magnetic field (P and S) as a function of consecutive days of exposure.

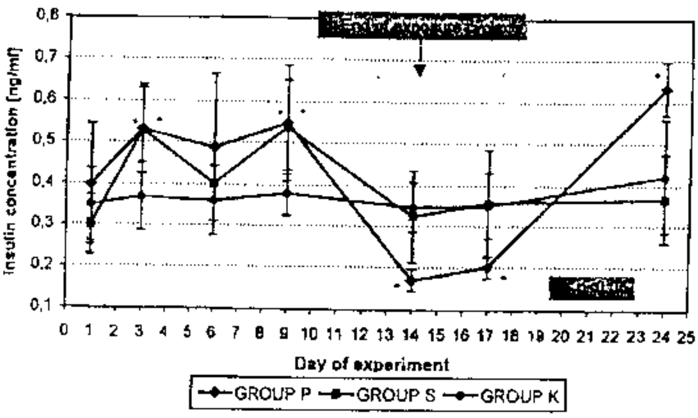

Fig. 2. Insulin concentration (mean value and SD) in serum of rats in groups exposed to magnetic field (P and S) as a function of consecutive days of exposure.

Single exposure of animals to either magnetic field caused no significant changes of insulin concentration as compared to the control group. But on 3 and 9 day of exposure cycle insulin concentration was significantly higher ($P<0.05$) in both groups of exposed rats than in the control group.

In group P, insulin concentration on the last day of exposure and on 3rd day after the end of exposure cycle was significantly lower ($P<0.05$), compared to the control group. Within day 10 after the end of exposure cycle, significantly higher ($P<0.05$) insulin concentration was observed in this group. In group S, insulin concentration on the last day of exposure cycle and during the whole period after end of the exposure cycle was comparable to control.

No significant correlation was observed between serum glucose and insulin concentrations in groups of rats exposed to magnetic field and in the control group (Fig. 3). The correlation coefficients showed no statistical significance ($P>0.05$) and were lower than in the control group (Fig. 3).

The mean values of the insulin/glucose I/G index in serum of rats in both groups exposed to magnetic field and in control group are shown in Figure 4 as a function of exposure time. Statistical analysis confirmed that a single exposure of animals to magnetic field caused no significant changes of I/G index value in groups P and S as compared to the control group. In the later phases of the exposure cycle a significant increase in the I/G index was observed as compared to the control group.

In group P the values of I/G index on the 3 and 9 day of the exposure cycle were significantly higher ($P<0.01$) than in the control group. In group S the values of the I/G index on days 3, 9, and 14 of exposure sessions were significantly higher than in the control group ($P<0.05$ or $P<0.01$). After the end of the exposure cycle, the changes of values of I/G index in groups P and S had the same tendency as the insulin concentration, but the differences were not statistically significant.

Measurements of Enzymatic Activity of Pancreas

No significant differences of α-amylase and lipase serum activity were observed between either experimental group and the control group (Figs. 5 and 6).

Ultrastructure of Langerhans Islets

The submicroscopic structure of Landerhans' islets of pancreas in animals from the control group displayed the normal structure of Langerhans' islets of rat, and it did not change significantly during the consecutive days of sham exposure (Fig. 7).

Electron micrographs of Langerhans' islets in rats exposed to either magnetic field showed only minimal ultrastructural changes, which mostly concerned β cells of pancreatic islets (Fig. 8). In group P on 1st day of exposure ultrastructural changes were related to extension of clear space "halo" surrounding granules in β cells and extension of rough endoplasmatic reticulum. On the 3rd day of exposure considerable extension of a "halo" surrounding granules gave foamy character to β cells. Cytoplasm of β cells on day 6 of exposure was vesiculated, resulting from a great number of clear vesicles without visible content. On day 9 of exposure greatly expanded Golgi apparatus and rough endoplasmatic reticulum, numerous granules of different density, surrounded by a "halo" and swollen mitochondria were observed in β cells. A great number of endocrine granules surrounded by a "halo" and swollen mitochondria were also observed on day 14 of exposure. Submicroscopic images of β cells on 3rd and 10 day after the end of exposure cycle did not differ significantly from typical images in the control group. Ultrastructural changes of β cells in group S were similar to those in group P. However, numerous vesicles without granules were observed, creating a picture of cytoplasm vesiculation only on the 3rd day of exposure, and a lower number of granules surrounded by a "halo" than in group P was observed within day 14 of exposure.

Ultrastructure of Excretoric Part of Pancreas

The typical image of the ultrastructure of acinar cells in excretoric part of pancreas in control animals showed the well known architecture (Fig. 9). In group P the ultrastructural image of acinar cells in excretoric part of pancreas on the 1st day of exposure did not differ from the picture observed in the control group.

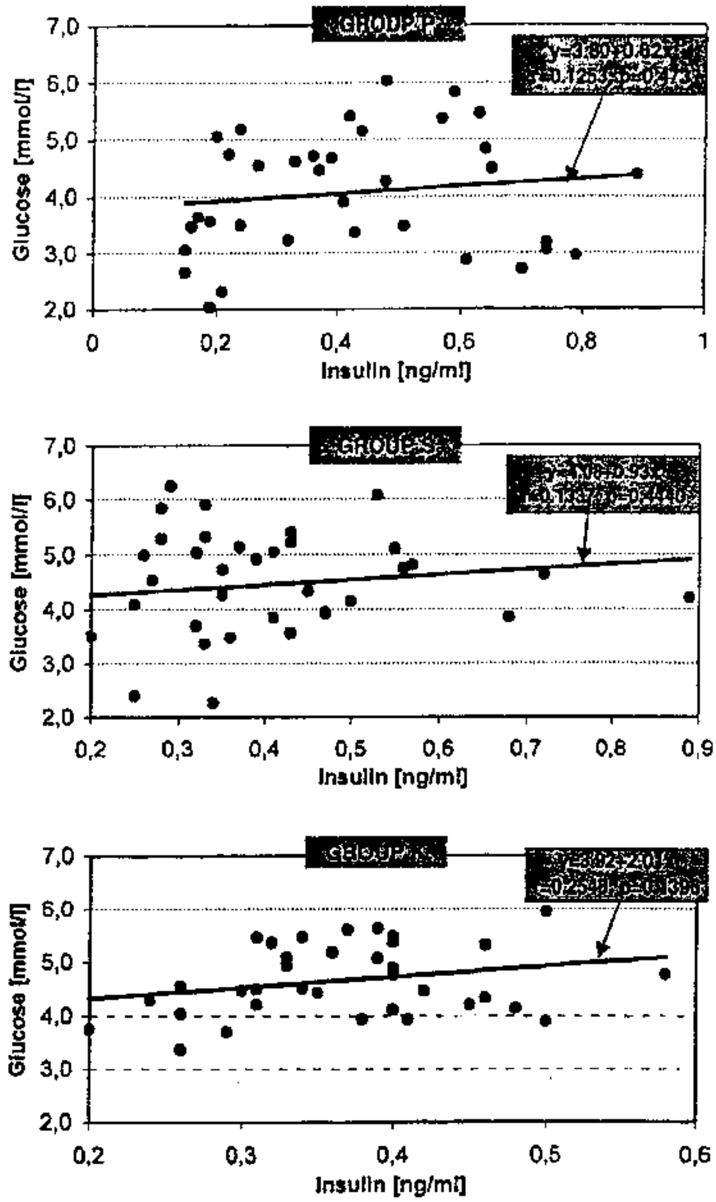

Fig. 3. Correlation between glucose and insulin concentration in serum of rats in groups exposed to magnetic field (P and S) and in the control group (K).

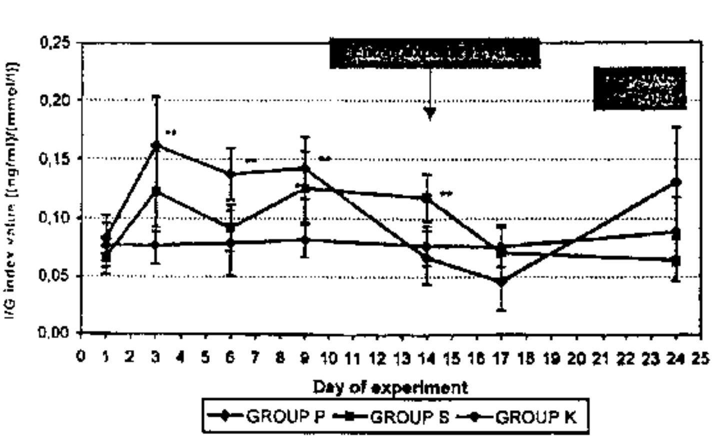

Fig. 4. Insulin/glucose index I/G (mean value and SD) in serum of rats in groups exposed to magnetic field (P and S) as a function of consecutive days of exposure.

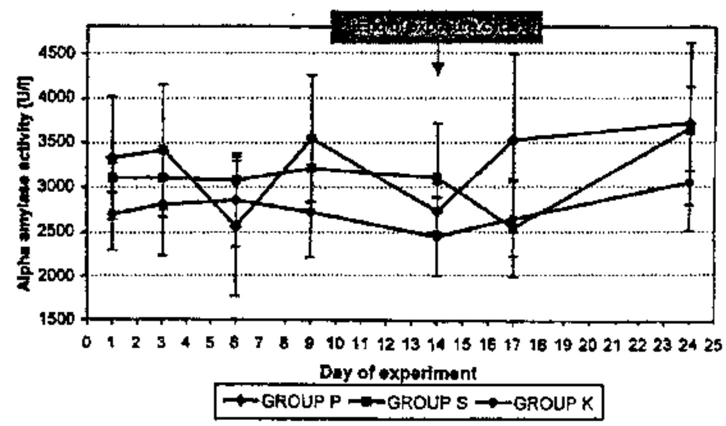

Fig. 5. α-amylase activity (mean value and SD) in serum of rats in groups exposed to magnetic field (P and S) as compared to the control group (K) as a function of consecutive days of exposure.

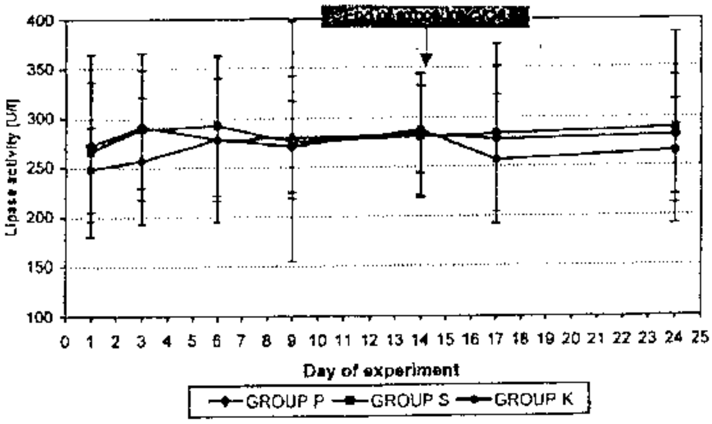

Fig. 6. Lipase activity (mean value and SD) in serum of rats in groups exposed to magnetic field (P and S) as compared to the control group (K) as a function of consecutive days of exposure.

On 3rd day of exposure, swelling of mitochondria was observed, in extreme cases creating the impression of vacuoles in the cytoplasm (Fig. 10). On day 6 of exposure, in addition to swollen mitochondria, extension of tubules of rough endoplasmatic reticulum was observed. On days 9 and 14 of exposure, swollen mitochondria and extension of tubules of rough endoplasmatic reticulum were evident, as well as an increase in the number of zymogen granules. On 3rd day after the end of exposure cycle, a slight swelling of mitochondria was visible, while other cellular elements of acinar cells did not show any alterations. The ultrastructural image of excretoric part of pancreas of rats on day 10 after the end of exposure cycle did not differ from the one observed in the control group. Ultrastructural changes in exocrine acinar cells in group S were similar to that in group P. However the extension of tubules of the rough endoplasmatic reticulum was observed on day 9 of exposure, and the blurring of structure of mitochondrial crests accompanied by marked swelling of mitochondria. was noted on days 9 and 14 of exposure and on the 3rd day after the end of exposure cycle.

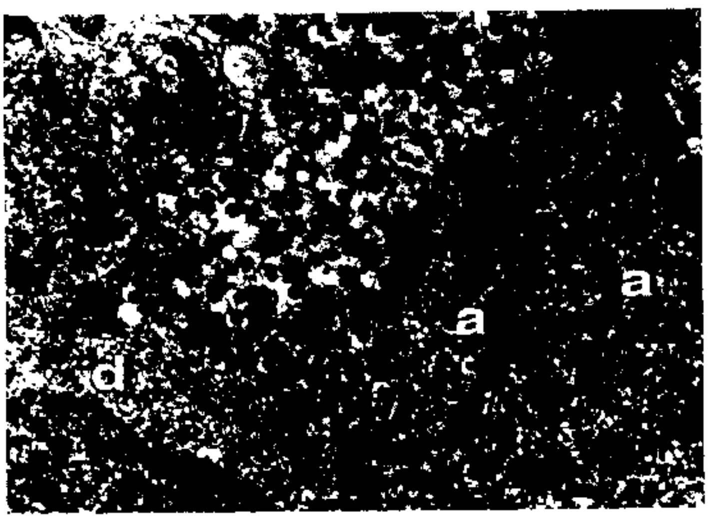

Fig. 7. Electron micrograph of Langerhans islet in control rats showing normal ultrastructure of rat islet of Langerhans; (a) -α cell, (b) β cell, (d) δ cell.

DISCUSSION

The results of this experiment suggest that adaptative changes of the hormonal function of the pancreas can occur in rats subjected to long term exposure to ELF magnetic fields. The starting point of such changes is probably stimulation of synthesis and excretion of insulin in β cells of the pancreatic islets. Ultrastructural changes of β cells with signs of extension of the rough endoplasmatic reticulum, which were observed especially in the initial phase of exposure, may indicate stimulation of preproinsulin and proinsulin synthesis. On the other hand, significant expansion of the Golgi apparatus, observed in both groups of rats exposed to magnetic field, is probably related to storage of increased amount of proinsulin in the form of small vesicles [Tartakoff, 1980; Go, 1993]. After transformation of proinsulin into insulin, such vesicles move to the cytoplasm, creating characteristic insulin granules. Significant extension of a "halo" around the granules, observed mainly in the initial phase of exposure, suggests the accumulation of a great quantity of insulin in the β cells. Presence of a great number of electron-empty vesicles, a remnant after secretion of insulin granules outside the β cells, as observed in the later phases of exposure to magnetic field, may indicate an intensification of the hormone secretion processes. Final and direct proof of a stimulating influence of ELF magnetic fields on synthesis and secretion of insulin may be provided by results of insulin blood concentration analysis, since during the whole exposure cycle a significant increase in blood concentration of this hormone was observed in both groups of experimental rats.

Magnetic fields with a rectangular pulse waveform generally cause more pronounced changes of structural properties and permeability of biological membranes [McLeod, 1992; Tenforde, 1991]. Since it seems this effect may be responsible for the stronger stimulation of the insulin secretion process, with a subsequent faster exhaustion of the cellular reserve of this hormone and a secondary lowering of the insulin blood concentration in rats exposed to the rectangular pulsed magnetic field. Notably greater numbers of electron-empty vesicles, remnants of secreted insulin granules, and a lower number of typical insulin

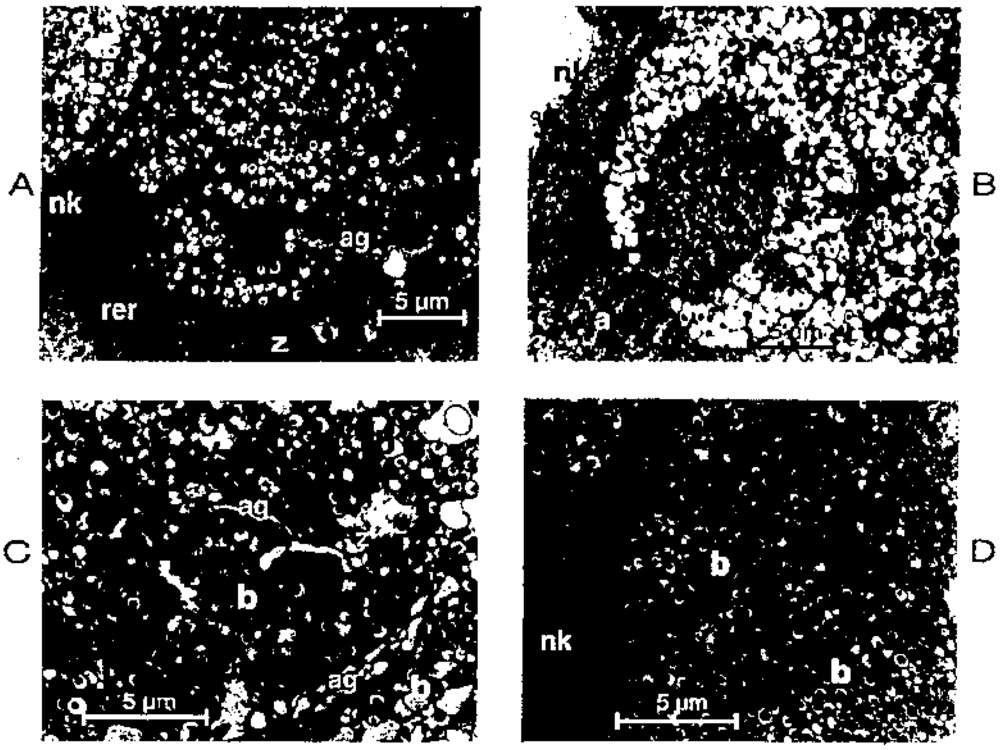

Fig. 8. Electron micrograph of Langerhans islets in rats exposed to magnetic field. **A.** First day of exposure, showing extension of "halo" surrounding granules in β cells (b) and extension of rough endoplasmatic reticulum (rer); (ag) Golgi apparatus, (nk) capillary vessel, (z) zymogen granules. **B.** Day 6 of exposure, showing great number of vesicles without granularity giving vesicular character to β cells (b); (nk) capillary vessel, (a) α cell. **C.** Day 9 of exposure, showing greatly expanded Golgi apparatus (ag), numerous granules of different density surrounded by "halo" and swollen mitochondria in β cells (b). **D.** Day 14 of exposure, showing numerous granules surrounded by "halo" and swollen mitochondria in β cells (b); (nk) capillary vessel.

granules in later phases of exposure cycle, as observed in group of rats exposed to the rectangular magnetic field, may confirm this hypothesis. The increase in insulin blood concentration on day 10 after the end of exposure cycle noticed in this group seems to be of compensating character in relation to the greatly lowered reserve of this hormone and the subsequent relatively higher glycaemia.

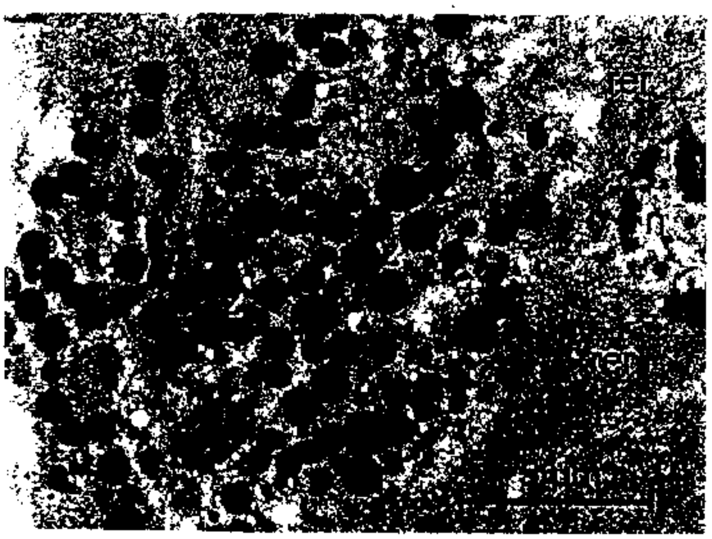

Fig. 9. Electron micrograph of excretoric part of pancreas in control rats - normal ultrastructure of acinar cell. Zymogen granules (z) point toward secretory pole near normal rough endoplasmatic reticulum (rer) and nucleus (n).

Regression of ultrastructural changes and normalization of insulin blood concentration immediately after the end of exposure sessions indicates the functional and adaptative character of observed hormonal changes.

Since endocrine and excretoric function of the pancreas, as well as homeostasis of carbohydrate metabolism, are subjected to complex neuro-humoral regulation, establishment of the mechanisms responsible for stimulating effect of ELF magnetic fields on insulin synthesis and secretion is difficult. The main stimulus of insulin secretion is increased concentration of glucose circulating in blood. A sensitive marker of β cells, responsiveness to changes of glycaemia is the insulin/glucose index, representing the correlation of insulinaemia and glycaemia [Go, 1993]. Increased values of this index indicate destabilisation of carbohydrate metabolism regulation. Significantly increased values of the insulin/glucose index without correlation between glycaemia and insulinaemia in both experimental groups may indicate lack of correlation of insulinaemia and glycaemia under the influence of

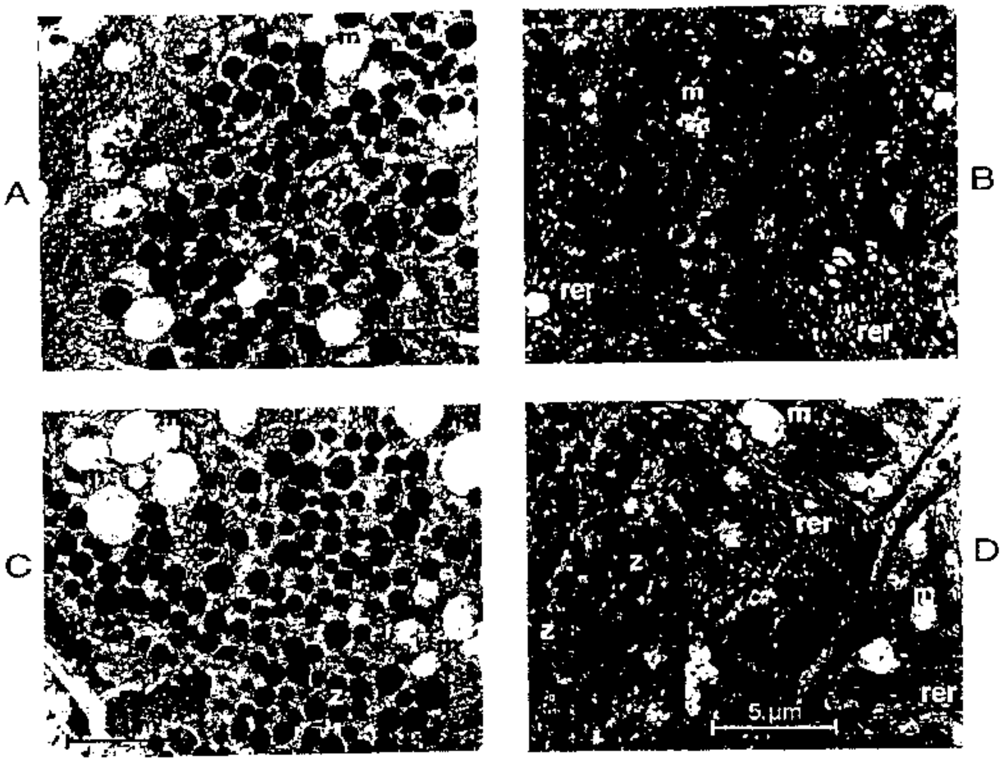

Fig. 10. Electron micrograph of excretoric part of pancreas in rats exposed to magnetic field. **A.** Third day of exposure, showing swollen mitochondria (m) creating impression of vesicular cytoplasm in exocrine acinar cells; (z) zymogen granules. **B.** Day 6 of exposure, showing swollen mitochondria (m) and extension of tubules of rough endoplasmatic reticulum (rer) in acinar cells; (z) zymogen granules. **C.** Day 14 of exposure, showing swollen mitochondria (m), extension of tubules of rough endoplasmatic reticulum (rer) and a great number of zymogen granules (z) in acinar cells. **D.** Day 9 of exposure, showing marked swelling of mitochondria (m) with blurring of structure of mitochondrial crest and evident extension of rough endoplasmatic reticulum (rer), as well as a great number of zymogen granules (z) in acinar cells.

magnetic field. These results, therefore, do not support the possibility that glycaemia would be the primary mechanism of magnetic fields' influence insulin secretion, especially in the initial phase of exposure. According to some authors [Cassiano et al., 1967; Hefco et al., 1969], the influence of ELF magnetic fields on carbohydrate metabolism and the secretion of pancreatic hormones may be indirectly related to activation of the parasympathetic part of the vegetative nervous system, which is one of most significant factors stimulating hormonal activity of pancreas.

Reiter (1993) has shown that exposure of animals to alternating magnetic fields causes reduction of cAMP and melatonin contents in the pineal gland with a subsequent decrease in melatonin and increase in serotonin blood concentration. Because serotonin is an important agent for stimulating insulin secretion [Vadakekalam, 1997], it is possible that increased serotonin production in pineal gland may be another mechanism of magnetic field stimulation of insulin secretion.

It is generally assumed that the final result of activation of the β cells of pancreatic islets by various secretive stimuli is stimulation of adenyl cyclase activity, resulting in increased concentration of cAMP and calcium ions in cytoplasm of these cells [Gagliardino and Rossi, 1994; Henquin, 1994]. The activity of Ca^{2+} dependent insulin secretion regulators is modified by cAMP dependent albumin kinase. Results of numerous experiments have shown that exposure to alternating magnetic fields may reduce activity of adenyl cyclase [Reiter, 1993] and numerous cAMP-dependent albumin kinases [Goodman et al., 1993; Uckun et al., 1995]. In turn lowering of insulin secretion under the influence of glucose stimulus in the presence of magnetic field was accompanied by a decrease in intracellular concentration of calcium ions in the β cells of pancreatic islets [Jolley, 1983]. Taking this into account it may be assumed that another mechanism of influencing insulin secretion may be related to effect of the magnetic field on the system of cellular transmitters (cAMP, albumin kinases, Ca^{2+} ions).

The transitory character of the observed ultrastructural changes of exocrine acinar cells, as well as the absence of marked changes of membranous structures in these cells, suggests that the ELF magnetic field did not have a destructive influence on the tissues of the excretoric part of pancreas.

The absence of significant changes of α-amylase and lipase activity in the blood of animals exposed to magnetic field excludes the induction of an acute pancreatitis under the influence of magnetic field. Also no significant changes of α-amylase activity were observed by other authors [Barroncelli et al., 1985], when investigating the influence of an alternating magnetic field at 50 Hz and 5–20 mT on healthy volunteers.

Structural changes of exocrine acinar cells, in the form of a slight extension of the rough endoplasmatic reticulum with an accompanying increase in zymogen granule size, indicate the stimulation of synthesis processes of digestive enzymes under the influence of magnetic field. They were irregularly present in electron micrographs of pancreatic islets in animals exposed to magnetic field and disappeared after the removal of the field. The phenomenon appears to be adaptative, similar to the reaction of pancreatic islet cells to the action of ELF magnetic fields. As some investigations show, isulin strongly stimulates pancreatic secretion [Vadekekalam, 1997]. A significant increase in insulin concentration in serum during the exposure to ELF magnetic field may, therefore, be another potential mechanism whereby the field influences the excretoric function of pancreas.

The electron microscope pictures also demonstrate a strong swelling of mitochondria in acinar cells of rats exposed to magnetic field, similar to observation after oxidative stress and several other injuries [Blank, 1998]. These changes were reversible, but probably not harmful.

The ultrastructural and functional changes of pancreas observed in this experiment were reversible and probably not harmful. Even when transfer of results of research on animal model directly to humans is not fully possible, it seems that results of this investigation may provide another argument against treating diabetes as on implicit contraindication for application of magnetotherapy. This result is of special, practical importance, on account of beneficial therapeutical effects of alternating magnetic fields in the treatment of organic complications of diabetes, described in detail in the introduction.

Nevertheless, since there is a possibility of temporary disorders in insulin secretion and changes of glucose concentration in blood during exposure to ELF magnetic field, the results of the present experiment indicate the need for glycaemia level monitoring in diabetic patients treated with magnetic fields. Monitoring will enable possible correction of hypoglycaemising drugs and/or insulin doses during magnetotherapy, increasing the safety of treatment in these patients.

CONCLUSIONS

First, the long-term exposure of rats to ELF magnetic fields with therapeutical parameters causes reversible changes of the ultrastructure of β cells in pancreatic islets and leads to increased synthesis and secretion of insulin, accompanied by secondary hypoglycaemia in the initial phase of exposure. Second, the effect of magnetic fields on the function of β cells depends on parameters of the magnetic field, since only a rectangular waveform caused a compensating decrease in insulin concentration in the final phases of the exposure cycle as well as a subsequent increase after the end of the exposure cycle. Third, long-term exposure to ELF magnetic field causes reversible structural changes of the rough endoplasmatic reticulum and mitochondria of acinar cells, without significant changes of α-amylase and lipase activity in the blood of rats exposed to this field. Fourth, it is necessary to monitor glycaemia level in humans treated with magnetic fields, especially when using a rectangular pulse waveform.

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