

Euro Endocrinology 2018 : Placental fatty acid transporters in obese pregnancy women - Alvarez Da - University of Chile

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Statement of the Problem: Diabetes control remains a challenging problem regardless of many advances made. Stress adds extra burden. Positive attitude promotes health and reduces stress in a fundamental basis, and can result in permanent changes in as short as 3 weeks because of neuroplasticity. Its contribution to diabetes control remains unknown. In this study, we aim at encouraging patients practicing positive attitude in their daily life, and explore its impact on diabetes control in patients with type 2 diabetes. **Methodology & Theoretical Orientation:** One hundred and twenty type 2 diabetic subjects were enrolled, assigned into two groups, one test and one control, with 60 subjects for each, well matched for age and diabetes control, informed consent form signed and ethical committee review obtained. Blood glucose (FBG, 2hr PPG), HbA1c, C peptide, Insulin, and other labs were tested before and after practicing positive attitude. Positive attitude practice includes confidence, gratitude, adaptable, generous, lovable, forgivable, courageous, compassionate, healthy, connected and meaningful, for 3 weeks. Other treatment remains the same as that prior to the study. Statistical analysis was performed with SAS, and compare was between groups, before and after practicing positive attitude. Sub-layer analysis is also performed.

Findings: Prior to practicing positive attitude, all the lab values are well matched between two groups, without significant difference for glucose level or HbA1c. With 3 weeks practice, the test group had significant decrease with blood glucose and HbA1c ($p < 0.01$ before vs. after), while no significant change in the control group. The difference between the test group and control group after 3 weeks is also significant ($p < 0.05$ test vs. control). The more positive attitude they practice, the better glucose control.

Conclusion & Significance: Practicing positive attitude can significantly improve glucose control in patients with type 2 diabetes. It should be strongly encouraged.

INTRODUCTION

Maternal fatness could cause serious health complications for mother and foetus. It will increase the incidence of maternal physiological condition complications like physiological state polygenic disorder and toxemia additionally to

maternal health complications, there's additionally a substantial increase within the risk of foetal complications.

These embrace miscarriage spontaneous abortions and foetal physiological state, additionally as accrued risk of delivery of little for age or giant for age babies. within the semipermanent, the offspring of weighty mothers have a better risk of fatness in adult life, and this can be seemingly because of the combined effects of genetic science and surroundings. Given these factors, understanding however maternal fatness may need a bearing on offspring health is of major public health importance.

Pregnancy could be a important amount of physiological modification for each the mother and therefore the foetus. The placenta, the interface between the maternal and foetal blood circulations, is liable for the maternal-to-fetal transfer of nutrients that ar essential for foetal growth and development. foetal growth is directly associated with maternal nutrient convenience and therefore the placental ability to move these nutrients from maternal circulation to the foetus. Glucose, amino acids, and fatty acids ar essential macronutrients for adequate foetal growth. All of those traverse the placental syncytiotrophoblasts (SCTB) mediate by specific transporters. Placental aldohexose transport happens by expedited diffusion on a amount gradient through members of the aldohexose transporter (GLUT) family. organic compound transport across the human placenta could be a advanced method as a result of over twenty completely different organic compound transporters with overlapping specificities ar expressed within the SCTB. for instance, system A could be a sodium-dependent accumulative transport system that mediates the uptake of neutral amino acids (both essential and nonessential) with short and branchless aspect chains, principally L-alanine, glycine, L-serine, L-methionine, and L-glutamine. In recent years, a factor family of sodium-coupled neutral organic compound transporters [(SNAT); (SCL38 factor family)] secret writing for proteins that possess the classically represented system A transport

activities (in terms of their practical properties and patterns of regulation) has been cloned. SNAT-2 is wide expressed in rat tissues, and its template RNA concentration will increase in refined cells throughout adaptative regulation or with the addition of cAMP. The proteins related to carboxylic acid transport embrace carboxylic acid transport proteins (FATP), carboxylic acid translocase (FAT/CD36), cell wall carboxylic acid binding supermolecule (FABPpm), and alternative FABP. FATPs, six members (FATPs1-6), are integral membrane proteins that are of importance for the uptake of long-chain fatty acids. Five members (FATPs1-4, and 6) are known in placental trophoblasts. FATP-1 and FATP-4 are oftentimes studied in placental tissue as their expression correlates with omega-3 fatty acid levels in maternal plasma, cord blood, and placental phospholipids, suggesting a vital role within the transfer of long-chain unsaturated fatty acids. Of note, previous studies have investigated the association between maternal fatness and placental nutrient transporters, however results are inconsistent. Reynolds et al have reported that maternal high-fat (HF) consumption induces sex-specific nutrient transport within the rat placenta. During this study, maternal HF consumption was found to be related to accrued placental CD36 template RNA expression solely in feminine placentas, and placental GLUT1, GLUT4, and SNAT2 template RNA expression considerably accrued solely in HF male placentas. This sex distinction could also be driven by sexually polymorphic placental alterations that occur as a result of maternal physiological state diets. Farley et al reported that maternal fatness was among reduced placental SNAT activity though the offspring grew commonly. In a very Canadian study in humans, it absolutely was found that maternal fatness was related to accrued placental CD36 template RNA and supermolecule expression and reduced FATP-4 template RNA and supermolecule and FABP3 supermolecule expression. However, Zhu et al, operating with sheep, showed that maternal fatness increased the template RNA expression and supermolecule content of FATPs within the placenta. These advanced and conflicting results raise vital doubt on whether or not placental nutrient transport is related to maternal fatness. Therefore, during this study, we have a tendency to developed a model of maternal fatness during which rats are fed a HF diet and used this model to

see however maternal fatness influenced foetal growth, placental weight, additionally as placental factor and supermolecule expression of nutrient transporters.

Methods

All animal procedures were approved by the Animal ethics panel of Anhui Medical University (approval number: 20131188). feminine Sprague-Dawley rats, half dozen weeks recent, were obtained from the Experimental Animal Center of Anhui Medical University. The rats were maintained in controlled temperature (23-25 °C), lightweight (12-hr lightweight - dark cycle), and wetness (55±5%) conditions with access to food and water spontaneously. Behind a seven day adaptation amount, animals got spontaneously access to either a bearing (CON; n=40) diet of ordinary placental mammal chow (3.435 kcal/g; twelve-tone music energy as fat, Jiangsu Xie Tong Biological Engineering Co., Ltd.) or a HF; (n=53) diet that contained seventieth traditional chow, 10% lard, 1% Chronicles sterol, 3% casein, 100 percent ingredient powder, and 6 June 1944 whole-milk powder (4.487 kcal/g; forty fifth energy as fat, Jiangsu Xie Tong Biological Engineering Co., Ltd.). weight of every dam was monitored weekly. when seven weeks of feeding, rats fed the HF diet exhibited variable corporeal weight modification in response to the diet. in line with the approach undertaken in previous studies eighteen rats with the best weight gain were selected as diet-induced fatness (DIO) rats, whereas eighteen rats with lowest weight gain were selected as diet-induced obesity-resistant (DIR) rats. throughout the eighth week, the food intakes of the CON, DIO, and DIR rats were measured. At the top of the eighth week, the CON, DIO, and DIR rats were mated with age-matched Sprague-Dawley male rats fed the CON diet. sex was confirmed by the presence of spermatozoon in a very canal flush; the day of sex was selected physiological state day (GD) zero. when sex, the CON rats were divided into 2 cluster: [*fr1] were switched to the HF diet (CON-HF group, n=10), whereas [*fr1] were maintained on the CON diet (CON-CON cluster, n=10). The DIO (n=10) rats and DIR (n=10) rats were maintained on the HF diet throughout physiological condition. Food intakes throughout physiological condition were measured. Body weights were monitored weekly. At the top of GD21, all rats were fasted nightlong before being euthanized with depressant that was additionally employed in previous studies Blood samples of rats were obtained

from the common aorta for measurements of hypoglycemic agent levels. Fetuses in every litter were counted and weighed, so crown-rump length was measured. foetal blood samples were additionally collected for measurements of hypoglycemic agent level. Maternal associated foetal blood sugar levels were measured like a shot exploitation an Accu-Chek blood sugar monitor (Accu-Chek; Roche medicine, Mannheim, Germany) humour hypoglycemic agent level made up our minds by immunoassay (Beijing North Biotechnology analysis Institute, Beijing, China). Placental weights were recorded, and placentas were snap frozen in atomic number 7 and hold on at -80°C till more analysis.

Isolation of Total ribonucleic acid and time period enzyme Chain Reaction Total ribonucleic acid was extracted from placental tissues, and time period enzyme chain reaction (rt-PCR) performed as antecedently represented. Total ribonucleic acid was extracted exploitation TRI chemical agent (Molecular analysis Center). Ribonuclease-free deoxyribonuclease-treated total ribonucleic acid ($1.0\ \mu\text{g}$) was reverse-transcribed with Aves white cell cancer of the blood virus polymerase (Promega). RT-PCR was performed with a LightCycler 480 SYBR inexperienced I kit (Roche medicine GmbH) exploitation gene-specific primers as listed in Table one. Specific primers were synthesized by Shanghai Sangon Biological Engineering Technology (Shanghai, China). The amplification reactions were administered on a LightCycler 480 Instrument (Roche medicine GmbH) with associate initial hold step (95°C for five minutes) and fifty cycles of a three-step PCR (95°C for fifteen seconds, 60°C for fifteen seconds, 72°C for thirty seconds). The comparative cycle threshold technique was wont to verify the number of target, normalized to associate endogenous reference (GAPDH) and relative to a calibrator exploitation the LightCycler 480 code. Western Blot

Total lysate from rat placentas was ready by homogenizing fifty mg placenta tissue in three hundred three hundred lysis buffer (50 metric linear unit Tris-HCl, pH 7.4, 1 mM EDTA, a hundred and fifty metric linear unit NaCl, 0.1% metal dodecyl sulphate, I Chronicles Triton X-100, I Chronicles metal deoxycholate, one metric linear

unit phenylmethylsulfonyl fluoride) supplemented with a cocktail of peptidase inhibitors (Roche). supermolecule concentrations were determined exploitation bicinchoninic acid (BCA) supermolecule assay reagents (Pierce, Rockford, IL) in line with manufacturer's directions. the amount of CD36, FATP1, and FATP4 in placental tissue were quantified exploitation Western blot, as antecedently represented.

Briefly, associate quantity of supermolecule ($40\sim 80\ \mu\text{g}$) was separated electrophoretically by SDS-PAGE and transferred to a polyvinylidene halide membrane. Membranes were blocked in five-hitter non-fat milk in tris buffered saline (TBST) ($137\ \text{metric linear unit NaCl}$, $2.7\ \text{mM KCl}$, twenty five metric linear unit Tris-Cl, pH 8.0) supplemented with zero.1% Tween-20 nightlong at four $^{\circ}\text{C}$. The membranes were incubated for two hours with the subsequent antibodies: CD36 (1:500; Abcam INC, Cambridge, MA), FATP1 (1:500; Abcam INC, Cambridge, MA), and FATP4 (1:1000; Abcam INC, Cambridge, MA). β -actin (1:2000; Santa Cruz Biotechnologies, CA, USA) was used as a loading management. when being washed in TBST containing zero.05% Tween-20 fourfold for ten min every, the membranes were incubated with secondary protein (goat anti-rabbit immunoglobulin G or goat anti-mouse IgG; each from Santa Cruz Biotechnologies, CA, USA) for two hours. The membranes were then washed for fourfold in TBST containing zero.05% Tween-20 for ten min every.

Finally, increased luminescence resolution (ECL kit; Pierce Biotechnology, USA) was additional, and Fine-do X6 visualiser was used for the photographing (Tanon, Shanghai, China).

Statistical Analysis All applied mathematics analysis was performed exploitation the SPSS thirteen.0 code (SPSS INC, Chicago, IL). For animal experiments, the litter was thought of the unit for applied mathematics analysis among completely different teams. For foetal weight and crown-rump length, the means that were calculated per litter. All values ar expressed because the mean \pm variance (SD). Comparisons between CON and HF teams were compared exploitation 2 freelance sample t-test. unidirectional ANOVA was wont to verify variations among 3 or a lot of teams and more comparison between 2 teams was assessed with least vital distinction (LSD) logical fallacy check. A p-value <0.05 was thought of statistically vital.

DISCUSSION

We report the result of maternal HF, DIO on foetal growth and placental nutrient transport. We have a tendency to found correlation between maternal HF, DIO and reduced foetal growth. However, in animals proof against elicited fatness, no reduction in foetal weight was determined. Meanwhile, maternal HF, DIO down-regulated the expression of placental carboxylic acid transporters. Obesity results from advanced interactions of environmental associated genetic elements that facilitate the event of an weighty composition. Diet is that the most significant environmental issue resulting in fatness, and models of HF DIO are normally employed in studies. when feeding with a high fat diet, rats exhibited completely different phenotypes in response to the diet. Therefore, we have a tendency to chosen the DIO and DIR rats in line with weight gain when seven weeks of HF feeding. we have a tendency to found that food intake and energy intake of DIR rats were below those of DIO rats, in step with previous reports. Liu et al reported that DIR rat has the flexibility to sense and reply to energy imbalance accurately, whereas the flexibility in DIO is dulled. Despite having identical feeding conditions because the DIO cluster, DIR rats ar sensitive to the energy balance system and may modify their energy expenditure to take care of a standard weight looking on the extent of energy intake. Previous studies have investigated the association between maternal fleshiness and vertebrate growth, however results are contradictory. redoubled risks for each vertebrate macrosomia and intrauterine growth restriction (IUGR) are reported within the current study, vertebrate weight of DIO dams was considerably reduced, Associate in Nursingd a transparent association between maternal fleshiness and an redoubled the danger for IUGR were shown. moreover, DIO dams had traditional blood sugar and humor endocrine levels in our study, suggesting the absence of physiological condition DM despite the rotund composition. In previous studies, rotund mothers typically developed abnormal aldohexose physiological condition Thus, reports show inconsistencies which can result to review style (contents of HF diet, time of HF diet feeding), degree of fleshiness in subjects, or species distinction. Our results conjointly demonstrate that vertebrate growth is totally different in DIO and DIR dams. Despite having constant feeding conditions because the DIO cluster, the offspring of

DIR rats appear to be healthier compared with DIO offspring, in keeping with previous reports. in a very future study, the main target are going to be on the difficulty of however the DIR rats square measure protected against the injurious effects of a HF diet.

The vertebrate to placental weight quantitative relation has been thought of to be a marker of placental nutrient transporter potency. A lower vertebrate to placental weight quantitative relation might indicate below average placental nutrient transport potency. In our study, vertebrate to placental weight quantitative relation was lower in DIO dams indicating that placental nutrient transport potency in DIO dams was remittent.

Fetal growth is especially keen about vertebrate nutrient availableness, that is decided by the capability of the placenta to move nutrients. The transport of placental fatty acids is vital for vertebrate growth, notably in late gestation. A previous study found that maternal fleshiness was related to remittent FATP-4 messenger RNA and macromolecule expression, whereas CD36 expression was redoubled. we tend to found that the carboxylic acid transporters (CD36, FATP-1, and FATP-4) messenger RNA and macromolecule expression were down-regulated within the DIO placenta. Thus, maternal fleshiness was related to remittent placental carboxylic acid transporter messenger RNA and macromolecule expression. it's been reported that many placental transport functions square measure altered in pregnancies sophisticated by IUGR. Placental carboxylic acid transporters might have a crucial role to play within the method of IUGR evoked by maternal fleshiness. Our results square measure inconsistent with antecedently reported results, which can result to species distinction (rat, sheep, human, etc.), degree of fleshiness in subjects, study style, or age studied (mid-gestation, late physiological state, delivery, etc.). Study Limitations There square measure many limitations of the present study. because of the character of our fleshiness model, we tend to square measure restricted by the amount of rats in our study, that left North American nation underpowered to totally assess variations between male and feminine fetuses. Thus, although we tend to didn't notice any trends, we tend to cannot once and for all rule out the impact of vertebrate sex on these

relationships. additionally, some metabolic factors (i.e. leptin, inflammation, lipids and fatty acids levels) in

maternal circulation weren't measured in current study. we tend to square measure presently unable to establish however maternal fleshiness affected placental carboxylic acid transport. more studies are going to be designed to explore the mechanism.

Conclusion

In summary, the present study indicates that maternal HF, DIO diode to vertebrate growth retardation. Moreover, maternal fleshiness inhibits placental nutrient transport potency. specially down-regulation of the carboxylic acid transporters (CD36, FATP-1, and FATP-4) messenger RNA and macromolecule expression might have a crucial role within the development of IUGR within the offspring of rotund mothers. one in every of the foremost elementary queries arising from the study is however DIO and DIR dams and their offspring dissent in terms of their various metabolic response to a HF diet. In more studies, the

metabolic distinction between the DIO and DIR dams ought to be investigated comprehensively.

Growth and development variations in their offspring ought to be conjointly explored. These variations could also be elementary to future understanding of the impact of diet on fleshiness and health.

Biography :

Daniela Álvarez was born in Santiago, Chile, She studied Nutrition and Dietetics at the University of Valparaíso graduated in 2015. She is currently studying the PhD program in Nutrition and Food of the University of Chile. She devoted herself to study the reproductive alterations of gestational obesity in female offspring in a rat model. She is currently doing research on a mouse model of gestational obesity and study the placental transport of fatty acids and the metabolic alterations at the fetal liver level.

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