Review
article

Effects of intrauterine malnutrition on the renal morphology of Wistar rats: a systematic review

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Abstract

Introduction: Many epidemiological studies suggest that the intrauterine environment is extremely important to the determination of the individual's future health. Alterations in the maternal nutritional state, reflected on the weight on birth, may program the litter for the development of diseases on the adult age. Studies with animals exposed to intrauterine malnutrition have suggested a reduction in the number of glomeruli, as well as arterial pressure increase. To review in the literature the alterations of the renal physiology of adult Wistar rats exposed to malnourishment during intrauterine life. Material and methods: A search was performed in the following databases: SciELO, MEDLINE, PUBMED, SCIENCE DIRECT and LILACS. The main search terms were "malnutrition" and "renal function" both in Portuguese and in English. Were included original articles involving albino rats. Were excluded the review articles as well as those involving human beings. Results: According to Franco et al. (2009) the renal function and the number of glomeruli were reduced by the intrauterine malnutrition, predisposing the adult animals to renal diseases. For Chen and Chou (2009) the glomerular ultrastructure is not affected by maternal undernutrition, suggesting that this factor does not contribute to the hypertension pathogenesis after maternal malnutrition. Conclusion: Intrauterine malnourishment seems to interfere in the renal functions programming with alterations to the glomeruli morphology, but its mechanisms are yet uncertain. More randomized studies and clinical essays are suggested in order to comprehend the factors that cause such process.

Keywords: malnutrition, renal diseases, Wistar rats.

1 Introduction

Malnutrition is caused by a qualitative and quantitative unbalance of nutrients in the organism. These unbalances are mainly sustained by protein, fat and carbohydrate lack, which debilitates its physiological process. This protein-energy malnutrition is the most frequent kind, reaching over 800 million people in the world (RAMIREZ, ROCHA, ROCHA et al., 2007).

Many epidemiological studies suggest that the intrauterine environment is extremely important to determine the individual's future health (DODIC, MORTIZ, KOUKOULAS et al., 2002). Alterations to the maternal nutritional state, reflected on the weight on birth, may determine the development of diseases in the adult life (BOMFIM and LACERDA, 2005; MARISTELLA, RICHARDT, SONIA et al., 2008). The effects of intrauterine malnutrition depend on the development phase in which the fetus or the organ is, being the effects as intense and permanent as how precocious occurs this malnourishment and how later occurs the nutritional recovery (MARISTELLA, RICHARDT, SONIA et al., 2008).

In studies with animals, a reduction in the number of glomeruli, along with hypertrophy and arterial pressure increase has been suggested. For Chou, Wang, Lu et al. (2008), however, the altered glomerular ultrastructure is not a contributing factor for the hypertension pathogenesis after the maternal undernutrition stage (EVANS, LANGLEY-EVANS and MARCHAND, 2003; CHOU, WANG, LU et al., 2008; VIEIRA, LARA, SILVA et al., 2009).

This study had as objective to review the literature about the renal morphological alterations in Wistar rats subjected to intrauterine malnutrition.

2 Material and methods

To do this study were consulted the following databases: SciELO (Scientific Eletronic Library Online); MEDLINE (US National Library of Medicine); PUBMED (National Library of Medicine and The National Institute of Health); SCIENCE DIRECT; LILACS (Latin American and Caribbean Health Sciences). The searching strategy involved the following databases, explored with these respective search terms: on SciELO, "intrauterine malnutrition and kidney"; on MEDLINE, "fetal malnutrition" [subject descriptor] and "kidney" [subject descriptor]; on PUBMED, "intrauterine malnutrition and kidney and rat". On SCIENCE DIRECT, "intrauterine malnutrition and kidney and morphology and rats". On LILACS "malnutrition" [subject descriptor] and "kidney". Were included original articles involving albino

Table 1. Studies that evaluated the morphological and physiological alterations to the kidneys of Wistar rats exposed to malnutrition during intrauterine life (IU).

Study	Sample	Material and methods	Main results
Chen and Chou (2009)	Sprague-Dawley rats	The authors evaluated the glomerular ultrastructure of adult litters from malnourished rats, compared to the adult litters of nourished rats.	The glomerular ultrastructure is not affected by the maternal undernutrition, suggesting that this factor does not contribute to the pathogenesis of hypertension after maternal undernutrition.
Chou, Wang, Lu et al. (2008)	Sprague-Dawley rats	Investigated the angiotensin levels on the adult offspring of animals malnourished during gestation.	The malnourished-during-gestation offspring had lower glomeruli number, higher systolic pressure and greater production of angiotensin II.
Paixão, Maciel, Teles et al.(2001)	Wistar rats	Studied the effects of IU malnutrition and malnutrition during both IU life and lactation on the renal morphology and function.	The malnourished litter showed lower nephrons number, glomerular hypertrophy and arterial vasoconstriction, alterations compatible with chronic renal insufficiency.
Evans, Langley-Evans and Marchand (2003)	Wistar rats	Verified the nephron number on the full-term rats with 4 weeks of life.	Maternal undernutrition may program the number of renal nephrons and, thus, the impact on the arterial pressure of adult rats and the development of renal disease.

rats. Were excluded review articles as well as those involving human beings and animals different from rats, as well as the articles that related malnutrition that was not intrauterine. Those articles that were found in more than one of the explored databases were counted only once.

On the SCIELO, PUBMED, LILACS and SCIENCE DIRECT databases no limits were established, whereas on the MEDLINE databases were explored the articles published on the 1966-2009 period. 16 articles were found on PUBMED, 2 on MEDLINE, 216 on SCIENCE DIRECT, 0 on SciELO, 0 on LILACS, totalizing 234 articles. The abstracts were used for applying the inclusion and exclusion criteria and 4 articles were selected for analysis.

3 Results

After applying the inclusion and exclusion criteria the selected articles were summarized on Table 1.

In many animal models, low weight on birth has been associated to the reduction in the nephron number, as this fact has been suggesting a predisposition of these descendants to Hypertension (PAIXÃO, MACIEL, TELES et al., 2001; EVANS, LANGLEY-EVANS and MARCHAND, 2003; CHOU, WANG, LU et al., 2008; FRANCO, PONZIO, GOMES et al., 2009). The total nephron number is a biological variable that is defined, in human beings, before birth. Approximately 60% of the nephrons may develop during the third month of gestation (HAYCOCK, 2001), therefore not forming more nephrons after birth. Besides, a reduction in the number of nephrons on birth may be associated to a decrease in the resistance to the renal lesion mechanisms during adult life (FRANCO, PONZIO, GOMES et al., 2009). Studies suggest that the rats intrauterine growth restriction may be associated to a deficient nephrogenesis, causing a subsequent increase in the arterial pressure. For Paixão, Maciel, Teles et al. (2001), besides the reduction in the nephrogenesis, a glomerular hypertrophy was observed, fact that may be associated to a compensatory mechanism for the reduced glomerular number. For Chen and Chou (2009) however, the glomerular ultrastructure of the adult offspring that was subjected to nutritional deficiencies during intrauterine life was not altered. It is not possible, therefore, to associate the arterial pressure increase with the glomerular genesis. This compensatory hypertrophy may balance the renal functions with those of individuals that have normal levels of nephrons number.

This compensatory hypertrophy can balance the renal functions with those of subjects who present number of nephrons within normal limits, however, the compensatory glomerular hypertrophy can lead to a progressive deterioration of renal function over time (DOUGLAS, McNAMARA and HOY, 2006).

4 Conclusion

A reduction in the nephron number is observed in various animal models with low weight on birth, suggesting that an adverse fetal environment during a critical development period alters the renal morphological structure. It is suggested, however, that more studies be done in order to clarify the gaps.

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