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The Effect of Extremely Low Frequency Electromagnetic Field on Angiogenesis

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Abstract: In this study, we studied electromagnetic field effect on angiogenesis. Ross fertilized eggs were used that divided into 3 random groups 42 consisted of control, sham-exposed and a test group which treated by 0.04 T electromagnetic field. In day 10 members of test group was occurred in 0.04 T electromagnetic fields for 4 h. Members of sham-exposed group was occurred in the same electromagnetic field but in turn off condition. In day 12 chorioalantoic membranes were examined and photographed in all cases. The numbers and lengths of vessels in four random same areas were measured and compared with each other by t-test ($p<0.05$). Comparison between average number and length of vessels in controls and sham-exposed didn't show any significant differences. In test group we saw a significant decrease in average number (26.69±7.88) and length (44.41±9.88 cm) of vessels in comparison with controls. As a result 0.04 T electromagnetic field has an inhibitory effect on angiogenesis in chick chorioalantoic membrane.

Key words: Angiogenesis, electromagnetic field, chorioalantoic membrane, ross

INTRODUCTION

Angiogenesis, the sprouting of capillaries from pre-existing venules, orchestrated by a plenitude of different molecules and pathways, including Vasculo-Endothelial Growth Factor (VEGF) (Breier, 2006), Stem Cell Factor (SCF), Epithelial Growth Factor (EGF), Transforming Growth Factor β (TGFβ) family (Lioyd *et al*., 2003), FGF, extracellular matrix (ECM) (Li *et al*., 2003), angiopoietins and other cytokines (Hiromatsu and Toda, 2003). In the adult organism, new blood vessel formation is tightly controlled and occurs only under certain physiological and pathological conditions, such as pregnancy, wound healing (Li *et al*., 2003) diabetic retinopathy, or solid tumor growth (Srivastava *et al*., 2002; Breier, 2006). Balasubramanian and Reed (2003) showed that following embryonic and postnatal development, blood vessel endothelial cells proliferate and may remain quiescent for several years, in physiological conditions, a fine balance of pro- and anti-angiogenic factors is maintained as part of normal homeostatic mechanisms.

Electromagnetic fields, constant and alternating, are a static element of the environment. They originate from both natural and man-made sources. Depending on the type of the field,

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its intensity and time of activity, they exert different effects on the natural world (plants and animals). Some animals utilize magnetic field of the earth for their own purposes (Rochalska, 2007). Several reports have shown that weak, Extremely-Low-Frequency (ELF), Pulsed Magnetic Fields (PMFs) can adversely affect the early embryonic development of the chick, PMFs can induce irreversible developmental alterations and the pulse waveform can be a determinant factor in the embryonic response to ELF magnetic fields (Ubeda *et al.*, 1994). *In vitro* or *in vivo* studies in nonhuman species can be used to study mechanisms and the effects that have been suggested by human investigations. The studies dealing with mutagenesis, cell death and cell proliferation using *in vitro* systems do not indicate that EMFs have the potential for deleteriously affecting proliferating and differentiating embryonic cells at the exposures to which populations are usually exposed. Of course, there is no environmental agent that has no effect, deleterious or not, at very high exposures. The animal and *in vitro* studies dealing with the reproductive effects of EMF exposure are extensive (Brent, 1999).

Several mechanisms, both thermal and nonthermal, are were established by which electromagnetic fields can interact with biological systems. Thermal mechanisms are related to heating of tissue and generate when electrical energy change to heat. Nonthermal mechanisms directly depend on electromagnetic field itself and low frequency electric fields interfere to cell membrane stimulation and decrease it (Litvak *et al.*, 2002). A report was published in 2004 that referred to effect of 0.2 T electromagnetic field on angiogenesis in chick chorioallantoic membrane (Ruggerio *et al.*, 2004). In this study we analyze the effects of 0.04 T electromagnetic field on angiogenesis with this hypothesis that if 0.04 T electromagnetic field has inhibitory effect on angiogenesis.

MATERIALS AND METHODS

This research was executed in Research Laboratory in Biology Department of Mashhad Islamic Azad University (Mashhad, Iran, 2008-2009). We used 42 fertilized Ross eggs that hold in an incubator with 38°C temperature and 65% moisture. In day 2 of incubation, windows were opened on eggs under sterile condition (Ruggerio *et al.*, 2004; Laminair flow,

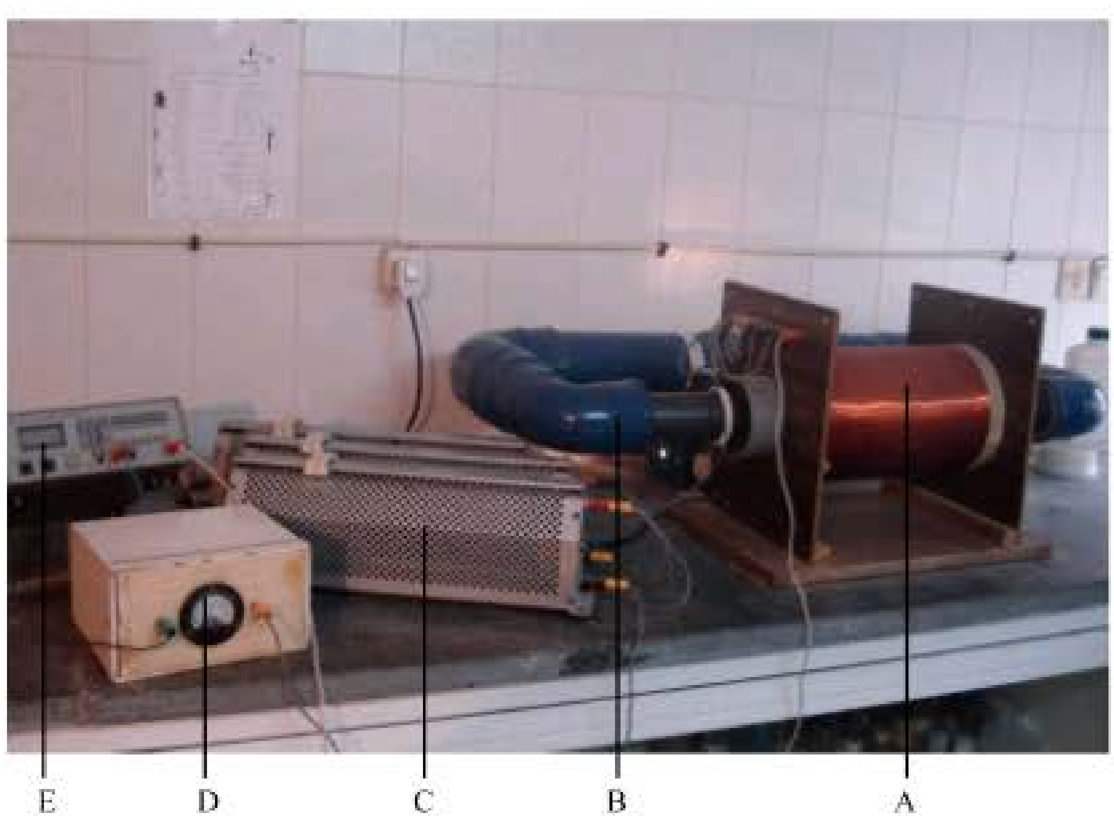

Fig. 1: The electromagnetic system with incubator. A: Electrical coiling, B: Incubator, C: Resistant, D: Condenser and E: Amper meter

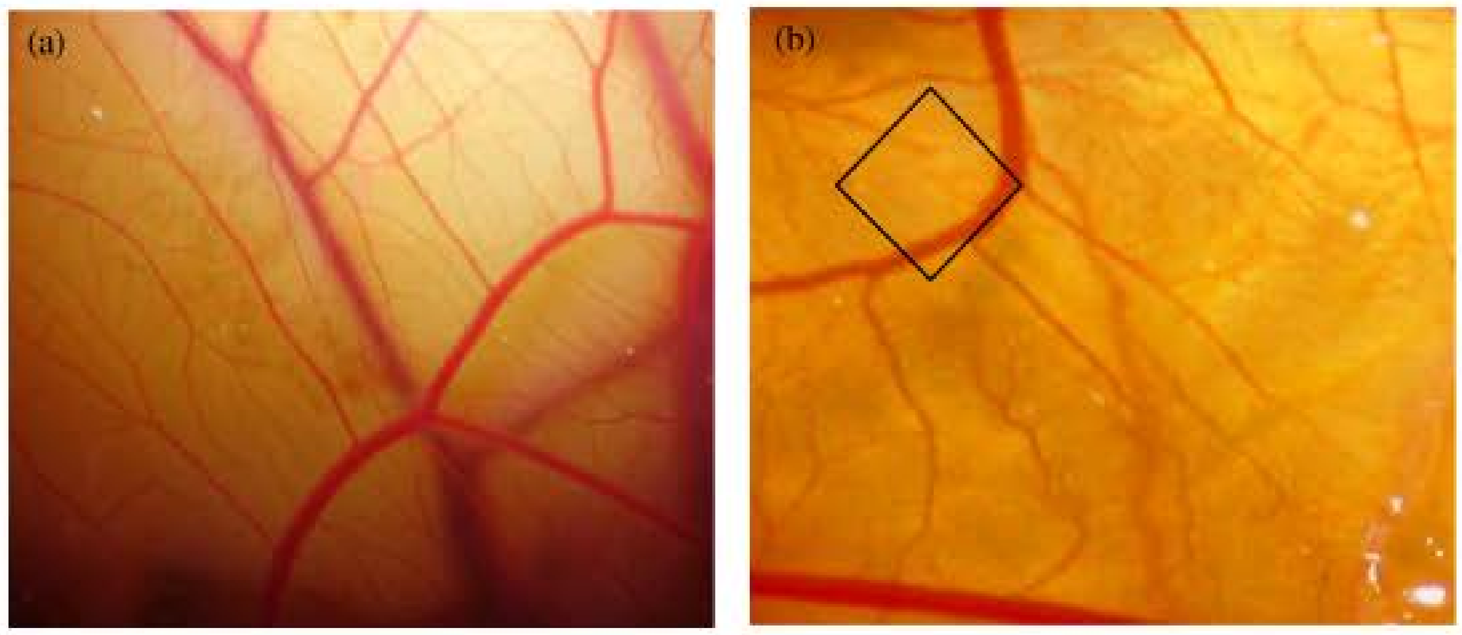

Fig. 2: Chorioalantoic membrane in experimental groups. (a) Control case and (b) test case (treated by 0.04T electromagnetic field). Black quadrate show one of the measured area

Teslar AV-100, Spain) and eggs were considered in 3 random groups include of, 1) control, that hold in normal condition; 2) sham-exposed, that were placed in electromagnetic field, but in turn of position and 3) test, treated by 0.04 electromagnetic field. In day 10 members of group 2 were occurred in 0.04 T electromagnetic field (made in biology research lab of Islamic Azad university of Mashhad, Iran) for 4 h, but in turn off position (Fig. 1) and members of group 3 were occurred in this electromagnetic field in turn on position (0.04 T for 4 h). Chorioalantoic membrane were examined daily and photographed (by photo-stereomicroscope, Zeiss, Germany) at day 12 in 0.65×10×4 magnification (Fig. 2a, b). Four equal random area (quadrate shape) were selected and data were analyzed for the number and length of angiogenic blood vessels by software programs and t-test.

RESULTS AND DISCUSSION

As shown in Table 1, there was not any differences between the average number (42.00±7.26) and length (57.25±5.05 cm) of blood vessels in control and average number (42.93±6.73) and length (58.22±6.40 cm) of blood vessels in sham-exposed, so electromagnetic field in turn off position has not any effects on blood vessel formation. In test group which treated with 0.04 T electromagnetic field (MF) there was a significant decrease in average number (26.69±7.88) and length (44.41±9.88 cm) of vessels in comparison with control.

In the extremely low frequency (ELF, <300 Hz) part of the electromagnetic spectrum, experimental therapies have been emerging for a variety of medical conditions, such as non-union bone fractures, skin ulcers, migraines and degenerative nerves (Shupak, 2003). Williams and his co-workers reported reduction of angiogenesis in breast adenocarcinoma cells treated by 10, 15 and 20 µT electromagnetic fields, Okano *et al*. (2007) showed that 10 and 15 mT static electromagnetic fields reduce angiogenesis in rats with experimental hypertension (McKay *et al*., 2007). Okano *et al*. (2007) demonstrated that 120 mT Static Magnetic Field (SMF) significantly reversed the inhibitory effects of TGF-β1 arteriogenesis *in vitro*, suggesting that SMF could have potential to modify tubular formation, depending on the origin of the cells and the experimental conditions, including angiogenesis inhibitors or stimulators in the medium used for incubation, field intensity, localization of exposure, exposure duration and heterogeneous or homogeneous magnetic fields (Okano *et al*., 2007).

Table 1: Average number and length of vessels in experimental groups (±SD), control, sham-exposed and test (treated with 0.04 T electromagnetic field)

Experimental groups	Average number ±SD	Average length ±SD
Control	42.00±7.26	57.25±5.05
Sham-exposed	42.93±6.73	58.22±6.40
Test	26.69±7.88	44.41±9.88

Del Monache *et al.* (2008) showed that some important functions of human microvascular endothelial cells (*in vitro*), including proliferation, migration and tubule formation increased under the influence of a sinusoidal electromagnetic field (1 mT, 50 Hz) and the organization of the actin and local adhesion inside the cell, the state of activation and the distribution of VEGF receptors were also affected. It was reported that angiogenesis increased in rat subcutaneous tissue when exposed to 0.1 mT for 30 min twice daily for 8 or 12 weeks (Weber *et al*., 2004). Tepper *et al*. (2004) showed that 1.2 mT pulsed electromagnetic fields (PEMF) increased angiogenesis in transgenic mice (8 h day^{-1} whole body exposure for 3, 10 or 14 days) (Tepper *et al*., 2004). There are several factors that make different effects of electromagnetic fields on the basis of intensity and exposure time of electromagnetic field and the hereditary characteristics of the treated cases too (Lahijani and Sajadi, 2004). In this study we found when eggs were exposed to 0.04 T electromagnetic field, angiogenesis was inhibited and the number of blood vessels were decreased. Bare (2004) suggested that by creating a synergism of biochemical, electrochemical and electronic principles, the practitioner should be able to achieve a superior treatment outcome; reporting that present chemotherapy regimens can cause permanent damage to various vital organs including the heart, lung and kidneys; even without such permanent damage, short term toxicity manifested as repression of the hematopoietic system and other type of physical unpleasantness.

CONCLUSION

The 0.04 T sinusoidal electromagnetic field can inhibit angiogenesis in chick chorioalantoic membrane which appear as a significant decrease in numbers and lengths of blood vessels. Based on different results in different studies, we purpose that electromagnetic fields with different densities and shape of waves can use for treated some pathological conditions that involve with angiogenesis as solid tumor and metastasis (inhibitory effect) or wound healings (stimulatory effect).

REFERENCES

Balasubramanian, S.P. and M.W. Reed, 2003. Ischemic vascular disease and solid cancers opposing ends of the angiogenic spectrum. Med. Hypothesis, 67: 1317-1319.

Bare, J.E., 2004. Pulsed field assisted chemotherapy. http://www.quress.com/artsen/images/PDF/quress_pulsed_field_assisted_chemotherapy.pdf.

Breier, G., 2006. Vasculogenesis. In: Cell Signaling and Growth Factors in Development, Unsicker, K. and K. Kriegistein (Eds.). Willey-VCH, Verlag, Weinheim, pp: 909-917.

Brent, L.R., 1999. Reproductive and teratogenic effects of low-frequency electromagnetic fields a review of *in vivo* and *in vitro* studies using animal models. Teratology, 59: 261-286.

Del Monache, S., R. Alessandro, R. Lorio, G. Gualtieri and R. Colonna, 2008. Extremely low frequency electromagnetic fieldes (ELF-EMFs) induce *in vitro* angiogenesis process in human endothelial cells. Bioelactromagnetics, 29: 640-648.

Hiromatsu, Y. and S.H. Toda, 2003. Mast cells and angiogenesis. Microsc. Res. Tech., 60: 64-69.

Lahijani, M.S. and K. Sajadi, 2004. Development of preincubated chicken eggs following exposure to 50 Hz electromagnetic fields with 1.33-7.32 mT flux densities. Ind. J. Exp. Boil., 42: 858-865.

Li, J., Y.P. Zhang and R.S. Krisner, 2003. Angiogenesis in wound repair: Angiogenesis growth factors and the extracellular matrix. Microsc. Res. Tech., 60: 107-114.

Lioyd, R., S. Vidal, E. Horvath, K. Kavacs and S. Bernd, 2003. Angiogenesis in normal and neoplastic pituitary tissues. Micros. Res. Tech., 69: 244-250.

Litvak, E., K.R. Foster and M.H. Repacholi, 2002. Health and safety implications of exposure to electromagnetic fields in the frequency range 300 Hz to 10 MHz. Bioelactromagnetics, 23: 68-82.

McKay, J.C., F.S. Prato and A.W. Thomas, 2007. A literature review: The effects of magnetic field exposure on blood flow and blood vessels in the microvasculature. Bioelectromagnetics, 28: 81-98.

Okano, H., N. Tomila and Y. Ikada, 2007. Breif communication: Effects of 120 mT static magnetic field on TGF-β1-inhibited endothelial tubular formation *in vitro*. Bioelectromagnetics, 28: 497-499.

Rochalska, M., 2007. The effect of electromagnetic fields on living organisms plants birds and animals. Med. Pr., 58: 37-48.

Ruggerio, M., D. Bottaro, G. Liguri, M. Gulisano, B. Peruzzi and S. Pacini, 2004. 0.2 T magnetic field inhibits angiogenesis in chick embryo chorioalantoic membrane. Bioelactromagnetics, 25: 390-394.

Shupak, N., 2003. Therapeutic uses of pulsed magnetic field exposure: A review. Rad. Sci. Bull., 307: 9-30.

Srivastava, A., R. Ralhan and J. Kaur, 2002. Angiogenesis in cutaneous melanoma: Pathogenesis and clinical implications. Micros. Res. Tech., 60: 208-224.

Tepper, O.M., M.J. Callaghan, E.I. Chang, R.D. Galiano, K.A. Bhatt and S. Baharestani *et al.*, 2004. Electromagnetic fields increase *in vitro* and *in vivo* angiogenesis through endothelial release of FGF-2. FASEB J., 11: 1231-1233.

Ubeda, A., M. Trillo, L. Chacón, M. Blanco and J. Leal, 1994. Chick embryo development can be irreversibly altered by early exposure to weak extremely-low-frequency magnetic fields. Bioelectromagnetics, 15: 385-398.

Weber, R.V., A. Navarro, J.K. Wu, H. Yu and B. Strauch 2004. Pulsed magnetic fields applied to a transferred arterial loop support the rat groin composite flap. Plast. Reconstr. Surg., 114: 1185-1189.