

Available online at www.sciencedirect.com

ScienceDirect

Biomedical Journal

journal homepage: www.elsevier.com/locate/bj

Letter to the Editor

Melatonin as fetal neuroprotection: Links and risks



Fahimeh Ghotbizadeh Vahdani ^a, Sedigheh Hantoushzadeh ^a,
Farzaneh Nazari ^{b,*}

^a Department of Gynecology and Obstetrics, Tehran University of Medical Sciences, Medical School, Tehran, Iran

^b Department of Gynecology and Obstetrics, Bushehr University of Medical Sciences, Medical School, Bushehr, Iran

ARTICLE INFO

Article history:

Received 7 October 2020

Accepted 14 October 2020

Available online 16 October 2020

Keywords:

Melatonin

Fetal

Neuroprotection

Dear Editor,

We have read the review article entitled “Neurocritical care of premature infants” by Reyin Lien published in *The Biomedical Journal* 2020; 43(3):259–67. We want to congratulate the author for this successful review article, and make some contributions.

In the review article, it has been indicated that one of the future directions of neuroprotection in the premature infants is aiming at pharmacological prevention, specifically using agents with anti-inflammatory (e.g. melatonin) [1]. We think melatonin has many biologically possible behaviors that may effectively protect premature neonatal brains. Melatonin has been shown to act as a vasodilator, protect tissues from the activity of free radicals, reduce vascular dysfunction, prevents hypoxic injury, attenuates cell injury induced by excitatory amino acids or cytokines, and have antiapoptotic effects. But there are some controversial matters on melatonin effect. N Merchant et al. demonstrated that the neuroprotective effects

of melatonin in premature infants less than 31 weeks of pregnancy did not have a beneficial effect on the MRI parameters of the immature brain at term equivalent age [2]. Also further important consideration is the use of ethanol as a diluent due to the hydrophobicity of melatonin. Immature brains are detrimentally affected by ethanol. While an extremely small volume of ethanol in one sample of preterm fetal sheep had beneficial regional effects to enhance the survival of neurons in the caudate nucleus, it increased hippocampal neuron loss [3]. Melatonin triggered a slight contractile response in bronchial smooth muscle [4]. Also, melatonin contributes to a reduction in the concentration of vascular endothelial growth factor (VEGF), production of NO, and, consequently, vascular permeability, resulting in higher hypoxic condition [5]. To evaluate melatonin as a fetal neuroprotective agent, however, several properly designed randomized clinical trials (RCTs) with an appropriate sample size and confirmed clinical outcome measurements should be conducted.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- [1] Lien R. Neurocritical care of premature infants. *Biomed J* 2020;43:259–67.
- [2] Merchant N, Azzopardi D, Counsell S, Gressens P, Dierl A, Gozar I, et al. Melatonin in as a novel neuroprotection in

* Corresponding author. Department of Gynecology and Obstetrics, Bushehr University of Medical Sciences, Medical School, Moallem St., Bushehr, Iran.

E-mail address: Nazarif78@yahoo.com (F. Nazari).

Peer review under responsibility of Chang Gung University.

<https://doi.org/10.1016/j.bj.2020.10.006>

2319-4170/© 2020 Chang Gung University. Publishing services provided by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

- preterm infants-a double blinded randomized controlled trial (mini study). *Arch Dis Child* 2014;99:A620.
- [3] Drury PP, Davidson JO, Bennet L, Booth LC, Tan S, Fraser M, et al. Partial neural protection with prophylactic low-dose melatonin after asphyxia in preterm fetal sheep. *J Cereb Blood Flow Metab* 2014;34:126–35.
- [4] Weekley LB. Influence of melatonin on bovine pulmonary vascular and bronchial airway smooth muscle tone. *Clin Auton Res* 1995;5:53–6.
- [5] Cheng J, Yang HL, Gu CJ, Liu YK, Shao J, Zhu R, et al. Melatonin restricts the viability and angiogenesis of vascular endothelial cells by suppressing HIF-1 α /ROS/VEGF. *Int J Mol Med* 2019;43:945–55.