The effect of perinatal ground and water exercises on the pregnant female mouse obesity gene

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A Dissertation
Submitted to the
Graduate School of Sungshin University

in partial fulfillment of the requirements
for the degree of
Doctor of Physical Education

Kim Sun Hwa

02. 2015

This is to certify that we have examined the

Doctoral Dissertation of

Kim Sun Hwa

Submitted to Department of Physical Education

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Abstract

The obesity gene (PPARs, Adiponectin) expression levels in prenatal rats were observed by differentiating the exercise type, and investigated how it affects on the mother mice. The goal of this study is to provide a preliminary data for the effective exercise routine and exercise prescription for pregnant women.

The animals used in this study were 7-week-old male (n = 10) and female(n = 40) ICR type mice, which were supplied by an animal handling company (DY Biotech). After breeding, the pregnant mosue were randomly selected and divided into the Control Group(n=9), Ground Exercise Group (n=10), and Water Exercise Goup(n=10). The Ground Exercise and Water Exercise were conducted for 9-weeks at the frequency of 3days/week.

.All data were analyzed utilizing the Statistical Package for the Social Sciences(SPSS, v.20.0). One-way analysis of variance(ANOVA) was used for inter-group comparisons. Statistical significance was considered when p value was less than 0.05(p <.05).

1. There is no statistical difference of the expression of PPAR- β in PPARs of muscles in the Control group and Ground Exercise group, but both groups have an increasing tendency. The statistical significance is(p<.05) between a Control group and WAter Exercise group that there are differences in the expression tendency depending on types of exercises.
2. There is no statistical difference of the expression of adiponectin of muscles in the Control Group and Ground Exercise Group, but both groups

have an increasing tendency. The statistical significance is (p <.05) between the Control Group and Water Exercise Group that there are differences in the expression tendency depending on types of exercise.

The results conclude that the Ground exercise and water exercise positively affect pregnant mouse prior and after pregnancy. The water exercise increases the obesity genes, PPARs, and the expression of adiponectin that it prevents an excessive weight increase or obesity, thus, it affects positively on the health of a pregnant and embryo.

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Ⅰ. Introduction

1. Research necessity

Fetal health is the biggest concern of pregnant women. In many cases, exercise is carried out during pregnancy to maintain a better condition and health of the fetus. Healthy childbirth through various activities, such as good environment, food, music, and sports Kim., 2011), relieving the pain of childbirth and safe birth, and returning to pre-pregnant state are also the wishes of many pregnant women. When women get pregnant, however, the physical and physiological changes causing a weight in crease gradually reduce thephysical activity, and they aree asily subjected to being overweight and obese due to disharmonious eating habits during pregnancy(Parketal.,2013).

Domestically, the exact incidence of obesity in pregnant women is not clearly reported, but the fact is that living conditions are increasingly more Westernized than in the past(Park, 2013). According to the national health and nutrition survey 2011, the body mass index(BMI) based on overweight and obesity prevalence rate of childbearing age women from 19 to 39 years were reported as high as 28.5% and 10.1% respectively, implying that the provision of nutrition promotion programs and education are urgently needed(Department of Health and Human Services, 2011).

The negative side effects of pregnancy on pregnant mothers, such as discordant of diet and physical activity reduction due to the weight increase, require a proper management because the side effects might result in obesity during pregnancy, causing gestational diabetes and adverse effects on maternal-child health(Canadian Diabetes Association Clinical

Practice Guidelines Expect Committee, 2003).

In response to these problems, physical activities can bring positive effects to pregnant women and fetus. The improvement of muscular strength and endurance, prevention of excessive weight gain and obesity, back- and pregnancy-associated pain relief, fetal and placental growth, and increase of birth weight can be achieved through exercise(Clapp et al. ,2002; Clapp et al., 2001).

Exercising during a pregnancy gives a lot more positive impact for both mother and baby and diverse results of exercising based on the type of movement, time, and intensity have been reported(Koshino, 2003). Aerobic exercise, as one of example, gives positive effects in the reduction of excessive weight gain, reducing back pain, and relieving depression in healthy women(Polley et al., 2002); low-intensity aerobic exercise during pregnancy can help in preventing or treating gestational hypertension and diabetes(Wolfe & Weissgerber, 2003). The positive effects of other weight bearing exercises, such as walking and low intensity running, and non-weight bearing exercise, such as swimming, have also been reported (Clapp et al., 2001).

Among these exercises, swimming has the advantages of heat dissipation and water buoyancy(Hartman et al., 1999) and of water pressure that moves the extracellular fluid into the vessels, helping blood flow to the uterus and placenta(McMurray et al., 1990). The underwater exercise is better than any other exercises in terms of efficacy and safety stocks due to the nature of the water and greater exercise adherence from a positive body image during exercise in which one's own shape moving in the water is unexposed(Basmajian, 1987).

Aquatic exercise that has been reported to be suitable for pregnant women increases the physical factors, such as flexibility, strength, and balance(2009), helps the physical challenges related to late pregnancy and enables the continuous dynamic balancing exercises(Eo, 2011).

It also has been reported on how to have less physical demands on pregnant women(Lynchetal, 2003; .San,Cecatti, Sarno, Cavalcante & Marussi, 2007).The underwater condition reduces the effort to move against gravity ,and buoyancy provides the advantage of reducing the weight load as well as the force acting less as a stress on joints. The aquatic aerobic exercise for pregnant women appeared to have no risk during childbirth and was confirmed as a safe exercise for both maternal and fetal health(Silveira, Pereira, Cecatti, Cavalcante & Pereira, 2010). management from

According to recent report from the National Health Insurance Corporation(2012), diabetes during pregnancy has increased 5.8 times larger than the previous nine years, and the management from pre-pregnancy and early pregnancy has been recommended.

About 25% of the pregnant women with gestational diabetes in early pregnancy might develop into the non-insulin-dependent diabetes(type 2) or diabetes within four years after the birth(kelly & Mandarino, 2000). The offspring gestational diabetes mellitus(GDM) also have been reported to have an increased risk of type 1 and type 2 diabetes(Canadian Diabetes Association Clinical Practice Guidelines Expect Committee, 2003).

In two different studies conducted to prevent the risk of diabetes, a short-term yoga practice targeted to two pregnant women groups of impaired glucose tolerance and normal showed a significant increase of Adiponectin expression levels(Im, 2008), and the significantly increase of Adiponectin level was observed in the weight-loss group from a 6 months aerobic exercise program targeted to 11 healthy men and women(Hulveretal. 2005).

The human Adiponectin, which was referred to as Apm1(adipose most abundant gene transcript 1) and GBP28(gelatin-binding protein 28), appeared very low in the obese, with 55-93% of strong hereditary. The polymorphic genotype of Adiponectin regulates the levels and influences the development of insulin resistance and type 2 diabetes(Jang et al, 2006; Pollin et al, 2005). The polymorphic genotypes of Adiponectin in rat, Acrp30 and AdipoQ(Hu, Liang, & Sipcgelman, 1996), also have been reported to increase the body insulin resistance and to be greatly reduced in the obese (Maeda et al., 1996).

The PPARs(peroxisome proliferator-activated receptor) is one of the important genes that is involved in the metabolism of adipose tissue and diabetes, and exercise during pregnancy has been reported to have a positive impact on this gene. Kannisto et al.(2006) reported a decreased expression of mRNA of PPAR-α and significantly increased expression of PPAR-β when exercising. PPAR-ɣ, through an experiment with rats, is known to involved in the fat cell differentiation, the process of insulin resistance and blood sugar level Control, and in storing surplus energy as a form of fat Barak et al., 1999); it is also associated with the pathogenesis of many diseases, such as atherosclerosis and cancer, as an active material of obesity, diabetes, and anti-inflammatory(Berger et al., 2002). Also, n an experiment where before and after pregnancy aerobic exercise of pregnant rats was conducted, a tendency of increased PPAR-α and PPAR-γ expression in the muscle PPARs was reported(Yun, 2012).

PPAR-β that is expressed in the intestines, kidney, and heart has a cellular sensor sensing the fat contained in food and it slow downs the progression of lesions that cause heart disease. The weakening of the PPAR-β due to the high fat, lack of exercise, infection, and stress has been reported(Lee et al., 2003). Also, a significant increase of PPAR-β by a sustained low-intensity exercise during pregnancy was reported(Kim Dong-Hyun,2011).

To sum up the results of the previous studies, the expression level of PPARs gene changes through exercising before and after impregnation, and exercising gives a positive impact on obesity-related genes and brings a change of superior genes. Therefore, it is considered that exercise during pregnancy will deliver good genetic information to the fetus.

Conducting an exercise and genetic testing on pregnant women, however, may be a safety issue in the experiment so that the effect was verified via animal-testing.

The effectiveness of Ground Exercise and underwater Exercise for pregnant women has been verified separately in many studies or rather intermittently, but only a few studies that identified an efficient way to exercise by comparing the two types of exercises have been conducted.

Therefore, more in-depth research is needed for an organized maternal exercise program.

2. Research Purpose

The obesity gene(PPARs, Adiponectin) expression levels in prenatal prenatal mouse were observed by differentiating the exercise type and investigated in how it affects mother mice. The goal of this study is to provide preliminary data for an effective exercise routine and exercise prescription for pregnant women.

3. Research hypothesis

1) The difference in the expression of PPARs gene in muscle and fat cells will be observed, depending on the type of the Group exercise.

2-1) The difference between the expression of PPAR-α will exist between the groups.

2-2) The difference between the expression of PPAR-β will exist between the groups.

2-3) The differencebetweentheexpressionofPPAR-ɣ will exist between the groups.

2) The difference in the expression of obesity-related Adiponectin gene will exist between the groups with different exercise type.

4. The definition of the terms

The concept and operational definition of the terms used in this study are as follows.

1) PPARs

PPARs (peroxisome proliferator-activated receptors) have six main domains comprised of twelve alpha-helixes, of which four domains have their key features. Since these are the acceptors combined in the nucleus, they have a domain that binds with DNA, and another domain that binds with PPAR agonist comes from either inside or outside. In X-ray, they form a three-dimensional shape with a ligand acceptor. When the ligand is attached, they activate the DNA transfer mechanism and act as a gene that Control the lipoprotein metabolism and maintain the homeostasis of the lipid and cholesterol.

2) PPAR-α

PPAR-α is the nuclear receptor with a unique transcription that is present in the liver, kidney, and muscle cells. This gene is related to weight loss.

3) PPAR - β

PPAR-β has a same role as PPAR-δ, but it is named as aβdue to its' different shape. This gene is distributed in most of the organs.

4) PPAR-γ

PPAR-γ has three isoforms, and it presents in the liver and kidney in addition to fat cells and skeletal muscle. PPAR-γ is the gene that is involved in the differentiation of adipocytes.

5) Adiponectin

Adiponectin enhances the responsiveness to insulin by increasing the glucose and lipid metabolism. Adipocyte controls the lipid storage by involving hormone regulation of the physiological response to fat intake. The concentration in blood is reduced in the patients with obesity, diabetes, and heart disease; in the contrast to this, the concentration increases when the weight is lost.

Ⅱ. Theoretical Background

1. Type of PPARs and mechanisms

PPARs are transcription factors belonging to the nuclear hormone receptor family, and are activated by ligands to control the transcription of genes related to lipid and glucose metabolism, as well as energy homeostasis. They also have a role in controlling the proliferation and differentiation of cells. There are three forms of PPAR isomers, α, β, and ɣ, each of which are expressed by different genes(Dong Hyun Kim, 2011).

PPARs are largely divided into the N-terminal region, DNA binding domain, ligand binding domain, and active domain present in C-terminal. Among these, the sequences of amino acids in the DNA binding domain are well-preserved in the three isomers of PPARs; however, differences in the ligand binding domain cause each of the PPARs to bind to different ligands. This fact suggests that PPARs can detect the amounts of fat metabolites, which are main nutrients in the body, and play an important role in controlling their metabolism(Fajas et al., 2001).

2. Exercise and PPARs

1)Mechanisms and Exercise of PPAR-α

PPAR-α is mostly expressed in the skeletal muscles of the human body, and activates the transcription of many genes, including fatty acid translocase, fatty acid binding protein, carnitine palmitoyltrasferase 1, and pyruvate deehydrogenase kinase-4. This is known to enhance the oxidation of fatty acids within the skeletal muscles(Campbell et al., 2002; Muoio et al., 2002).

In addition, PPAR-α is expressed in various metabolically active tissues in rodents and humans, including kidney, heart, skeletal muscle, and brown adipose tissue(Braissant et al., 1996). The hepatocellular expression of PPAR-α particularly occurs most actively, and extensive research related to fat metabolism is currently in progress.

Iemitsu et al.(2002) reported that nerve stimulation through exercise or long-term exercise has the effect of improving reduction of protein content and PPAR-α m-RNA in cardiac tissues, which occur due to aging. Wv14643 and linoleic acid are also known as representative ligands which activate PPAR-α. In addition, hypolipidemic fibrate and compounds such as deformed fat metabolites, which are structurally variable, have also been reported to combine with PPAR-α as inhibitors of lipid metabolism(Linton et al., 2000).

Fibrate, known as a ligand for PPAR-α, is a hypolidenic drug used to treat cardiovascular disease. It stimulates fatty acid oxidation, mediated by PPAR-α. This reduces the expression of apo-Ⅲ to lower the plasma triglyceride concentration, and induces the expressions of apolipo-protein A and AⅡ, which increase the amount of high density lipoprotein(HDL) in the plasma. The over-production of fatty acid drops insulin sensitivity in the fat, liver, and muscle tissues, and induces insulin resistance. Therefore, the effect of increasing fatty body concentration due to fibrate treatment facilitates insulin sensitivity in the liver and muscle tissues to display hypoglycemic effects, which can lower the blood sugar levels. This ligand of PPAR-α can be presented as a potential treatment for suppression of obesity through dissociation of fat(Dong Hyun Kim, 2011).

PPAR-α is an important factor that controls metabolic syndrome, and is known as a primary controller for genes related to fatty acid oxidation, which occurs in microsomes within mitochondria and peroxisomes (Reddy et al., 2001). The transcription of key enzymes or proteins involved in Beta-oxidation are direct targets of PPAR-α, including Acy1 CoA oxidase (ACO) or CPT-1(Guan et al., 2001).

As the expression of these genes increases, the ligand of PPAR-α activates fatty acid oxidation. On the other hand, deactivation of PPAR-α causes the accumulation of large amounts of lipid in the liver, which induces low ketosis, hypoglycemia, and hypothermia, as well as increases the level of free fatty acids in the plasma(Leone et al., 1999). Such data clarify that PPAR-α is a key factor which controls the metabolic adaptation to enhanced fatty acid concentrations.

Thus, PPAR-α affects both obesity and insulin resistance(Seedofr et al., 2001), While its activation reduces weight in rodents, deactivation becomes a sign of obesity(Costet et al., 1998).

PPAR-α plays a crucial role in lipid metabolism, and is involved in the majority of processes in lipid metabolism, including lipid absorption and combination, fatty acid oxidation, composition of lipoproteins, and lipid transport(Neve et al., 2001). In addition, the ligand fibrate increases the combination of high density lipoprotein(HDL) through different PPAR target genes, such as Apo-Ⅰ, Apo-Ⅱ, and low density lipoprotein(LDL). This maintains and promotes the HDL levels, bringing out the key benefits of the treatment.

The activation of PPAR-α enhances fatty acid uptake while simultaneously reducing triglyceride(TG) levels, and facilitates the dissociation of very low density lipoprotein(VLDL) (Neve et al., 2002). Therefore, has been suggested that PPAR-α has a role as a lipid sensor and exerts positive metabolic effects in lipid metabolism.

Nerve stimulation through exercise or long-term exercise affects the expression of PPAR-α within skeletal muscle. Russell et al.(2003) conducted a study on male subjects examining endurance exercise(60～80% VO_2max)for 6 weeks. He reported that the levels of PPAR-αmRNA andprotein were significantly increased due to exercise. In comparison of the level of PPAR-α protein expression by muscle contraction characteristics, expression was found to be significantly high in type I, which has high oxidative metabolic activity. He reported that significant expression of PPAR-α occurred according to the muscle contraction characteristics. Furthermore, through astudy on pregnant mice subjected to 8 weeks of aerobic exercise, significant differences in PPAR-α expression were shown between the Control Group and Exercise group. As the exercise time increased, the PPAR-α expression was also shown to increase(Sang-Yong Park et al.,2013).

2) Mechanisms and Exercise of PPAR-β

PPAR-β, which is also known as PPAR-δ, is currently known to be expressed in almost all tissues, and has been reported to be activated by the ligands of saturated fatty acids and unsaturated fatty acids(Oliver et al., 1999). It regulates various metabolic processes related to cholesterol transport, using the fatty acid-oxidation process and glucose(Friedmann, P.S., Cooper H.L., Healy, F., 2005).

According to PPAR-δ activation, the expressions of genes related to the lipid catabolism and control of energy uncoupling in the skeletal muscle cells are known to be enhanced(Dressel et al., 2003; Tanaka et al., 2003; Wang et al., 2003).

Genetic and pharmaceutical research related to PPAR-β has found that it strengthens fat metabolism, reduces weight, and enhances sensitivity to insulin. These results indicate that a PPAR-β agonist has the potential to be used in the treatment of dyslipidemias, obesity, or type 2 diabetes (Wang, D., Wang, H., Guo, Y., Ning, W., Katuri, S., Wahli, W., Desvergne, B., Dey, SK, Dubois, RN 2006).

In the obesity model, the increase in the levels of HDL-cholesterol due to PPAR-β activation was shown to be much higher than for the effects of treatment with fibrate, the ligand of PPAR-α. In the majority of research related to PPAR-β, it was reported to be related to placentation, obesity, colon cancer, and diabetes(winegar, D, A. 2001).

3)Mechanisms and Exercise of PPAR-ɣ

PPAR-ɣ is highly expressed mainly in adipose tissue, but its mRNA is also expressed in other tissues such as skeletal muscle, large intestine, and lungs(Lazar et al., 2005). PPAR-ɣ plays an important role in the production of fat and dissociation of adipocytes, and is usually abundant in adipose tissue where it functions as an important factor in adipocyte dissociation(Lowell et al., 1999).

The relationship between PPAR-ɣ and adipocytes has been revealed by many studies. The adipose tissue was mostly unformed in PPAR-ɣ null-mice, and also remained developed in the embryonic stem cells in which PPAR-ɣ was removed(Rosen et al., 1999). This fact presents that PPAR-ɣ is a transcriptional regulatory factor for fat production, which contributes to obesity.

PPAR-ɣ, when plasma TG is increased and HDL is reduced, is known to play a central role in controlling fat metabolism and fat production. Accordingly, mutations of PPAR-ɣ cause loss of function, which causes an increase in the TG level and decrease in the HDL level(Savage et at., 2003).

PPAR-ɣ is known to be expressed in the skeletal muscle, where it is well-known to have a role in gene regulation. Through recent studies, PPAR-ɣ in the skeletal muscle was found to play a crucial role in the regulation of genes involved in lipid metabolism, predicted by the expressions of three genes: LPL, mCFT-1, and FABP(Lapsys et al., 2000).

After 3 hours of exercise, the expression of PPAR-ɣ in skeletal muscle was observed to increase by 2.7 times(Mahoney et al., 2005). In the skeletal muscle of rats trained in treadmill running for 16 weeks, enhancement in PPAR-γ protein was also observed. Therefore, PPAR-γ was suggested to be expressed after exercise or training(Kawamura et al., 2004), through which it contributes to fat metabolism which occurs after one-time or long-term training.

3. Mechanisms and Exercise of Adiponectin

Adiponectin was first reported by Scherer et al.(1995), after which it was found by many researchers and reported in the following terms: adipocyte complement-related protein of 30 kDa(ACRT30), adipose most abundant gene transcript1(apM1), gdlatin binding protein of 28 kDa(GBD28), adipoQ, collagen containing domain(ACDC), etc.(Derek et al., 2004).

Adiponectin is created as a homotrimer, and higher oligomeric structures are formed through interactions with collagen within the same region (Shapiro and Scherer, 1998). In humans and in nature, this protein exists in the forms of three small fusions, including trimers(Low Molecular Weight: LMW), hexamers (Medium Molecular Weight: MMW), and larger multimeric(High Molecular Weight: HMW) forms(Kishida et al., 2003;. Pajvani et al, 2003). The full-length adiponectin protein splits into smaller forms, including a globular domain, and a very small amount was confirmed to be present in the plasma of both humans and mice(Fruebis et al., 2001). Globular Adiponectin and full-length Adiponectin stimulate the activation of AMPK phosphorylation. On the other hand, full-length Adiponectin is only known to have this function in the liver. Through activation of AMPK, Adiponectin stimulates ACC phosphorylation, fatty acid consumption, intake of glucose, and lactate production in the muscles. In the liver, it phosphorylates ACC and reduces the molecules involved in glucose expression. Adiponectin can be a critical cause of glucose-lowering effects(Yamauchi et al., 2002).

Adiponectin is secreted from adipose tissue, but the concentration was shown to be lower in the obese compared to the general population(Meier &Gressner 2004; Ouch et al., 2003). Therefore, it has been suggested that adiponectin enhances fat oxidation to regulate the level of circulating fatty acids, and reduces intracellular triglycerides in the cells of the liver and skeletal muscle to enhance insulin sensitivity(Saltiel, 2001).

Adiponectin is present in high concentrations of 5~30㎍ / ㎖ in the blood of normal people, with significantly higher concentrations in women compared to men. In adipocytes, adiponectin is a site-specific protein, and is currently receiving considerable amounts of attention in studies on obesity and metabolic syndrome(Chandran et al., 2003; Wong et al., 2002). These available data have suggested that adiponetcin regulates the body energy metabolism, and that its expression is regulated by nutritional status. In addition, adiponectin is known to have anti-diabetic action, anti-atherosclerotic effects, and anti-inflammatory activity in the adipose tissue of the human body, which has caused it to attract attention as a hormone with a central role in metabolic syndrome(Korean Society for the Study of Obesity, 2005).

Matthew et al.(2002) conducted a study on a group of subjects who received 6 months of endurance training and a subject group who lost weight after receiving stomach reduction surgery due to morbid obesity. As a result, the change in adiponectin concentration was clearly higher in the weight loss group compared to the Exercise Group; therefore, adiponectin was reported to be inversely correlated to weight.

Adiponectin also enhances the expression of genes(CD36, acyl-CoA, oxidase, uncoupling protein 2) related to fatty acid transport and oxidation in muscle. This increases fat burning and energy dissipation, and suppresses the inactiveness of triglycerides in the muscle to overcome insulin resistance(Chandran et al., 2003; Yamauchi et al., 2001).

Ⅲ. Methods

1. Animals

The animals used in this study were 7-week-old male(n = 10) and female(n = 40) ICR type mice, which were supplied by an animal handling company(DY Biotech). After providing the animals with an adaptation period, the male and female mice were cross-bred for 48 hours at the proportion of 1:4. Female mice were each placed in a cage with the following conditions: thermostatic(22 ± 2 ℃), humidity of 50 ± 15%, and 12 hours of day/night intervals. During the experiment, all animals had free access to pellets(Carbohydrate 66.8%, Protein 18%, Fat 5%, Fibrin 5%, P 0.2%, other 5%) and water.

After mating, the pregnant mouse were randomly selected and divided into the Control Group(CG), Ground Exercise Group(GEG), and Water Exercise Group(WEG). The characteristics of the animals used in this experiment are listed in <Table 1>, and their physical appearances are displayed in <Figure 1>

Table 1. Body weight(g) of 7-week-old rats used for experiments.

Treatment groups	Body weight(M±SD)	Sample number
CG	29.88 ± 1.20	9
GEG	29.54 ± 0.50	10
WEG	29.51 ± 1.81	10

Mean±SD,
CG: Control Group, GEG: Ground Exercise group, WEG: Water Exercise group

Figure 1. laboraBtory animals

2. Research procedures

The procedure used in this study is shown in <figure 2>. The pregnant mosue (n=29) were categorized into types of exercise. All experiments were conducted for 9 weeks at the frequency of 3days/week.

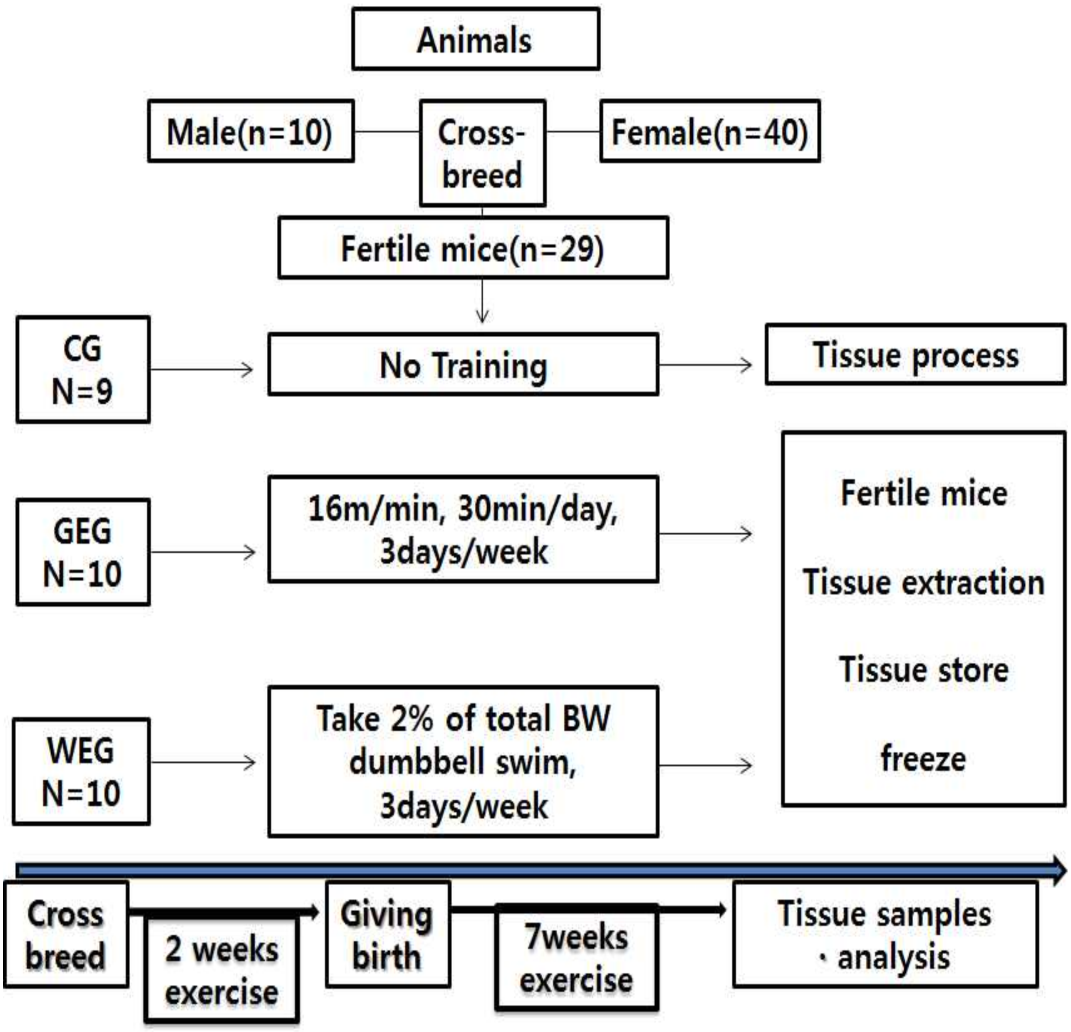

Figure 2 . Experimental design

3. Exercise method

Each group was subjected to 16m/min of adaptation training for 1 week. After breeding for 48 hours, the pregnant mosue were selected and randomly categorized into the Control Group(CG), Ground Exercise group(GEG), and Water Exercise group(WEG). All experiments were conducted for a total of 9 weeks at the frequency of 3 days/week, with a resting period of 2 weeks during fertility and 1 week after giving birth. Seven weeks of exercise was performed after the resting period. The Control Group(CG) was limited to having less movement.

To control the type of exercise for each group, variation was given with ground exercise and water exercise. The training profile of VO_2max 40~45% was applied according to the study reported by Bedford et al(1989). which was revised based on the exercise intensity. The ground Exercise group(GEG) was trained at a rate of 16m/min for 30minutes, and the Water Exercise group(WEG) was trained for 30minutes with the weight of 2%. The exercise protocol is shown in<Table2>.

Table 2. Exercise protocol

Group	Type	Speed(m/min)	Time(min)	Vo_2max
CG	-	-	-	-
GEG	treadmil	16m/min	30min	40~50%
WEG	Forced-swim	take 2% of total BW dumbell	30min	40~50%

CG: Control Group, GEG: Ground Exercise group, WEG: Water Exercise group

Figure 3 . Treadmil Exercise

Figure 4. force swimming Exercise

4. Extraction and preparation of tissue

50mg samples of liver and musculature were rapidly frozen in liquid nitrogen and stored in a deep freezer at -80℃. For analysis, 1ml RNA prep solution (Accuzol total RNA extraction solution, Bioneer, Korea) was added to the samples, after which they were pulverized with a tissue homogenizer. After the addition of 200ul chloroform, the samples were mixed well for 15 seconds. They were then stored on ice for 5 minutes, and then centrifuged for 15 minutes at 12,000rpm, 4℃. Next, isopropyl alcohol was added in the same amount as the mixture, which was mixed and stored for 10 minutes at -20℃. The mixture was then centrifuged again under the same conditions, after which the supernatant was removed, the pellet was washed with 80% ethanol, and the total RNA was extracted.

An RT premix kit(AccuPower cyclescript RT premix, Bioneer) was used for cDNA synthesis. The total RNA of 1ug was added as a template to a Premix tube to make the reaction volume of 20ul, and a PCR machine(Veriti 96well thermal cycler, Applied Biosystems, USA) was used for the cDNA synthesis. The PCR conditions were as follows. Step 1:20℃, 30sec(primer annealing); Step 2:45℃, 4min(cDNA synthesis); Step 3:55℃, 30sec(melting secondary structure); and Step 4:95℃, 5min(heat inactivation). Real-time PCR(Lightcycler 480, Roche) was conducted using the cDNA template produced. After preparing Lightcycler 480 SYBR green 1Master(vial 1) and PCR-grade-only water(vial 2), 20ul reaction volumes were made, to which 5ul of DNA template was added. The PCR conditions were as follows: pre incubation for 1cycle(95℃, 5min) and amplification for 45 cycles(95℃ 10sec, 54℃ 20sec, 72℃ 30sec).

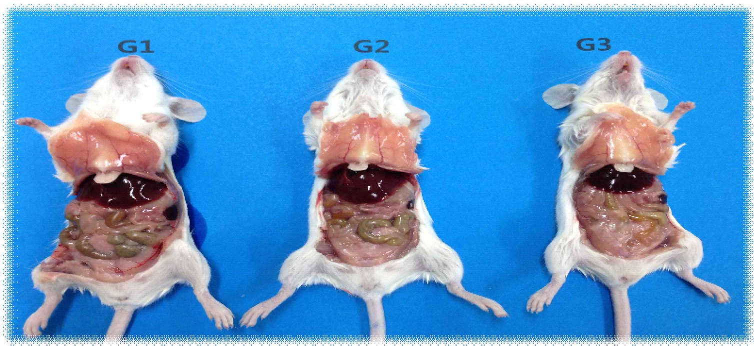

Figure 5. Rat dissection pictures

Figure 6. Extraction of rat liver pictures

5. Measuring Items

The experimental devices and their applications in the experiment are as shown in <Table 3>.

Table 3. Experimental equipments

Experimental item	Model(product)	Usage
Microbalance	bio-red(U.S.A)	weight measurement
Centrifuge	vs-15000cf(U.S.A)	centrifuge
PCR	Veriti(U.S.A) / LC 480(Germany)	quantiative analysis
Gudero	Bumyang(Korea)	quick-freeze
Alphamager2 200	U.S.A	expression analysis
Microplate reder	Bio-rad model 550(Japan)	obsorbance measurement

6. Data Processing

All data were analyzed utilizing the Statistical Package for the Social Sciences (SPSS, v.20.0).

The mean (M) and standard deviation (SD) of each variable were calculated by the groups, and one-way analysis of variance (ANOVA) was used for inter-group comparisons. Turkey's post hoc test was also carried out.

Statistical significance was considered when p value was less than 0.05 (p <.05).

Ⅳ. Results

This study aimed to determine how the type of exercise during fertility affects the expression of genes related to obesity. The exercises were conducted on ICR mice during fertility and after giving birth. In order to determine the expression of genes related to obesity between the Control Group(CG), Ground Exercise group(GEG), and Water Exercise Group(WEG), real-time qPCR was conducted for genetic testing, from which the following results were obtained.

1. PPARs protein expression in skleetal muscle

1) PPAR-α expression in skeletal

PPAR-α expression within the skeletal muscle is shown in <Table 4>. The expression of PPAR-α had a tendency to increase in the Exercise Group compared to the Control Group. The results of the post verification to identify the significant differences between groups are shown in <Table 4>. Significant differences were not found among the Control Group and Exercise Group; however, within the Exercise Group, the Water Exercise Group and Ground Exercise Group showed about two-fold higher expression compared to the Control Group.

Table 4. PPAR-α assay rsult (Unit: ㎛)

	N	*M±SD*		*SS*	*df*	*MS*	*F*
G1	8	0.999±.605	BG	17.666	2	8833	1.480
G2	8	1.520±1.534					
G3	8	3.023±3.897	WG	125.345	21	5.969	

Mean±SD

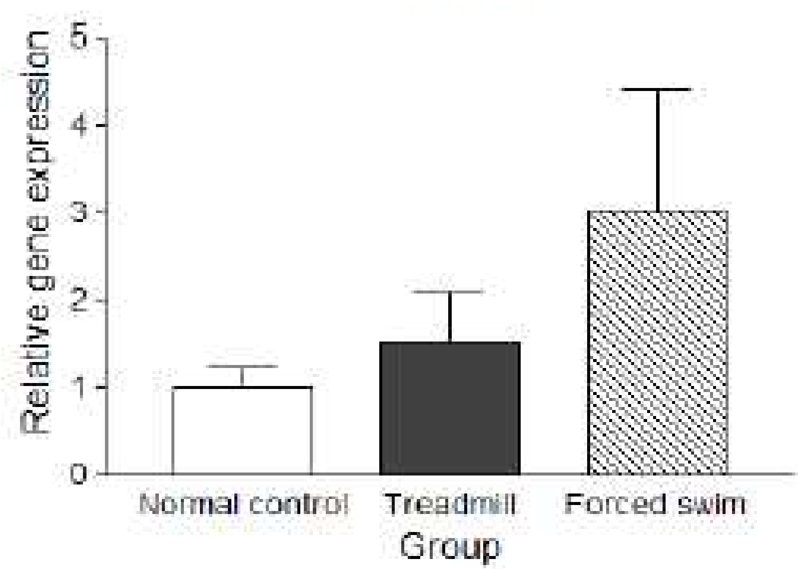

Figure 7. The expression of PPAR-α protein in skeletal mule by accumulation of short duration exercise and Control Group

2) PPAR-β expression in skeletal

The expression of PPAR-β within the skeletal muscle was as shown in <Table 5>. The expression of PPAR-β had a tendency to increase more significantly in the Exercise group than in the Control Group. Post verification regarding the significant differences between the groups revealed significant differences between the Control Group and Water Exercise group ($p<.05$), while the Ground Exercise group also displayed about two-fold higher expression than the Control Group.

table 5. PPAR-β assay rsult (Unit: ㎛)

	N	*M±SD*		*SS*	*df*	*MS*	*F*	*MC*
G1	8	0.999±.251	BG	3.319	2	1.660	2.380	A<C*
G2	8	1.384±.531						
G3	8	1.906±1.322	WG	17.963	21	.697		

Mean±SD, $^{*}p<.05$

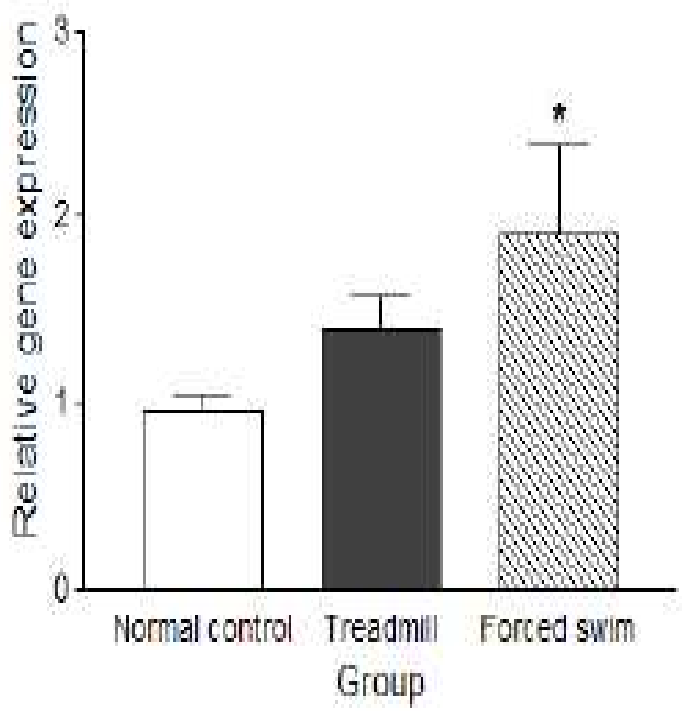

Figure 8. The expression of PPAR-β protein in skeletal mule by accumulation of short duration exercise and Control Group

3) PPAR-ɣ expression in skeletal

The expression of PPAR-ɣ within the skeletal muscle was as shown in <Table 6>. The expression of PPAR-ɣ had a tendency to increase in the Exercise group than in the Control Group. Post verification regarding the significant differences between the groups unrevealed significant differences between the Control Group and Exercise Group. However, within the Exercise Group, the water Exercise Group showed about 1.3-fold higher expression compared to the Control Group.

Table 6. PPAR-ɣ assay rsult (Unit: ㎛)

	N	*M±SD*		*SS*	*df*	*MS*	*F*
G1	8	0.952±0.615	BG	.637	2	.319	.305
G2	8	0.995±1.111					
G3	8	1.318±1.236	WG	21.974	21	1.046	

Mean±SD

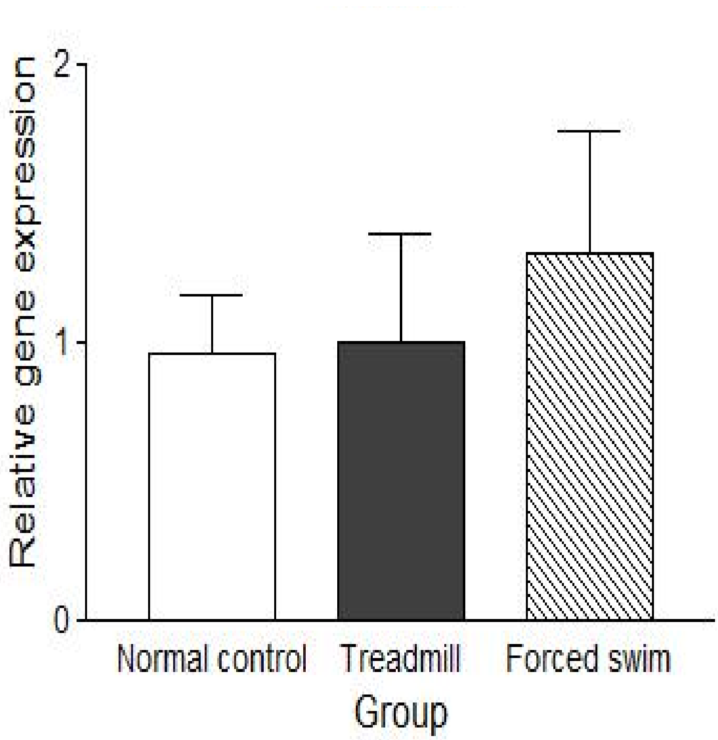

Figure 9 . The expression of PPAR-ɣ protein in skeletal muscle by accumulation of short duration exercise and Control Group

2. Adiponcetin expression in liver tissue

The expression of Adiponectin was as shown in <Table 7>. The expression of Adiponectin had a tendency to increase in the Exercise Group than in the Control Group. Post verification regarding the significant differences between the groups revealed significant differences between the Control Group ($p<.05$) and Water Exercise group ($p<.05$) as compared with the Water Exercise group. The Water Exercise group also displayed about 3.5-fold higher expression than the Control Group.

Table 7. Adiponectin assay rsult (Unit: μg/mL)

	N	*M±SD*		*SS*	*df*	*MS*	*F*
G1	8	1.159±1.020	BG	29.418	2	14.709	5.646*
G2	8	1.213±.627					
G3	8	3.534±2.526	WG	54.711	21	2.605	

Mean±SD, $^{*}p<.05$

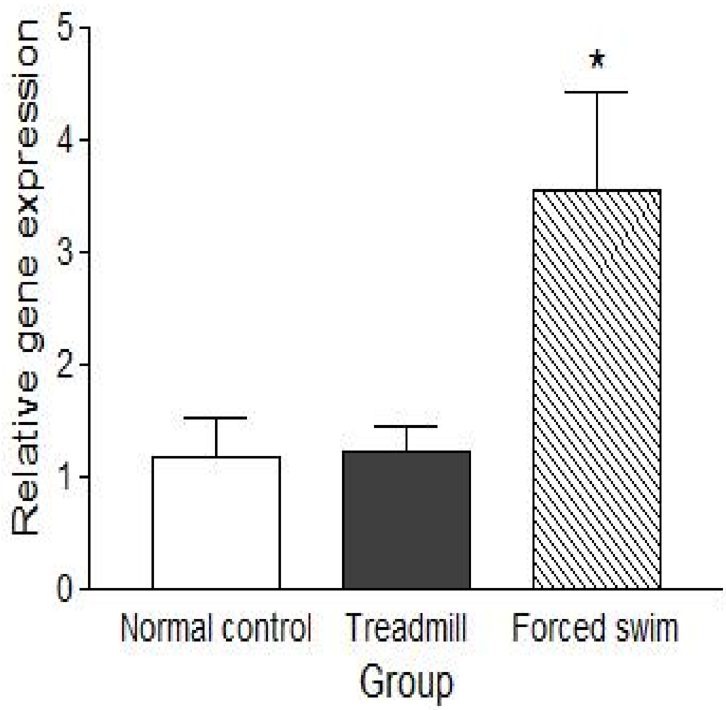

Figure 10 . Adiponectin assay graph

Ⅴ. Discussion

To determine the effects of different types of exercise on the expressions of obesity-related genes, including PPARs and perinatal adiponectin, in mice, 9 weeks of exercise was conducted by female ICR mice(n = 30). The following results of obesity-related gene expression in the muscle and liver for the Control Group(n = 10), Ground Exercise group(n = 10), and Water Exercise group(n = 10) were obtained.

1. The PPARs expression of the mice after giving birth

In this study, 9 weeks of exercise was conducted by the Ground Exercise Group and Water Exercise Group to examine the expression of obesity-related genes according to types of exercise carried out by the perinatal mice. The changes in expression levels of the obesity-related PPARs was observed in the muscle.

PPAR-α is mainly expressed in the skeletal muscle of the human body, where it activates the transcription of a number of genes to increase the oxidation of fatty acids in the skeletal muscle(Campbell et al., 2000; Motojima et al., 1998; Muoio et al., 2002). Horowits et al(2000) conducted a study on 12 weeks of endurance exercise in female subjects, and reported that the amount of PPAR-α protein in skeletal muscle was increased by two-fold.

In contrast, Gorla-Bajszak et al.(2000) reported that treadmill exercise caused increased expression of PPAR-α in the brown adipose tissue of mice, but no change in the expression levels in soleus muscle. Other studies reported that no significant changes(Tunstall et al., 2002) or reductions(Kannisto et al., 2006) in PPAR-α were observed after exercise.

Yun(2012) showed that the expression of PPAR-α showed significant differences according to the amount of exercise performed by pregnant mice (p<.01).During the 9 weeks of the present study, increase in PPAR-α expression was observed in the Ground Exercise Group and Water Exercise Group, which was in line with the results of preceding studies. Among them, while the Water Exercise group did not show a statistically significant difference in PPAR-α expression, an increase in expression was observed. These results indicate the need to reveal the correlating factors between gene expression and exercise in greater depth, through diversely selecting the type and intensity of exercise performed during maternity.

PPAR-β has been reported to be expressed in almost all tissues, and can be activated by the ligands of saturated fatty acids and unsaturated fatty acids(Oliver et al., 1999). It utilizes the fatty acid-oxidation process and glucose to regulate various metabolic processes related to cholesterol transport(Friedmann, PS, Cooper HL, Healy, F., 2005).

The increase in HDL-C due to PPAR-β activation in an obesity model was shown to be much higher compared to the increase due to fibrate, which is a known ligand of PPAR-α. The majority of research on PPAR-β has reported on the relationships of PPAR-β placentation, obesity, colon cancer, and diabetes(wineger, D, A. 2001).

Enhancement of the oxidative capacity through physical activity is important, especially in the treatment of metabolic diseases. Activation of co-activator for peroxisome proliferator activated receptors(PPAR) coactivator-1α (PGC-1α) nuclear receptors, PPAR-β / δ, and ɣ all have unclear interdependence, but were found to have a pivotal role in regulating oxidative metabolism in muscles(Perez-Schindler j, Svensson K, Varqas-Fernandez E, Santos G, Wahil W, Handschin C. 2014).

The expression of PPAR-β was shown to be increased after short-term exercise(Mahoney et al., 2005, Watt et al., 2004). A significant increase in PPAR-β was demonstrated in human subjects after walking 150 minutes per week for 4 months(Fritz et al., 2006).

In the present study, as a result of conducting exercise before and after giving birth, mice of the Water Exercise group showed significant increase in the levels of PPAR-β. The level of PPAR-β gene expression was increased by activity in the mid-strength Water Exercise group, which was similar to the results of preceding studies. Water exercise is a safe exercise with very low risk for damage to joints, bone, and muscles, and is an aerobic exercise recommended for the obese, women during maternity, and elderly men(Linattiniemi et al,, 2008; Juhl et al,, 2010; Williams, 1999). However, insufficient studies have been carried out on PPAR-β, so research needs to be carried out in greater depth using exercises of various intensity.

PPAR-ɣ has an important role in glucose and fat metabolism, the function of macrophages, adipose tissue decomposition, differentiation of adipocytes, cell proliferation, triglyceride homeostasis, cardiovascular function, lipogenesis, and improvement of insulin sensitivity(Kawamura et al., 2004; Bailey, 2001; Balasubramanyam & Mohan, 2001). In a study of treadmill running conducted on mice over 16 weeks, the level of PPAR-γ protein was increased in the muscle of the mice, and thus PPAR-γ was suggested as a very important protein expressed after exercise or training. In addition, the study of Mahoney et al.(2005) reported increase in PPAR-γ expression by approximately 2.7-fold 3 hours after exercising skeletal muscle. Therefore, PPAR-γ was suggested to be involved in converting to fat metabolism after short-term training and long-term aerobic training. Yun(2012) showed statistically significant differences (p <.05) in PPAR-γ expression between the Control Group and high Exercise group after 7 weeks of aerobic exercise. Although the low and mid-Exercise groups did not show significant differences, it was reported that the increase in PPAR-γ expression was proportional to increase of exercise. In the present study, a different form of aerobic exercise was conducted. Although no significant difference was shown in comparison of the Control Group with the Ground Exercise Group and Water Exercise Group, the Water Exercise Group exhibited an increasing tendency. It is suggested that this indicates that the expression level changed according to differences in the exercise protocol. Future studies should be conducted to determine the expression of obesity-related genes in more depth by using different forms and strengths of exercise.

2. The Adiponectin expression of the mice after giving birth

This study evaluates the exercise status of pregnant mosue' prior and after pregnancy to analyze the data of Ground Exercise group and aquatic Exercise group for 9 weeks to discover the changes of adiponenctin expression ratio in an organization during each exercise.

Pregnancy requires a great deal of physical exercise for a pregnant that insufficient physical activities lead to a decline in muscular strength and an increase in weight(Sungsoo KIM, Ilkyu JEONG, 1995), and lead to obesity during pregnancy that develop various complications including gestational hypertension, pre-eclampsia, and others that even need surgeries.

Therefore, an adequate physical exercise, improvement of muscular strength and endurance, and prevention of weight increase or obesity are important in ameliorating the pain relating backaches and pregnancy(Clapp, Kim, Bruciu, Schmidt, Petry, & Lopex, 2002; Bungum, Peaslee, Jadkson, & Perez, 2000).

Adiponectin is a protein, which although revels and secrets exclusively from adipose tissue, it is known that as body fat increases, the blood concentration decreases(Hyejin LEE, 2005). It is a protein hormone that also affects glucose and free fatty acid concentration that the concentration decreases as the weights of obese or diabetic patients decreases Hyunsuk CHO, 2006)

Esposito et al.(2003), a study analyzing the relationship between workouts and changes of adiponectin, reports that the concentration of adiponectin increased during the two-year experiment of aerobic exercise on obese middle-aged women. Hyunjoon KIM(2006) asserts that in his study where obese male elementary school students practiced 12 weeks of complex exercise, the concentration of adiponectin decreased at the beginning of a complex workout, but after 12 weeks, the concentration increased similarly compared to the concenteration prior to exercise. Furthermore, Hyejin LEE(2005) insists that the concentration of adiponectin at plasma similarly increased in the eight-week experiment of complex workout and aquatic aerobic exercise programs affect on obese middle-aged women under physical treatments. Similarly, in the study by Fatouros et al. (2005), elders in an acute resistance Exercise group had increased the concentration of adiponectin.

Ferguson et al(2004) says temporary workouts decrease the concentration of adiponectin that a high-level of calorie consumption in addition to persistent exercise are necessary for the changes in the concentration of adiponectin.

Similar research results are shown in both ground Exercise Group and Water Exercise Group and in particular, an Water Exercise Group also has an increasing result that it resembles the existing studies.

Nonetheless, Dongbok LEE(2010) reports that in the experiment on pregnant rats for analyzing the effect of exercise on the expression of adiponectin in muscles and the liver, as the exercise rate increased, the creation of adiponectin decreased. Sungjoon YOON(2012) argues that in his study, pregnant rats in the thirty-minute Exercise group had the most expression that adequate time of exercising maximizes the expression of adiponectin than the excessive or short-term exercising. Therefore, according to the research results, the concentration of adiponectin positively changes during medium-intensity or high-intensity of exercising than low-intensity and in the time frame that are long-term and persistent than short-term. In order to generalize the relationships between the exercise and the expression of adiponectin in the liver and blood influenced by types of exercises, it is necessary to identify and differentiate the intensity of exercise and durations.

Ⅵ. Conclusion

The 9 weeks experiment of ICR mouse female rats (n=29) proceeding Ground and aquatic exercise is conducted to prove the effects of exercise types on obesity-related genes, PPARs, and the expression of adiponectin in pregnant mosue prior and after pregnancy. The results of analysis on the expression of adiponectin in a Control Group, ground Exercise Group, and water Exercise Group are as follows

There is no statistical difference of the expression of PPAR-α in PPARs of muscles in a Control Group, Ground Exercise Group, and Water Exercise Group. A Control Group and Exercise Groups do not have any difference, but there is a greater increase of expression in the Ground and Water Exercise Groups than a Control Group.

There is no statistical difference of the expression of PPAR- β in PPARs of muscles in the Control Group and Ground Exercise Group, but both groups have an increasing tendency. The statistical significance is($p<.05$) between a Control Group and Water Exercise Group that there are differences in the expression tendency depending on types of exercises.

There is no statistical difference of the expression of PPAR- γ in PPARs of muscles in all Control, Ground Exercise, and Water Exercise Groups. Also, there is no difference between Control Group and Exercise Groups, but the Ground Exercise Group and Water Exercise Group have greater increases of expression ratio than a Control Group.

There is no statistical difference of the expression of adiponectin of muscles in the Control Group and Ground Exercise Group, but both groups have an increasing tendency. The statistical significance is ($p<.05$) between the Control Group and Water Exercise Group that there are differences in the expression tendency depending on types of exercise.

The results conclude that the Ground Exercise and Water exercise positively affect pregnant mouse prior and after pregnancy. The Water Exercise Group increases the obesity genes, PPARs, and the expression of adiponectin that it prevents an excessive weight increase or obesity, thus, it affects positively on the health of a pregnant and embryo.

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(국문 요약)

수태 쥐의 출산 전 · 후 지상운동과 수중운동이 어미 쥐의 비만 유전자에 미치는 영향

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이 연구의 목적은 수태한 쥐의 출산 전 · 후 운동 형태에 따른 비만 유전자 PPARs와 adiponectin 발현에 미치는 영향을 규명하여 임신 중 효과적인 운동 방법을 임산부에게 제시하는 데 있다.

본 연구에서 사용된 동물은 7주령의 ICR계 mice 수컷(n=10), 암컷(n=40)쥐로 동물 취급업체(두열 바이오텍)로부터 공급받았으며, 교배 후 수태 쥐는 무작위로 선별되어 비 운동집단(n=9), 지상 운동집단(n=10), 수중 운동집단(n=10)으로 나누어졌다. 지상운동과 수중운동은 9주간, 주 3회로 실시하였다.

유전자 발현의 비교 분석을 위하여 SPSS Win ver. 20.0 통계프로그램을 사용하였으며, 집단 간 분석을 위해 one-way ANOVA를 이용하였다. 유의 수준은 $p<.05$로 설정하였다. 결과는 다음과 같다.

1.운동 형태에 따른 근육 내 PPARs에서 PPAR-β 발현은 비 운동집단과 지상 운동집단간에서 통계적으로 유의한 차이를 보이지 않았지만 증가하는 경향을 나타내었고, 비 운동집단과 수중 운동집단간에는 통계적으로 유의한 차이($P<.05$)를 나타내어 운동 형태에 따른 발현량의 경향에서 차이가 나타났다.

2. 운동 형태에 따른 근육 내 PPARs에서 PPAR-β 발현은 비 운동집단과

지상 운동집단간에서 통계적으로 유의한 차이를 보이지 않았지만 증가하는 경향을 나타내었고, 비 운동집단과 수중 운동집단간에는 통계적으로 유의한 차이($P<.05$)를 나타내어 운동 형태에 따른 발현량의 경향에서 차이가 나타났다.

본 연구 결과를 통해 수태 전 · 후 지상운동과 수중운동은 임산부에게 긍정적인 영향을 미치며, 수중운동에서 비만 유전자인 PPAR-β와 adiponectin에서 발현을 증가시키는 것은 과도한 체중증가나 비만을 억제함으로써 임산부와 태아의 건강에 보다 유익한 것으로 사료된다.