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Prolonged Exposure to Extremely Low Frequency Electromagnetic Field Affects Endocrine Secretion and Structure of Pancreas in Rats

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ABSTRACT

There are several reports that indicate a linkage between exposure to Extremely Low Frequency Electromagnetic Fields (ELFEMF) with a variety of biological effects. The aim of this study was to evaluate the influence of ELFEMF on endocrine secretion and structure of pancreas in rats. Experimental adult male wistar rats were exposed to a 50 Hz ELFEMF ,1 mT (emitted from solenoid) for 24 h daily during 135 days. The sham rats were subjected to sham exposure and the control rats were kept in animal room. In final, blood samples collected for the determination of the insulin, glucagon and glucose concentration in the plasma. The pancreas was examined using light microscopy. Results showed that in EMF exposed group insulin level was increased ($p<0.01$) which was associated with increased size of pancreatic islets and glucose level was decreased ($p<0.01$) but glucagon level did not significantly change. In conclusion, long term exposure to EMF impacts insulin secretion by influencing the structure of pancreas.

Key words: Long term exposure, electromagnetic field, pancreas, insulin, glucagon

INTRODUCTION

There are several reports indicating that Extremely Low Frequency Electromagnetic Fields (ELFEMFs), such as those originating from power distribution systems, household electrical wiring, medical devices, cellular phone and wireless communication produce a variety of biological effects (Lacy-Hulbert *et al*., 1998; Lazetic *et al*., 1997; Blank and Goodman, 2002; Mostafa *et al*., 2006; Al-Akhras *et al*., 2006; Roushangar and Rad, 2007; Khaki *et al*., 2008; Kilicalp *et al*., 2009; Zamanian *et al*., 2010). These fields are defined as those having frequencies up to 300 Hz which is a non-ionizing radiation having photon energy too weak to break the atomic bonds (Lee *et al*., 2004). Fundamental researches are still required to investigate the influence of these fields on the cells, tissues and organs.

It is reported that ELFEMFs lead to decrease in glucose concentration in the serum of healthy volunteers and diabetics (Sieron *et al*., 2007) as well experimental animals (Laitl-Kobierska *et al*., 2002). Also, ELFEMF-induced increase in synthesis and secretion of insulin was reported both *in vivo* (Laitl-Kobierska *et al*., 2002) and *in vitro* (Sakurai *et al*., 2004). But, it has been reported that exposure to alternating magnetic field has no effect on serum concentrations of insulin and glucose of experimental animals (Laitl-Kobierska *et al*., 2002). Besides, there are other studies point to suppressing effect of exposure to ELFEMF on insulin secretion with secondary increase in serum glucose concentration (Gorczynska and Wegrzynowicz, 1991).

One of the other hormones of pancreas is related to glucagon that counter regulatory to insulin, produces an increase in blood glucose by stimulating glycogenolysis and gluconeogenesis in the liver (Parker *et al.*, 2000). The study on the rat has revealed an increase in glucagon content accompanied to a decrease in insulin release and increase in blood glucose (Gorczynska and Wegrzynowicz, 1991).

In the pancreas of rodents, β-cells form a core from which insulin can easily reach α-cells arrayed in the periphery of the islet through the intra islet microcirculation and manage their secretory activity before exiting the islet (Ungera and Orci, 2010). Histological studies have shown differences in size distribution, number and volume of rat pancreatic isles (Han-Hung *et al.*, 2011). Base on the report of MacGregor *et al.* (2005) an average pancreas yields three times more small islets than large and the smaller islets release more than two times the insulin when stimulated than large islets.

The endocrine pancreas is a plastic organ especially because of the high ability of the β-cell mass to change according to the insulin demand (Bonner-Weir, 2000). This property has been demonstrated in physiological as well pathophysiological conditions such as pregnancy (Scaglia *et al.*, 1995) and obesity (Bernard-Kargar and Ktorza, 2001). Glucose has potent effect on β-cell mass growth causes to both β-cell hyperplasia and hypertrophy (Bernard-Kargar and Ktorza, 2001). According to Karaca (2010) one group of β-cell population of healthy rat pancreas has a high capacity to metabolize glucose in an oxidative way and to produce energy with ATP synthesis allowing insulin release.

Since there are no reports in the published works concerning the effect of prolonged exposure to ELFEMF on number and volume of rat pancreatic isles as well on glucagon secretion, the evidence for effects of ELFEMF on function and structure of pancreas remains inconclusive. Thus, the current study was undertaken to further evaluate the influence of long-term exposure to ELFEMF on the endocrine secretory function and structure of pancreas in rats.

MATERIALS AND METHODS

This study was conducted in Shira University laboratory in autumn, 2009. EMF exposure unit (at a frequency of 50 Hz and 1 mT) was an open wooden box (100×100×35 cm). The distribution of EMF flux density was measured using a gauss meter.

The research material consisted of 45 male rats of the Wistar strain (234.4±12.6 g). During the experiment, rats were kept in either magnetic field chamber or a similar chamber without a magnetic field or in ordinary cages in the same animal room under controlled temperature of 21-22°C for 135 days. The lighting was turned off or on under a 12 h cycle. The rats were fed with standard granulated feed and had free access to water. The animals were randomly divided into three equal groups of 15 rats each; the groups had no significant differences in body weight. The local ethics committee approved the study.

At the end of experiment animals were weighed, anaesthetized with ethyl ether and blood (average 5 mL) was obtained from the right ventricle of heart and then decanted and centrifuged at 10000 rpm. The plasma was used to determine glucose, insulin and glucagon concentrations. After opening the abdominal cavity, samples of the pancreas body were taken which after appropriate fixation and preparation were used for structural examination in light microscope. Plasma concentrations of insulin and glucagon were determined with the radioimmunoassay method (Tabeshyarnoor Co., Hamedan, Iran). Plasma concentration of glucose was measured using the automatic analyzer (Technicon, RA-1000, America).

Statistical analysis: The results of plasma insulin, glucagon and glucose concentrations, in different groups, are presented as Mean values±SEM and were statistically analyzed with the ANOVA test, followed by the post hoc Duncan test. All data analyses were performed using spss ver. 17 software and significance was taken at $p<0.05$.

RESULTS AND DISCUSSION

This study set out to investigate the impact of exposure to ELF electromagnetic fields over 135 days on endocrine function of pancreas in rat. The pancreas is composed of two major types of tissues: the *acini* which secrete digestive juices into the duodenum and the islets of Langerhans which secrete insulin and glucagon directly into the blood. According to the results of this experiment (Table 1), the hormonal secretion of the pancreas can change in rats subjected to long term exposure to ELF magnetic fields. These changes begin probably with the stimulation of synthesis and excretion of insulin in β cells of the pancreatic islets, since at the end of the exposure time a significant increase in blood concentration of this hormone was observed in the EMF exposed rats (9.8±0.47 vs. 5.14±0.21, $p<0.01$). On the other hand, sever increase of the islet diameter was observed in the EMF exposed rats (Fig. 1). Therefore, two possibilities are to be considered: 1-The accumulation of a great quantity of insulin in the β cells because blood concentration of glucagon was unchanged in the EMF exposed group (Table 1). In this regard, further studies are required to examine ultrastructural changes of β cells. 2- The increase of β cells population. Since the pancreatic beta-cells are responsible for the maintenance of the body's glucose levels within a very narrow range, their population is dynamic and undergoes compensatory changes to maintain euglycemia (Bonner-Weir, 2001). In accordance with our results, Rafacho *et al.* (2007) and Rafacho *et al.* (2008) observed an increase in islet area and perimeter, as well as in the absolute mass and relative density, of the islets in the pancreas of dexamethasone-received rats.

Pancreatic islets play an essential role in regulation of glucose metabolism by way of the secretion of insulin and glucagon. The decrease in plasma glucose concentration (153±8.71 vs. 238.1±9.42, $p<0.01$) at the end of exposure duration noticed in this experiment (Table 1) probably was due to the increase in insulin blood concentration (Table 1). In agreement to our results, recently, Laitl-Kobierska *et al.* (2002) reported that long term exposure of rats to ELFEMF with therapeutical parameters led to increased synthesis and secretion of insulin. Furthermore, Sieron *et al.* (2007) hypothesized that ELFEMF increases glucose uptake via increased pancreatic secretion of insulin, increasing affinity of insulin receptors, increasing signal transduction in the target cells and insulin transporter function. Moreover, Sakurai and Miyakoshi (2009) showed that exposure to static magnetic field increased insulin secretion. It must be added that there are contradictory findings indicating that EMF attenuated insulin secretion (Sakurai *et al.*, 2004; Sakurai and Miyakoshi, 2009). Besides, decrease of plasma glucose levels in male mice exposed to electromagnetic fields (5 microT, 50-Hz for 109 days) has been also observed (Bonhomme-Faivre *et al.*, 2003). Since, the main stimulus of insulin secretion is the increase in

Table 1: Mean plasma concentration of insulin, glucose and glucagon of EMF exposed male rats (Mean±SEM)

Groups	Insulin (ng mL^{-1})	Glucose (mg dL^{-1})	Glucagon (ng mL^{-1})
Control	5.14 ± 0.21^{a}	238.1 ± 9.42^{a}	5.37 ± 0.30^{a}
Sham operated	5.26 ± 0.20^{a}	238.7 ± 8.73^{a}	6.24 ± 0.45^{a}
EMF exposed	9.80 ± 0.47^{b}	153.0 ± 8.71^{b}	5.91 ± 0.38^{a}

Means in a column with no common superscript differ ($p<0.05$)

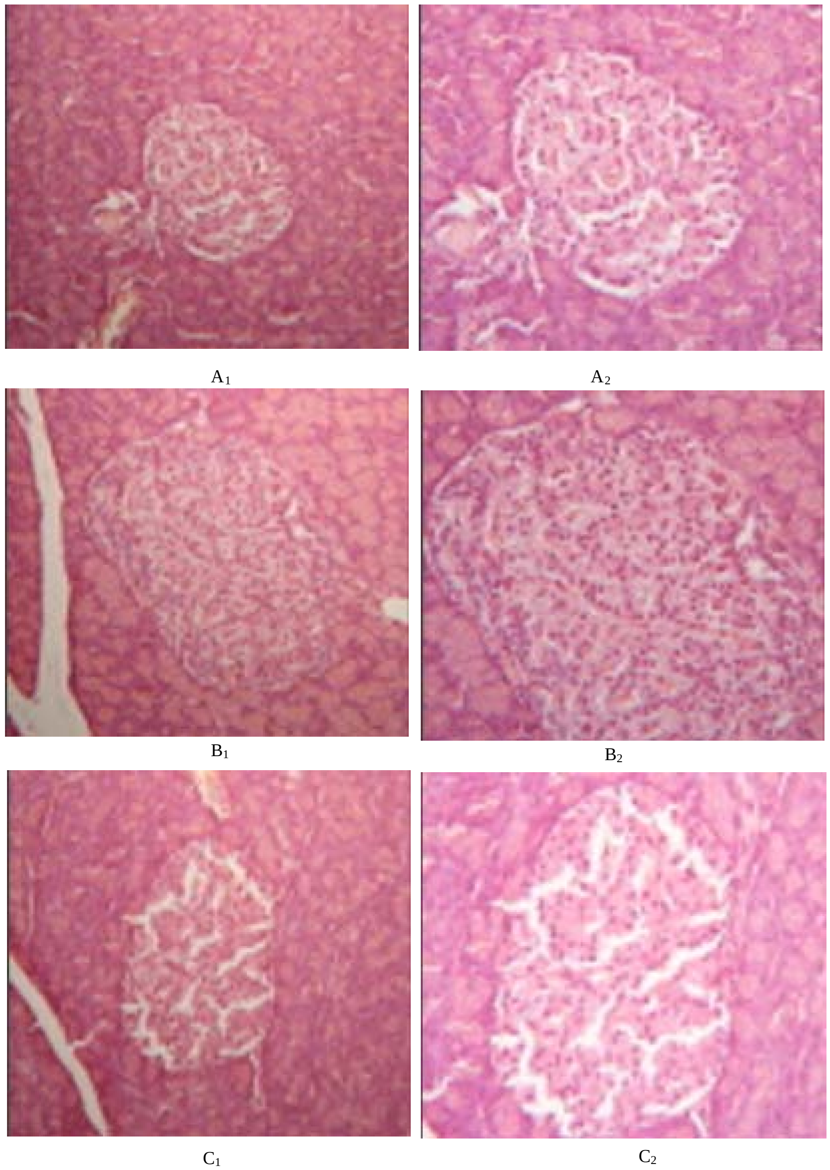

Fig. 1: Representative light microphotographs of Langerhans islet obtained from the control group (A_1 and A_2), EMF exposed group (B_1 and B_2) and sham group (C_1 and C_2); (H and E staining; A_1, B_1 and C_1,x160; A_2, B_2 and C_2,x250)

glucose blood concentration, decreased concentration of glucose circulating in blood may reveal destabilization of carbohydrate metabolism regulation under the influence of electromagnetic field. Moreover, as Laitl-Kobierska *et al.* (2002) supposed, activation of the parasympathetic nervous system which stimulates hormonal activity of pancreas, leads to this effect indirectly. In contradiction to our results, in other studies, no significant influence (Harakawa *et al.*, 2005) or increasing effect (Sedghi *et al.*, 2006; Anselmo *et al.*, 2007) was seen on glucose level in the blood of experimental animals after exposure to ELFEMF.

It has been well shown that glucose exerts important control over alpha cell secretion in a manner nearly the reverse of glucose control over insulin release from the beta cell. At low glucose levels, glucagon secretion is enhanced and at higher levels suppressed. But our results showed that blood concentration of glucagon was unchanged in the EMF exposed group inspite of decreased blood glucose concentration (Table 1). Inconsistent to our result, Gorczynska and Wegrzynowicz (1991) reported that magnetic fields cause to glucagon increasing in the rats (Shahryar *et al.*, 2008). Catecholamines may be as important as glucose in the control of glucagon secretion. It's shown that both epinephrine secretion by the adrenal medulla and norepinephrine secretion by sympathetic nerve terminals stimulate glucagon secretion (Weir *et al.*, 1974). On the other hand, previous investigations have shown that EMF stimulation alters catecholamine metabolism. Yim and Jeong (2006) showed that dopamine levels in PC12 cells were significantly reduced within 10-15 min under 60 Hz, 8 mT sinusoidal field. Besides Chiang and Yao (1987) observed decrease in catecholamine levels in the hypothalamus of the offsprings of Kumming mice after exposure to EMF from the first day of gestation throughout the pregnancy. Thus, it seems likely that long term exposure to ELFEMF prevents from increase of glucagon secretion due to low glucose levels via decreasing catecholamine levels. Besides, as insulin is a powerful glucagon suppressor (Ungera and Orci, 2010), an increase in insulin has probably prevented from increase of glucagon secretion.

The hypoglycemic effect of ELFEMF accompanied by an increase in insulin secretion reported here is in agreement with the report of Mansi (2006) about the antidiabetic effect of Nigella sativa in experimental diabetes through decreasing oxidative stress. As it's postulated that long-term exposure to EMF produces high levels of oxidative stress (Khaki *et al.*, 2008) and is reported that the effect of the EMF is critically dependent on the duration of exposure and strength of the field (Attia and Yehia, 2002), long- term exposure to ELF EMF (50 Hz, 1 mT) may have a potential role to exert a therapeutic protective effect in diabetes.

CONCLUSION

In total, the results of this study for the first time showed that long term exposure to ELFEMF led to the increase of insulin blood concentration accompanied to the reduction of glucose blood concentration, without changing in glucagon blood concentration and resulted in increasing of the size of the pancreatic islets. It's concluded that chronic exposure to 50 Hz EMF induces adaptive changes in structure and function of pancreas.

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