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Copper Deficiency and its Relation with Preeclampsia. A Systematic Review.

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Introduction

Micronutrient deficiencies are of great importance in Public Health when considering women of reproductive age within low and middle-income countries (PBMR). Preeclampsia (PE) is a condition defined by the International Society for the Study of Hypertension in Pregnancy (ISSHP)[1]. PE is characterized by systolic blood pressure at ≥140 mmHg and/or the diastolic blood pressure at ≥90 mmHg on at least two occasions with a four-hour interval in previously normotensive women. Furthermore, the diagnosis of PE requires the presence of ≥1 of the following new-onset conditions at or after 20 week´s gestation: Proteinuria (i.e., ≥30 mg/mol protein: creatinine ratio; ≥300 mg/24hr; or ≥2+ dipstick); Evidence of other maternal organ dysfunction, including: acute kidney injury (creatinine ≥90umol/L; 1 mg/dL), liver involvement with or without right upper quadrant or epigastric abdominal pain, neurological complications, or hematological complications. Uteroplacental dysfunction, which can be evidenced by fetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or stillbirth[1]. The present work aims to conduct a systematic review using Cochrane risk of bias tool and the Joanna Briggs Critical Appraisal Tools to answer the question if the copper´s deficiency in pregnant women may develop/induce PE, to support governmental health care action.

Results and Discussion

The search was based on literature published during January 2000 to April 2022 in databank Pubmed/ Medline, Embase, Lilacs, Cochrane Library, Clinical.trials.gov, by the keywords: micronutrients, preeclampsia, eclampsia, copper, woman and pregnant. The original review was performed according PRISMA guidelines and was register in PROSPERO (CRD42022302298). Within the base article, 256 articles were peer-reviewed and tabulated. When specifically examining copper, we analyzed 31 articles. All the studies analyzed Copper in association with other micronutrients, never it alone. For this summary, five articles were chosen, can be observed in Table 1, with one of them being the only one among all the copper-related articles that received the highest quality score and a bias risk [2], while the other three received good ratings [3, 4, 5]. Articles of good quality and low bias risk mostly yielded similar results and conclusions. Mistry et al. 2014[3] presented results and serum copper levels indicating more elevated in the study group at

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Table 1 – Results. *JB: Joanna Briggs Critical Appraisal Tools Quality,*

Author	Population	Outcomes	JB	Bias
Fenzl et al 2013	127 patients . 30 PE . 30 GH . 37 CG . 30 NP	Cu (µmol/L): . PE: 33.91 . GH 33.32 . CG 32.04 . NP 15.3		
Mistry et al 2014	716 patients . 244 SG . 472 CG	Cu (µg/L): . CG: 1850 (1663.5-2051.5) . SG: 1957.4 (1787-2177.5)		
Rafeeinia et al 2014	100 patients . 50 CG . 50 PE [35 Mild (M), 15 Severe (S)]	Cu (mg/L) CG: 1.32 ± 0.34 PE: . M: 2.26 ± 0.48 . S: 2.70 ± 0.85		
Polat et al 2015	130 patients . 70 PE . 60 CG	Cu (µgr/dl): . PE: 210.95 ± 56.58 . CG: 121.21 ± 25.08		
Choi et al 2016	245 pregnant 227 NP 300 men	Cu (µg/dl): . Pregnant: 165 (144-187) . NP: 100 (86,3-120) . Men: 91,5 (81-105,5)		

PE: preeclampsia, SG: study group, CG: control group, GH: gestational hypertension, NP: non-pregnant.

1957.4 µg/L (1787-2177.5 µg/L) when compared to the control group at 1850 µg/L (1663.5-2051.5 µg/L). The same way, Rafeeinia et al. 2014[4] observed a relationship between elevated copper levels and the severity of the condition, with patients with severe conditions having even higher levels (2.70 ± 0.85) compared to moderate cases (2.26 ± 0.48). Polat et al. 2015[5] reported results that corroborated with earlier studies[3, 4]. In the control group, they observed an almost halved average (121.21 ± 25.0) when compared to pregnant women with PE (210.95 ± 56.58). However, in Fenzl et al. 2013[2], no significant difference was observed in serum copper levels between the sample groups, only higher levels compared to non-pregnant women, which was considered a physiological alteration. It is necessary to note that some articles are designed in a confusing and contradictory manner. We included Choi et al. 2016[6], which compares pregnant women, non-pregnant women, and men while attempting to relate serum levels to the development of pregnancy-related changes. Thus, it becomes unfeasible to use these articles for data and result analysis between unrelated groups.

Conclusions

After analyzing, it was possible to conclude that most studies carried out have a great risk of bias and were not so elucidated. So, we have already observed the need to have more studies on copper in a solitary way, and there is a need for more clear studies on these substances to clarify doubts about their uses.

References

[1] ISSHP, 2018: Brown, M., Pregnancy Hypertension (2018), https://doi.org/10.1016/j.preghy.2018.05.004

[2] Fenzl V, et al Trace elements and oxidative stress in hypertensive disorders of pregnancy. Arch Gynecol Obstet. 2013 Jan;287(1):19-24.

[3] Mistry HD, et al. SCOPE Consortium. Association between maternal micronutrient status, oxidative stress, and common genetic variants in antioxidant enzymes at 15 weeks' gestation in nulliparous women who subsequently develop preeclampsia. Free Radic Biol Med. 2015 78:147-55.

[4] Rafeeinia A, et al. Serum copper, zinc and lipid peroxidation in pregnant women with preeclampsia in gorgan. Open Biochem J. 2014 1; 8:83-8. doi: 10.2174/1874091X01408010083.

[5] Polat M, et al. Coexistence of preeclampsia and inherited thrombophilia in Turkish pregnant women. Turk J Med Sci. 2016 Jun 23;46(4):1094-100.

[6] Choi R, et al.A Prospective Study of Serum Trace Elements in Healthy Korean Pregnant Women. Nutrients. 2016 Nov 23;8(11):749. doi: 10.3390/nu8110749.