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Maternal separation aggravated pancreatic oxidative and inflammatory damage in chronic socially defeated adult male rats

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Background: It is believed that psychosocial stress as one of the main sources of stress in humans may play an essential role in developing chronic degenerative metabolic diseases. Early life adverse experiences were supposed to affect the response to stress in later life.

Aim: This research was done to test the effect of maternal separation on the metabolic response to chronic social defeat stress (CSDS) at young adulthood. In this respect, the possible contribution of oxidative stress and inflammatory damage to the pancreas along with insulin resistance in response to CSDS exposure in young adult male rats who experienced early life maternal separation was explored.

Method: During the first 2 weeks of life, male Wistar rats were exposed to either maternal separation (MS) or left undisturbed with their mothers (Std). Starting on postnatal date 50, the animals of each group were either left undisturbed in the standard group housing (Con) or underwent chronic social defeat stress (CSDS) for 3 weeks. Thus, totally there were 4 groups (n=6/group). Then, fasting plasma corticosterone, insulin, and glucose levels were measured and insulin resistance was calculated. Pancreatic Catalase (CAT) activity, reduced Glutathione (GSH), Malondialdehyde (MDA) and interleukin-1 beta contents were measured.

Results: In this study, MS-CSDS animals showed an elevated fasting plasma corticosterone and insulin levels along with insulin resistance in comparison with standard-reared controls (Std-Con); however, neither early nor adult life adversity affected fasting glucose levels. Likewise, CAT activity, MDA, and IL-1 β contents of pancreatic tissue were increased only in MS-CSDS rats compared to Std-Cons.

Discussion: The finding of this study shows that maternal separation intensifies vulnerability to develop HPA axis over-activation, insulin resistance, pancreatic oxidative and inflammatory damage associated with chronic exposure to social defeat stress

in young adult male rats, which could play an important role in mediating the effects of chronic stress-related risk of diabetes mellitus.

Abnormal responses to stress in adults, who were exposed to stress in early life, almost occurred because of increasing basal tone of central CRFergic activity and coincident intensified HPA axis responsiveness. It may be secondary to facilitation of norenergic neurocircuits, central glucocorticoid resistance, and/or dampened regional GABAergic tone that have been observed to happen in response to maternal separation stress. Elevated levels of circulating glucocorticoid have been reported to influence the insulin signaling cascade at the level of insulin receptor and insulin-sensitive glucose transporter 4 (GLUT4) functionality, which may contribute to insulin resistance. In the face of insulin resistance, the β cells adapt by increasing insulin secretion, leading to peripheral compensatory hyperinsulinemia as a protective measure to maintain normal glucose concentrations without hypoglycemia. Augmented pancreatic oxidative stress in MS-CSDS animals may exceeded the increased compensatory antioxidant mechanisms, as evidenced by excessive peroxidation of cell membrane lipids. Based on the central role of IL-1 β in the destruction of pancreatic β cells, raised pancreatic IL-1 β content could be related to oxidative stress-mediated β cell damage and development of diabetes in response to CSDS exposure in young adult rats who underwent early life maternal separation.

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More than a third of SACA countries (South and Central America) do not have coverage of insulin, supplies and lab exams

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Background: The IDF Diabetes Atlas 2019 points out that SACA is the region with the highest percentage of health expenditures

on diabetes, 19.4%. The total number of individuals with diabetes in the region is 31.6 million, which means a prevalence of 9.4%. Countries with the largest percentage of expenditures are Cuba (24.3%), Brazil (24.2%), and Costa Rica (21.3%), while the lowest estimates are for Argentina (5.0%) and Uruguay (6.1%).

Aim: Identify if insulin, oral medicines, supplies (syringes, test strips, needles, etc.) and lab exams are fully provided (free of charge) in those countries and if there is an association between percentage of expenditures on diabetes and care provision.

Method: A digital online survey with 12 multiple choice questions was shared by e-mail and WhatsApp with all IDF members organizations in the SACA region. It was open for answers between April 4th and May 5th, during the COVID-19 pandemic. The question of interest for this abstract was specifically about access to medicines and lab exams. Mean diabetes-related expenditure (USD) per person with diabetes (20–79 years) was based on IDF Diabetes Atlas 2019 data. Wilcoxon signed-rank test was used to compare expenditures of countries providing free supplies with those without free medical supplies.

Results: The questionnaire was answered by 16 of the 18 IDF SACA region countries. Colombia and El Salvador were the only countries with no response. Most of the countries reported free access to oral medicines (69%), insulins (63%), supplies (syringes, needles, test strips, etc. - 56%) and lab exams (63%). Honduras was the only country where free access started because of the COVID-19 pandemic. Associations between expenditures and provision of free oral medicines, insulins, medical supplies or exams were not statistically significant, i.e. free provision of any of the four items was not associated with higher expenditures.

Discussion: Our study revealed that expenditure does not determine whether medicines, supplies and exams are provided for free or not. We hypothesize that countries spending less in providing these essential items for free are still spending similar amounts due to the high costs of treating diabetes chronic complications caused by lack of access to insulin, oral medicines, supplies and lab exams. At the same time that most of the SACA countries already count on full coverage of essential diabetes medicines and supplies, such as insulin, metformin, test strips, and exams, there are still 6 countries (Bolivia, Cuba, Dominican Republic, Ecuador, Peru and Puerto Rico) lacking coverage of 3 out of four or of all essential items. It is especially worrisome that 100 years after the discovery of insulin more than a third of the countries in SACA regions still do not count on full provision of this essential life-saving medicine.

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Effects of structured education program on Time in Range for people with type 1 diabetes

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Background: The percentage of time in target glucose range (TIR) from continuous glucose monitoring (CGM) system is more specific and sensitive than HbA1c detection, and can better reflect the effects of acute hyper- and hypoglycemia. However, the successful utilization of CGM technology in routine clinical practice remains relatively low.

Aim: To explore the effect of structured education on Time in Range for people with type 1 diabetes in a real-time CGM (rtCGM) combined with insulin pump (CSII) therapy.

Method: A convenience sampling method was performed in 42 people with type 1 diabetes who were hospitalized in Chengdu Ruien Diabetes Hospital in Sichuan Province, China from June to December 2020. Diabetes structured education program was offered to the participants by medical team. Participants received the insulin administration and guidance by physicians and proper operation of rtCGM and CSII by diabetes educator at first 2 days. Then during the following 3 days, participants were taught to match insulin doses from their food choices by dietitians, the exercise prescription specialists offer individualized exercise programs and the diabetes educator invited 5-6 participants each time for group discussion. Participants and caregivers gave feedback and summarized the day's lessons at the end of every day. Participants continued to receive education and psychological support through the Internet for 3 months after discharge. Paired t-test was used to detect glycemic outcomes of the adult group and the children and adolescents group at 3 months after the intervention. Correlation variables of TIR at 0 days, 14 days, 30 days, 60 days, and 90 days were compared by repeated measures analysis of variance.

Results: Compared with the baseline, TIR increased from 73.12 ± 8.57% to 79.20 ± 8.44% (P=0.000). Time above target glucose range (TAR) (Level 1, 10.1-13.9 mmol/L and Level 2, >13.9 mmol/L) decreased from (21.53 ± 8.48 to 16.29 ± 8.29)% (P=0.000) and (4.20 ± 2.51 to 3.03 ± 3.19)% (P<0.01). Time below target glucose range (TBR) (Level 2, <3.0 mmol/L) reduced from (1.60 ± 2.27 to 1.05 ± 1.17)% (P<0.05). There were 14 participants TIR <70% at baseline then only 2 participants (15%) did not meet the target after the intervention. In subgroup analysis, there were significant differences in TIR increased (P<0.01) and Level 1 TAR decreased (P<0.01) in the two groups, and Level 2 TAR decrease (P<0.01) in the adult group. TIR increased and Level 1, 2 TAR decreased over time in all groups with significant time effects (p<0.001). TBR (Level 1, 3.0-3.9 mmol/L) (P<0.05) and Level 1, 2 TAR (P<0.01) with significant differences observed intra groups. No significant interaction effects were observed inter groups.

Discussion: Structured education can improve TIR and reduce hyperglycemia in people with type 1 diabetes in a real-time continuous glucose monitoring system combined with insulin pump therapy. It has a low correlation with hypoglycemia in this study. Therefore, it may take longer CGM to evaluate the quality of blood glucose control in people with higher risk of hypoglycemia in future study.

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