J Pediatr (Rio J). 2017;xxx(xx):xxx–xxx

SOCIEDADE BRASILEIRA DE PEDIATRIA

Jornal de Pediatria
www.jped.com.br

ORIGINAL ARTICLE

Serum levels of melatonin may contribute to the pathogenesis of heart failure in children with median age of 1 year☆

Yao Wu[a,b,c], Feifei Si[a,b,c], Li Luo[a,b,c], Qijian Yi[a,b,c,*]

[a] *Key Laboratory of Pediatrics in Chongqing, Chongqing, China*
[b] *Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Chongqing, China*
[c] *Children's Hospital of Chongqing Medical University, Department of Cardiovascular Medicine, Chongqing, China*

Received 15 February 2017; accepted 14 June 2017

KEYWORDS
Melatonin;
Myeloperoxidase;
Capsase-3;
Heart failure;
Pediatric patients

Abstract

Objective: Melatonin has a protective role in adults with cardiovascular disease, but the effects of melatonin in children with cardiac dysfunction are not well understood. This study was designed to explore the variations in melatonin, myeloperoxidase, and caspase-3 levels in children suffering from heart failure.

Methods: Seventy-two pediatric patients with heart failure and twelve healthy children were enrolled in this study. A modified Ross scoring system was used to evaluate clinical cardiac function. Patients with a score of >2 points were included in the study and were divided into three groups according to severity of heart failure: mild (score: 3–6), moderate (score: 7–9), and severe (score: 10–12). Echocardiographic parameters, laboratory data, and serum levels of melatonin, myeloperoxidase, and caspase-3 were measured and analyzed in all patients.

Results: Compared with patients with mild and moderate heart failure, patients in the severe heart failure group had significantly decreased left ventricular ejection fraction ($p < 0.001$), and significantly increased serum melatonin levels ($p = 0.013$) and myeloperoxidase levels ($p < 0.001$). Serum melatonin levels were positively correlated with serum caspase-3 levels ($p < 0.001$). The optimal cutoff values of serum melatonin levels for the diagnosis of severe heart failure and primary cardiomyopathy in pediatric patients with heart failure were 54.14 pg/mL and 32.88 pg/mL, respectively.

☆ Please cite this article as: Wu Y, Si F, Luo L, Yi Q. Serum levels of melatonin may contribute to the pathogenesis of heart failure in children with median age of 1 year. J Pediatr (Rio J). 2017. https://doi.org/10.1016/j.jped.2017.06.023

* Corresponding author.
E-mail: qjyi2003@hotmail.com (Q. Yi).

http://dx.doi.org/10.1016/j.jped.2017.06.023

Conclusions: Serum melatonin and myeloperoxidase levels were increased in children with severe heart failure. It is likely that increasing melatonin levels may act as a compensatory mechanism in pediatric children with heart failure.

PALAVRAS-CHAVE
Melatonina;
Mieloperoxidase;
Caspase 3;
Insuficiência cardíaca;
Pacientes pediátricos

Níveis séricos da melatonina podem contribuir para a patogênese de insuficiência cardíaca em crianças com idade média de 1 ano

Resumo
Objetivo: A melatonina possui um papel protetor em adultos com doença cardiovascular, porém os efeitos da melatonina em crianças com disfunção cardíaca não são bem entendidos. O estudo foi projetado para explorar a variação nos níveis de melatonina, mieloperoxidase e caspase 3 em crianças que sofrem de insuficiência cardíaca.
Métodos: 72 pacientes pediátricos com insuficiência cardíaca e 12 crianças saudáveis foram inscritos no estudo. Um sistema de classificação de Ross modificada foi utilizado para avaliar a função cardíaca clínica. Os pacientes com escore de > 2 pontos foram incluídas no estudo e foram divididos em três grupos de acordo com a gravidade da insuficiência cardíaca: leve (escore: 3-6), moderada (escore: 7-9) e grave (escore: 10-12). Os parâmetros ecocardiográficos, dados laboratoriais e níveis séricos de melatonina, mieloperoxidase e caspase 3 foram medidos e analisados em todos os pacientes.
Resultados: Em comparação aos pacientes com insuficiência cardíaca de gravidade leve e moderada, os pacientes no grupo de insuficiência cardíaca grave apresentaram redução significativa da fração de ejeção do ventrículo esquerdo ($p < 0,001$) e aumento significativo nos níveis séricos de melatonina ($p = 0,013$) e níveis de mieloperoxidase ($p < 0,001$). Os níveis séricos de melatonina foram positivamente correlacionados com os níveis séricos de caspase 3 ($p < 0,001$). Os valores de corte ideais dos níveis séricos de melatonina para diagnóstico de IC e cardiomiopatia primária em pacientes pediátricos com insuficiência cardíaca foram 54,14 pg/mL e 32,88 pg/mL, respectivamente.
Conclusões: Os níveis séricos de melatonina e mieloperoxidase mostraram aumento em crianças com insuficiência cardíaca grave. Especulamos se o aumento nos níveis de melatonina pode agir como um mecanismo compensatório em crianças pediátricas com insuficiência cardíaca.

Introduction

The prevalence of heart failure (HF) is rising; it poses an increasing burden in terms of both healthcare costs and mortality, especially when it occurs in young children. Consequently, a better understanding of the best way to evaluate and manage HF is required. While advances in diagnosis and treatment of HF in adults have been made, similar awareness is lacking for pediatric patients with HF.[1]

Melatonin (N-acetyl-5-methoxytryptamine), a secretory product of the human pineal gland, is well known for its influence on the cardiovascular system. Melatonin has a protective action on the heart that occurs through both receptor-mediated and receptor-independent mechanisms.[2] The receptor-mediated mechanism involves the classic melatonin membrane receptors (MT1 and MT2); however, the precise localization of these receptors has not been completely elucidated.[3] The receptor-independent mechanism of melatonin occurs through its function as a potent antioxidant and free radical scavenger.[4] Melatonin has been shown to reduce hypertension,[5] protect the ischemic/reperfused heart,[6] and resist the process of atherosclerosis.[7] Cardiomyocyte hypertrophy initially occurs as a compensatory response, but eventually becomes pathological and can lead to HF. Melatonin affects hemodynamic overload, nitric oxide (NO) availability, free radicals, and lipid profiles that may also modify cardiomyocyte hypertrophy.[8]

The association between melatonin and pediatric HF has not been fully understood. The authors performed a study to investigate the circulating levels of melatonin in children with HF.

Methods

This single-center pediatric study was approved by the Ethics Committee. All patient-derived blood samples were