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Research Article

STUDY OF THE IMPACT OF MICRONUTRIENT FOUND IN SPERAMAX® DURING PREGNANCY PERIODS ON EMBRYONIC DEVELOPMENT AND NEWBORN

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ABSTRACT

Objective: This paper aims at evaluating the benefits of vitamins and minerals found in the Speramax® supplement and the risks to mother and infants of additional supplementation and possible adverse interactions between micronutrients in pregnancy.

Method: A total of 30 male and 120 female albinos Swiss mice of 8–12 weeks of age weighing 25–35 g were used. Speramax® was administrated orally for 1, 2, and 4 weeks. Fertile female mice were classified into four main groups: Group 1 is spontaneously (SPO); Group 2 is administrated with Speramax® only; Group 3 is treated Speramax® with superovulation (SUO); and Group 4 is superovulated only without Speramax®.

Result: The results indicated that treatment with Speramax® showed a positive effect on neonatal development and an increase in the number of newborn SPO and SUO treated with Speramax® after 1 week and 2 weeks. The results showed high significance ($p<0.000$) compared with SPO and SUO mice not treated with Speramax® and with groups treated for 4 weeks.

Conclusion: Good nutrition found in Speramax® may, therefore, be especially important to this group of infants and must be instituted alongside other nutritional supplements.

Keyword: Speramax®, Infant growth, Antioxidant, Micronutrients, Nutritional, Requirements.

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INTRODUCTION

Micronutrients are minerals and vitamins important, in minute sums, for ordinary working, development, and improvement. Vitamins and minerals bolster each phase of maternal, placental, and fetal connection to empower a solid incubation. Females in low-pay nations frequently eat lowered levels of micronutrients because they are limited to specific types of food and have little access to natural products, vegetables, and invigorated foods [1]. Micronutrients are very significant to pregnancy and regularly given as supplements such as Vitamins E, folate, zinc, and selenium [2]. Poor maternal health status, alongside maternal body synthesis, digestion, and placental supplement supply are the primary factors that can adversely impact fetal improvement and have been entirely identified with unfriendly pregnancy result and articulation of fetal hereditary potential [3]. Folic corrosive is a Vitamin B that assists the body in making solid new cells. The human body is in need of folic corrosive, particularly those females who may get pregnant [4]. It is also a cancer prevention agent, critical for DNA combination and cell replication, and diminishes risks of ovulatory barrenness [5]. Speramax® is a new medicine containing a number of various vitamins and L-carnitine, and all involved in cell metabolism and used for men. The L-carnitine is involved in fatty acid oxidation; the vitamins act as antioxidants in the anabolism of body [6].

Vitamins and antioxidant

In the female reproductive system, high convergences of ROS in the female conceptive tract could likewise adversely affect the preparation of oocytes and cause hindrance of embryonic implantation [7,8]. They play a significant role in the pathogenesis of subfertility in both men and women [9-11]. There is now a great deal of scientific knowledge about the use of nutritional complements and their advantageous effects on both female and male fertilities [12]. Studies have shown that vitamins and minerals can increase your chances of success of staying pregnant.

Studies on infertile woman have shown that pre-conception folic acid supplementation increases folate levels and decreases homocysteine level in follicular fluid (FF) [13], and it enhances embryo quality and the chance of pregnancy [14]. In addition, folate is vital for quality and development, implantation, placentation, fetal development, and organ advancement [15]. Selenium (Se) is a component of enormous significance for human health. It is effectively exchanged over the placenta into embryo amid gestation; the overall maternal selenium content is emphatically connected with fetal and infant selenium state [16]. Se plays a key role in the effectiveness of the reproductive system and male and female fertilities. Based on this purpose, supplementation in the case of selenium is of maximum significance [17]. Studies on animals and humans show that the use of hormones more efficiently may help to prevent miscarriage or fetal death [18,19].

Vitamin E is a vital antioxidant for reproduction and fertility; this powerful antioxidant can play a critical role in oocyte maturation because the FF found in oocyte is rich with Vitamin E. The environment of FF is thought to play a role in oocyte maturation and eventual development of an embryo [20].

L-carnitine-interceded beta-oxidation of unsaturated fats has a well-built-up part in vitality supply of oocytes and embryos [21] and the amount in the body peaks in your twenties and then decreases and becomes short supply as you age. It plays a role in increasing chances of pregnancy [22]. L-carnitine might be positive in advancing improvement in neonates [23,24].

METHODS

Fertile female mice were classified into four main groups: Group 1 is spontaneously (SPO); Group 2 is administrated with Speramax® only; Group 3 is treated Speramax® with superovulation (SUO); and Group 4 is superovulated only without Speramax®.

Ovarian stimulation (SUO induction)

SUO was performed by intraperitoneal (IP) shot of 7-point five international unite (I.U.) of pregnant mare's serum gonadotropin

Table 1: Newborn obtained from SPO and SUO female mice following (1, 2 and 4 weeks) of treatment with Speramax®

Period of treatment	Number of newborn				p value
	SPO (control)	SPO with Speramax®	SUO with Speramax®	SUO	
1 weeks	40	120	120	72	0.000
2 weeks	36	84	100	68	0.000
4 weeks	52	60	72	80	0.071

Chi-square test at 0.05 of significant, number of mice for each group 10, SPO: Spontaneously, SUO: Superovulated

(Folligon, Holland) and then followed 48 h later by IP injection of 7-point five I.U. of human chorionic gonadotropin (Pregnyl, Serono company).

Mating of the animals

After isolation of the sexually mature females which at the estrous stage by examining the vaginal smears under a light microscope, the isolated females were put in breeding cages, each two females with one mature male and left overnight.

Early in the next morning, copulation was confirmed by examining the females and noticing the incidence of the vaginal plug or the sperms in slides microscopically in the vaginal swabs.

In this work, the gestational day 0 was characterized as the day when spermatozoa were seen in a spread of the vaginal substance or potentially a copulatory attachment and/or sperm under a light microscope.

Statistical analysis

All statistical analysis was achieved using version 16.0 Minitab statistical program. Chi-square test was also utilized. $p<0.05$ was considered statistically significant in this study [25].

RESULT

Table 1 shows the number of newborn SPO and SUO mice treated with Speramax® after 1, 2, and 4 weeks.

DISCUSSION

This paper evaluates the supplementation of vitamins and minerals found in Speramax® on pregnancy. The study shows a significant increase in the number of neonatal with healthy feature. It does not record any state of congenital anomalies in groups treated with Speramax® supplements for 1 and 2 weeks in pregnant animals compared with an untreated group. The explanation for this feature is that the pregnant requires folic acid during and before pregnancy. The World Health Organization prescribes utilization of folic corrosive supplementation in females among pregnancy as a piece of regular antenatal care [26-28]. Its increase helps in expansion of red platelet mass, augmentation of the uterus, and the development of the placenta and embryo [29]. Another research found that the folic acid is of much importance to the synthesis of DNA and RNA [30]. Moreover, the previous study explained pregnant women treated with folic acid to prevent the occurrence of neural tube defect [31].

The paper also shows the importance of zinc oxide supplement during pregnancy for healthy neonatal. Several studies of investigational animals and humans reveal that severe zinc lack can have deep effects on pregnancy outcome [32]. Zinc is an important factor required for fertilization and pre-implantation development [33]. All instances of low birth weight could be counteracted by daily utilization of a multivitamin containing 15–20 mg of zinc among the main trimester of pregnancy [34].

Selenium also plays a role in reproduction rates in humans as well as animals [35]. Selenium is one of the minerals whose insufficiency is known to prompt confusions of female reproduction [36-42]. Selenium insufficiency has been related with a number of unfavorable pregnancy results, for example, preterm conveyances and miscarriages [43]. Several studies reported that selenium is important for normal reproductive function and for the prevention of compromised pregnancies as it reduces the risk of miscarriage, pre-eclampsia, gestational diabetes, pregnancy-induced hypertension, and early rupture of membranes [44,45].

Another study found that the decrease of selenium during pregnancy would lead to decrease of the weight of neonatal [46].

L-carnitine (L-Cn) is a fundamental compound to the cell delivering long 48 anchor unsaturated fatty acid to the β-oxidation pathway in the mitochondrial network for catabolism [47]. Various studies have shown a significant effect of L-carnitine supplement in embryogenesis and improving embryo development [48].

The importance of L-carnitine supplied to the maternal organism enhances intrauterine growth [49]. Carnitine can cross the placenta; therefore, a low carnitine level of the neonate can reflect both neonatal deficiency and maternal deficiency [50-52]. The significance of L-carnitine in enhancing oocyte quality and regenerative execution has been exhibited in creature and human investigations [53-58]. The umbilical string blood contains altogether larger amounts of free and aggregate L-carnitine than the relating maternal levels [59,60].

Vitamin E, the environment of the FF, is thought to play a pivotal role in oocyte maturation and later the eventual development of an embryo [61-63]. Furthermore, there are many antioxidants found in FF including Vitamin E, which promotes healthy oocyte maturation and oocyte viability; however, the results are conflicting [64-66].

Increased ROS levels have been related with poor oocyte quality, low fertilization rate, and impaired embryo development [67].

In a creature display, Train *et al*. [68] have demonstrated that oral organization of antioxidant (Vitamin E) decreased the negative impact of female maturing on the number and nature of oocytes.

CONCLUSION

This study concludes that Speramax® is not only used for male infertility but can also be used for female fertility potential because its contents are highly supplemental for oocyte maturation and embryonic development. Hence, good nutrition may, therefore, be especially important to this group of infants and must be administered alongside other nutritional supplements.

AUTHOR'S CONTRIBUTIONS

Speramax® is not only used for male infertility but can also be used for female fertility.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest.

REFERENCES

1. Huffman SL, Baker J, Shumann J, Zehner ER. The Case for Promoting Multiple vitamin/mineral Supplements for Women of Reproductive Age in Developing Countries. Available from: http//www.linkagesproject.org. [Last accessed on 2003 Apr 26].

2. Gernand AD, Schulze KJ, Stewart CP, West KP Jr., Christian P. Micronutrient deficiencies in pregnancy worldwide: Health effects and prevention. Nat Rev Endocrinol 2016;12:274-89.
3. Cetin I, Laoreti A. The importance of maternal nutrition for health. J Pediatr Neonatal Individ Med 2015;4:e040220.
4. Bailey SW, Ayling JE. The extremely slow and variable activity of dihydrofolate reductase in human liver and its implications for high folic acid intake. Proc Natl Acad Sci U S A 2009;106:15424-9.
5. Henmi H, Endo T, Kitajima Y, Manase K, Hata H, Kudo R, *et al.* Effects of ascorbic acid supplementation on serum progesterone levels in patients with a luteal phase defect. Fertil Steril 2003;80:459-61.
6. Generated on: This Page was Generated by TSDR; 2014.
7. Lee TH, Wu MY, Chen MJ, Chao KH, Ho HN, Yang YS, *et al.* Nitric oxide is associated with poor embryo quality and pregnancy outcome in *in vitro* fertilization cycles. Fertil Steril 2004;82:126-31.
8. Sharma RK, Agarwal A. Role of reactive oxygen species in gynecologic diseases. Reprod Med Biol 2004;3:177-99.
9. Ebisch IM, Thomas CM, Peters WH, Braat DD, Steegers-Theunissen RP. The importance of folate, zinc and antioxidants in the pathogenesis and prevention of subfertility. Hum Reprod Update 2007;13:163-74.
10. Joshi R, Adhikari S, Patro BS, Chattopadhyay S, Mukherjee T. Free radical scavenging behavior of folic acid: Evidence for possible antioxidant activity. Free Radic Biol Med 2001;30:1390-9.
11. Ruder EH, Hartman TJ, Goldman MB. Impact of oxidative stress on female fertility. Curr Opin Obstet Gynecol 2009;21:219-22.
12. Gunderson P. Nutrition during pregnancy of physically active women. Clin Obstetr Gynecol 2003;46:390-409.
13. Boxmeer JC, Brouns RM, Lindemans J, Steegers EA, Martini E, Macklon NS, *et al.* Preconception folic acid treatment affects the microenvironment of the maturing oocyte in humans. Fertil Steril 2008;89:1766-70.
14. Boxmeer JC, Macklon NS, Lindemans J, Beckers NG, Eijkemans MJ, Laven JS, *et al*. IVF outcomes are associated with biomarkers of the homocysteine pathway in monofollicular fluid. Hum Reprod 2009;24:1059-66.
15. Ebisch IM, Thomas CM, Peters WH, Braat DD, Steegers-Theunissen RP. The importance of folate, zinc and antioxidants in the pathogenesis and prevention of subfertility. Hum Reprod Update 2007;13:163-74.
16. Gupta RG. Reproduction and Developmental Toxicology. 2nd ed. New York: McGraw-Hill; 2013. p. 596-8.
17. Goldenberg RL, Tamura T, Neggers Y, Copper RL, Johnston KE, DuBard MB, *et al.* The effect of zinc supplementation on pregnancy outcome. JAMA 1995;274:463-8.
18. King JC. Determinants of maternal zinc status during pregnancy. Am J Clin Nutr 2000;71:1334S-43S.
19. Lydic ML, McNurlan M, Bembo S, Mitchell L, Komaroff E, Gelato M, *et al.* Chromium picolinate improves insulin sensitivity in obese subjects with polycystic ovary syndrome. Fertil Steril 2006;86:243-6.
20. Meldrum DR. Factors affecting embryo implantation after human *in vitro* fertilization. Am J Obstet Gynecol 1991;165:1896-97.
21. Várnagy Á, Bene J, Sulyok E, Gábor L Bódis J, Melegh B. Acylcarnitine esters profiling of serum and follicular fluid in patients undergoing *in vitro* fertilization. Reprod Biol Endocrinol 2013;11:67.
22. Eder K, Ramanau A, Kluge H. Effect of L-carnitine supplementation on performance parameters in gilts and sows. J Anim Physiol Anim Nutr (Berl) 2001;85:73-80.
23. Schmidt-Sommerfeld E, Novak M, Penn D. Carnitine and development of newborn adipose tissue. Pediatr Res 1978;12:660-4.
24. Arenas J, Rubio JC, Martín MA, Campos Y. Biological roles of L-carnitine in perinatal metabolism. Early Hum Dev 1998;53 Suppl: S43-50.
25. Minitab, Inc. Minitab Statistical Software, Release 13 for Windows. State College, PA: Minitab Inc.; 2000.
26. Black RE. Micronutrients in pregnancy. Br J Nutr 2001;85 Suppl 2:S193-7.
27. Botto LD, Mulinare J, Erickson JD. Occurrence of omphalocele in relation to maternal multivitamin use: A population-based study. Pediatrics 2002;109:904-8.
28. Caulfield LE, Zavaleta N, Shankar AH, Merialdi M. Potential contribution of maternal zinc supplementation during pregnancy to maternal and child survival. Am J Clin Nutr 1998;68:499S-508S.
29. Bailey LB. New standard for dietary folate intake in pregnant women. Am J Clin Nutr 2000;71:1304S-7S.
30. Sarheed O, Ramesh K, Shah F. *In vitro* evaluation of dissolution profile of two commercially available folic acid prepartions. Int J pharm pharm Sci 2015;7:473-5.
31. Vij S, Archana Agr. AH, Waheeta Ho. Computational analysis of interactions between antiepileptic drug and important placental proteins-passible roule for neural tube defects in Humans. Int J pharm pharm Sci 2018;8 suppl1:19-23.
32. Van Wouwe JP. Clinical and laboratory diagnosis of acrodermatitis enteropathica. Eur J Pediatr 1989;149:2-8.
33. Tian X, Diaz FJ. Acute dietary zinc deficiency before conception compromises oocyte epigenetic programming and disrupts embryonic development. Dev Biol 2013;376:51-61.
34. Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC, *et al.* Vitamin E consumption and the risk of coronary disease in women. N Engl J Med 1993;328:1444-9.
35. Tang CC, Chen HN, Rui HF. The effects of selenium on gestation, fertility, and offspring in mice. Biol Trace Elem Res 1991;30:227-31.
36. Mistry HD, Williams PJ. The importance of antioxidant micronutrients in pregnancy. Oxid Med Cell Longev 2011;2011:841749.
37. Palmieri C, Szarek J. Effect of maternal selenium supplementation on pregnancy in humans and livestock. J Elementol 2011;16:143-56.
38. Mistry HD, Broughton Pipkin F, Redman CW, Poston L. Selenium in reproductive health. Am J Obstet Gynecol 2012;206:21-30.
39. Ošt'ádalová I. Biological effects of selenium compounds with a particular attention to the ontogenetic development. Physiol Res 2012;61 Suppl 1:S19-34.
40. Rayman MP. Selenium and human health. Lancet 2012;379:1256-68.
41. Mehdi Y, Hornick JL, Istasse L, Dufrasne I. Selenium in the environment, metabolism and involvement in body functions. Molecules 2013;18:3292-311.
42. Ramos GB, Sia AJ, Callejas NA, Revilla CJ, Alfonso N, Sia SG. Pregestational and gestational maternal selenium-supplement: Influence on ethanol-induced dysmorphogenesis in murine postimplantation embryos. Asian J Exp Biol Sci 2013;4:361-8.
43. Mistry HD, Wilson V, Ramsay MM, Symonds ME, Broughton Pipkin F. Reduced selenium concentrations and glutathione peroxidase activity in preeclamptic pregnancies. Hypertension 2008;52:881-8.
44. Barrington J, Lindsay P, James D, Smith S, Roberts A. Roberts selenium deficiency and miscarriage: A possible link? BJOG 2014;103:130-2.
45. Palmieri C, Szarek J. Effect of maternal selenium supplementation on pregnancy in humans and livestock. J Elementol 2011;16:143-56.
46. van wouwe, Jacobus P. Clinical and laboratory assessment of zinc deficiency in Dutch children. J Trace Elem Med Biol 1995;49:211-25.
47. Kyvelidou C, Sotiriou D, Antonopoulou T, Tsagkaraki M, Tserevelakis GJ, Filippidis G, *et al*. L-carnitine affects preimplantation embryo development toward infertility in mice. Reproduction 2016;152:283-91.
48. Abdelrazik H, Agarwal A. L- carnitine and assist reproduction. Arch Med Sci 2009;5:s43-7.
49. Eder K, Ramanau A, Kluge H. Effect of L-carnitine supplementation on performance parameters in gilts and sows. J Anim Physiol Anim Nutr (Berl) 2001;85:73-80.
50. Lee NC, Tang NL, Chien YH, Chen CA, Lin SJ, Chiu PC, *et al.* Diagnoses of newborns and mothers with carnitine uptake defects through newborn screening. Mol Genet Metab 2010;100:46-50.
51. Schimmenti LA, Crombez EA, Schwahn BC, Heese BA, Wood TC, Schroer RJ, *et al*. Expanded newborn screening identifies maternal primary carnitine deficiency. Mol Genet Metab 2007;90:441-5.
52. El-Hattab AW, Li FY, Shen J, Powell BR, Bawle EV, Adams DJ, *et al*. Maternal systemic primary carnitine deficiency uncovered by newborn screening: Clinical, biochemical, and molecular aspects. Genet Med 2010;12:19-24.
53. Bremer J. Carnitine-metabolism and functions. Physiol Rev 1983;63:1420-80.
54. Mansour G, Abdelrazik H, Sharma RK, Radwan E, Falcone T, Agarwal A, *et al.* L-carnitine supplementation reduces oocyte cytoskeleton damage and embryo apoptosis induced by incubation in peritoneal fluid from patients with endometriosis. Fertil Steril 2009;91:2079-86.
55. Dunning KR, Cashman K, Russell DL, Thompson JG, Norman RJ, Robker RL, *et al.* Beta-oxidation is essential for mouse oocyte developmental competence and early embryo development. Biol Reprod 2010;83:909-18.
56. Dunning KR, Akison LK, Russell DL, Norman RJ, Robker RL. Increased beta-oxidation and improved oocyte developmental competence in response to l-carnitine during ovarian *in vitro* follicle development in mice. Biol Reprod 2011;85:548-55.
57. Wu GQ, Jia BY, Li JJ, Fu XW, Zhou GB, Hou YP, *et al.* L-carnitine enhances oocyte maturation and development of parthenogenetic embryos in pigs. Theriogenology 2011;76:785-93.
58. Somfai T, Kaneda M, Akagi S, Watanabe S, Haraguchi S, Mizutani E, *et al.* Enhancement of lipid metabolism with L-carnitine during *in vitro*

maturation improves nuclear maturation and cleavage ability of follicular porcine oocytes. Reprod Fertil Dev 2011;23:912-20.
59. Genger H, Sevelda P, Vytiska-Binstorfer E, Salzer H, Legenstein E, Lohniger A, Carnitinspiegel Wahrend der Schwangerschaft. Z Geburtsh Perinat 1988;192:134-6.
60. Salzer H, Hofbauer R, Karlic H. Pregnancy associated carnitine deficiency causes downregulation carnitine acyltransferase genes. FASEB (2001). abstract.
61. Agarwal A, Saleh RA, Bedaiwy MA. Role of reactive oxygen species in the pathophysiology of human reproduction. Fertil Steril 2003;79:829-43.
62. Ho HN, Wu MY, Chen SU, Chao KH, Chen CD, Yang YS, *et al.* Total antioxidant status and nitric oxide do not increase in peritoneal fluids from women with endometriosis. Hum Reprod 1997;12:2810-5.
63. Oyawoye O, Abdel Gadir A, Garner A, Constantinovici N, Perrett C, Hardiman P, *et al.* Antioxidants and reactive oxygen species in follicular fluid of women undergoing IVF: Relationship to outcome. Hum Reprod 2003;18:2270-4.
64. Paszkowski T, Traub AI, Robinson SY, McMaster D. Selenium dependent glutathione peroxidase activity in human follicular fluid. Clin Chim Acta 1995;236:173-80.
65. Pasqualotto EB, Lara LV, Salvador M, Sobreiro BP, Borges E, Pasqualotto FF. The role of enzymatic antioxidants detected in the follicular fluid and semen of infertile couples undergoing assisted reproduction. Hum Fertil (Camb) 2009;12:166-71.
66. Appasamy M, Jauniaux E, Serhal P, Al-Qahtani A, Groome NP, Muttukrishna S, *et al.* Evaluation of the relationship between follicular fluid oxidative stress, ovarian hormones, and response to gonadotropin stimulation. Fertil Steril 2008;89:912-21.
67. Das S, Chattopadhyay R, Ghosh S, Ghosh S, Goswami SK, Chakravarty BN, *et al.* Reactive oxygen species level in follicular fluid–embryo quality marker in IVF? Hum Reprod 2006;21:2403-7.
68. Tarín JJ, Pérez-Albalá S, Cano A. Oral antioxidants counteract the negative effects of female aging on oocyte quantity and quality in the mouse. Mol Reprod Dev 2002;61:385-97.http://www.rbej.com/content/11/1/67