

EFFECTS OF PROTEIN RESTRICTION ON GENERAL NUTRITIONAL PARAMETERS, GLUCOSE TOLERANCE AND COLON MORPHOLOGY IN MALE MICE

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Introduction: It has been reported that protein malnutrition induces damages in the gastrointestinal system and endocrine pancreas which have been correlated with the development of diseases such as type 2 diabetes mellitus. However, there is a lack of information regarding protein undernutrition actions on intestine morphofunction as well as their impacts on glycemic homeostasis. **Objectives:** To evaluate glucose homeostasis, cecum morphometry, and proximal colon morphology of protein-restricted mice. **Methods:** C57Bl/6 male mice from 30 to 120 days-old were distributed into control (C) group, which fed on a 14% protein diet; or protein restricted group (R), which fed on a 6% protein diet. Data were analyzed by Shapiro Wilk, followed by parametric (Student t) or non-parametric tests (Mann-Whitney U test; $P < 0.05$). **Results:** R mice higher total food ($364.2 \pm 2.1 \text{ g} \cdot \text{weeks}^{-1}$) and kilocalories intake ($96.5 \pm 0.5 \text{ kcal}$) during the experimental period, when compared to C ($298.8 \pm 7.1 \text{ g} \cdot \text{weeks}^{-1}$ and $79.3 \pm 1.9 \text{ kcal}$, respectively). Despite that, R mice exhibited lower body weight (BW; $24.6 \pm 0.6 \text{ g}$), feed efficiency ($29.3 \pm 0.3\%$), Lee Index (304.6) and mesenteric fat pad ($5.0 \pm 0.5 \text{ mg/g BW}$) when compared to C ($27.2 \pm 0.5 \text{ g}$, $41.4 \pm 0.2\%$, 312.6 ± 1.5 and $6.7 \pm 0.3 \text{ mg/g BW}$, respectively). Furthermore, R group presented increased glucose tolerance ($12175 \pm 536.7 \text{ mg/dL} \cdot \text{min}^{-1}$), insulin sensitivity ($2.8 \pm 0.1\% \cdot \text{min}$) and reduced pancreas weight ($8.0 \pm 0.3 \text{ mg/g BW}$) in R group compared to C group ($14291 \pm 698.0 \text{ mg/dL} \cdot \text{min}^{-1}$, $2.1 \pm 0.2\% \cdot \text{min}$ and $10.4 \pm 0.7 \text{ mg/g BW}$, respectively). Also, protein undernutrition led to higher intestinal permeability ($0.5 \pm 0.1 \text{ FITC } \mu\text{g/mL}$) in R group when compared to C group ($0.3 \pm 0.03 \text{ FITC } \mu\text{g/mL}$). Additionally, protein malnutrition diminished cecum weight ($5.3 \pm 1.3 \text{ mg/g BW}$) and length ($0.2 \pm 0.01 \text{ cm/CNA}$) in R mice in relation to C mice ($8.3 \pm 1.4 \text{ mg/g BW}$ and $0.3 \pm 0.01 \text{ cm/CNA}$). Proximal colon morphologic evaluation

showed that R group had higher submucosa thickness ($28.1 \pm 2.1\mu\text{m}$), colonocyte height ($35.7 \pm 1.9\mu\text{m}$) and number ($15.0 \pm 0.5\mu\text{m}$) than C group (24.4 ± 1.9 , $21.3 \pm 1.0\mu\text{m}$ and 10.3 ± 0.3 , respectively). In colonic crypts, protein restriction decreased the diameter ($37.0 \pm 0.8\mu\text{m}$), the depth ($138.6 \pm 2.1\mu\text{m}$), and the distance among crypts ($57.0 \pm 1.2\mu\text{m}$) in R mice in comparison to C mice ($41.7 \pm 1.2\mu\text{m}$), 143.6 ± 2.7 and $60.0 \pm 1.3\mu\text{m}$, respectively). Moreover, R mice colonic crypts displayed a higher number of goblet cells (GC; 17.2 ± 0.4), yet, these cells showed hypotrophy ($123.3 \pm 1.8\mu\text{m}^2$) when compared to C mice GC (16.3 ± 0.4 and $215.0 \pm 2.5\mu\text{m}^2$). Finally, R group had reduced neutral ($14.8 \pm 1.0\%$) and acid ($24.0 \pm 0.5\%$) mucins in colon crypts than C group (20.7 ± 1.0 and $27.5 \pm 0.7\%$). **Conclusion:** Protein-restricted mice had higher glucose tolerance due to increased insulin sensitivity. Also, R mice had increased intestinal permeability and morphologic abnormalities in colon. Further investigations are necessary to clarify if these morphofunctional alterations on both organs are correlated.

Key-words: endocrine pancreas, gut morphofunction, protein undernutrition,

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