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The Relationship Between Folic Acid and Spina Bifida

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ABSTRACT

Malformations known as neural tube abnormalities (NTDs) occur during the development of the embryo and are responsible for the majority of birth abnormalities involving the central nervous system. It has been shown that the development of non-traumatic diseases (NTDs) is influenced by both hereditary and environmental variables. The majority of neural axis defects occur in the caudal spinal or cranial regions, An opening in the vertebral arch is a characteristic of spina bifida, a kind of NTD, Although folic acid administration has been researched and documented inside the written works as a means of preventing NTDs, 88,000 people globally pass away from NTDs each year, It is suggested that Women should take 400 µg of folic acid or more every day, Prenatal vitamins are advised to offer the benefits of folic acid and taking supplements during pregnancy has been practiced in several countries for foods including cereal grain products; But not every nation has implemented folic acid fortification initiatives. neural tube development, vitamin B-12 pharmacology, spina bifida abnormalities, are all covered in this inquiry.key element in the global decline in spina bifida incidence is women's understanding of the function of the folic acid in shielding against the disease.

العلاقة بين حمض الفوليك والسنسنة المشقوقة

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الخلاصة:

تحدث التشوهات المعروفة باسم تشوهات الأنبوب العصبي أثناء نمو الجنين وهي مسؤولة عن غالبية التشوهات الخلقية التي تصيب الجهاز العصبي المركزي. وقد ثبت أن تطور الأمراض غير الرضحية يتأثر بكل من المتغيرات الوراثية والبيئية، تحدث غالبية عيوب الانبوب العصبي في المناطق الشوكية أو القحفية الذنبية، والفتحة في القوس الفقري هي سمة من سمات السنسنة المشقوقة، وهو نوع من تشوهات الأنبوب العصبي، وعلى الرغم من أن إعطاء حمض الفوليك تم البحث عنه وتوثيقه داخل الأعمال المكتوبة كوسيلة للوقاية من تشوهات الأنبوب العصبي، إلا أن 88000 شخص على مستوى العالم

يموتون بسبب هذه التشوهات كل عام، ويقترح أن تأخذ النساء 400 ميكروغرام من حمض الفوليك أو أكثر كل يوم، وينصح بتناول فيتامينات ما قبل الولادة لتقديم فوائد حمض الفوليك، وقد تم ممارسة تناول المكملات الغذائية أثناء الحمل في العديد من البلدان للأطعمة بما في ذلك منتجات الحبوب؛ ولكن لم تنفذ كل دولة مبادرات تحصين حمض الفوليك. تتناول هذه المقالة تطور الأنبوب العصبي، وعلم الأدوية الخاص بفيتامين ب 12، وتشوهات السنسنة المشقوقة. والعنصر الأساسي في الانخفاض العالمي في حدوث السنسنة المشقوقة هو فهم النساء لوظيفة حمض الفوليك في الحماية ضد هذا المرض

الكلمات المفتاحية: السنسنة المشقوقة، حمض الفوليك، تطور الأنبوب العصبي.

1. INTRODUCTION

Neural tube defects (NTDs) represent a failure of the neural plate to complete the developmental transition to a neural tube. NTDs are the most common birth anomaly of the CNS [1]. The caudal spinal or cranial regions are the sites of the majority of neural axis abnormalities [2, 3]. There are around 300,000 documented cases of NTDs annually. [4, 5], with an incidence of 0.1% in the Western world and 1.86% worldwide [6]. Approximately 88,000 deaths occur annually due to NTDs. A 1981 study examined the impact of 4,000 μg of folic acid per day on non-typing diabetes [7]. The study's that folic acid provided protection against NTDs. Another 1983 study found that taking a multivitamin before and throughout the first trimester of a subsequent pregnancy decreased the likelihood that women who had previously experienced pregnancies that resulted in children with non-traditional deliveries (NTDs) would experience this again. [8].

1.1. Disease Symptoms and Indications

There are various ways to categorize the Symptoms and Indications, including academic, executive, neurologic, and physical functioning**.**

1.1.1. Outward Signals: The most typical physical symptoms of spina bifida include club foot, weakness in limbs, paralysis, dislocation of the hip, scoliosis,, skin irritations, and irregularities in eye movements [9].

1.1.2. Signs of Neurology Lesions in the cerebellum**:** Are higher in patients with spina bifida and are smaller [10]. Neuron displacement may be the cause of cortical abnormalities [11]. The brain's in the corpus callosum [12]. Furthermore, myelomeningocele patients have less structured more damaged pathways connecting frontal regions and strands of white matter that link the anterior and posterior areas [10].

2. FOLATE

The naturally occurring form of vitamin B9, folate, is present in dishes like brussels sprouts, broccoli, and more lush green plants [13, 14]. In the US, fortification with folic acid is deemed necessary in light of flour, grain, additionally cereal goods labeled as "enriched." Mandatory micronutrient fortification schemes, as opposed to voluntary ones, generally produce more consistent distribution of a specific micronutrient to members of a population, in terms of coverage and degree of response. An investigation that is cross-sectional conducted in Ireland evaluated the folate and the vitamin B12 level as a consequence of supplement use and/or voluntary fortification. The study found which while the population's although the amount of folate consumed through fortified foods and supplements increased, this rise was not consistent. Remarkably, a large percentage of women who were able to procreate (66%) having folate levels in erythrocyte that were under the recommended threshold [14) In North America, folic acid fortification of food was first implemented ten years ago with the goal of lowering the incidence of neural tube abnormalities with every neural tube defect pregnancy that is avoided many hundred thousand people are subjected to a higher folic acid consumption when fortification is implemented. changing their phenotype in the offspring. Increased blood concentrations of unmetabolized folic acid and naturally occurring folates are observed in persons who consume more folic acid. Lower natural killer cell cytotoxicity has been connected to higher blood levels of folic acid, and higher levels of folate have been associated with a reduced response to antifolate drugs used to treat malaria, rheumatoid arthritis, psoriasis, and cancer [15].

The intestinal mucosal cells can easily absorb folic acid in its monoglutamate form, but the small intestine's brush barrier must first convert dietary types of folate, including polyglutamate derivatives, so as to enable their absorption. Since folates are typically found in polyglutamate forms, absorption requires hydrolyzing them into monoglutamates. Intestinal glutamate carboxypeptidase II, also referred to as folate hydrolase, is responsible for this. The monoglutamate forms can then be moved across the mucosa after this has happened [16]. The proximal section of the small intestine is **where folic acid and folate are absorbed [13] Additional studies conducted in the years** 1980 and 1990 showed which supplementing mothers Using folic acid-containing multivitamins decreases the development or recurrence of NTD [17], "The United States Preventative Services Task Force" USPSTF concluded with high confidence that

for women who are planned or capable of becoming pregnant, the net benefit of daily folic acid supplementation to prevent NTDs in the developing baby is substantial." according to a recommendation released by in January 2017 by the (USPSTF) [18]. Similar recommendations have been issued by other reputable institutions, such as the Institute of Medicine IOM formerly referred to as the U.S. Centers for Disease Control [19].

2.1. Sacral dimples

Sacral dimples are the more frequent cutaneous anomalies discovered when performing spinal exams on newborns. They are described as shallow or deep depressions that form in the lower sacral area, either inside or adjacent to the natal cleft. An opening in the vertebral arch that may allow for the herniation of meninges, cystic masses, the spinal cord, or nerves is a characteristic of spina bifida, a form of nontraumatic cerebral degeneration. The degree of severity varies according to the quantity of neural tissue. that emerges via the opening arch(es), Potential disabilities of spina bifida include hydrocephalus, motor function impairment, and bladder and bowel dysfunction , Sacral dimples on their own are harmless. Most of these pathways end in dermoid or epidermoid cysts [20].

3. TYPES SPINEA BIFIDA DERECT

Four defect-defined subgroups of spina bifida can be distinguished: occulta, closed spinal dysraphism, meningocele, and myelomeningocele. Spina bifida is marked by an aberrant spinal column opening (bifid) [21]. Occulta, the first type of spina bifida, is a closed, asymptomatic NTD caused by a vertebral abnormality that permits the vertebral column to open up. Usually hidden by a layer of skin, the deformity occasionally has a dimple or hairy patch next to it. Closed spinal dysraphism, the second kind of spina bifida, is a closed NTD that also involves abnormalities of the meninges covering the spinal cord, fat, or bone, and a deficit of at least two vertebral arches. The third type of spina bifida, known as meningocele, is a closed NTD caused by the extrusion of a cerebrospinal fluid pocket that is surrounded by the meninges through the posterior vertebrae or skull. A meningocele is an extrusion that lacks any neural components and can be skin-covered or uncovered. Myelomeningocele, the fourth kind of spina bifida, is an open or closed NTD that develops from meninges, neural components, and cerebrospinal fluid extruding through posterior vertebrae that may or may not be meningeally contained [21]. The most common and severe form of spina bifida is called myelomeningocele because amniotic fluid is exposed to the protruding

neural structures. Significant impairments such fecal incontinence, hydrocephalus, and dysfunction related to the urology, motor, musculoskeletal, and sensory systems may eventually arise from this exposure [22].

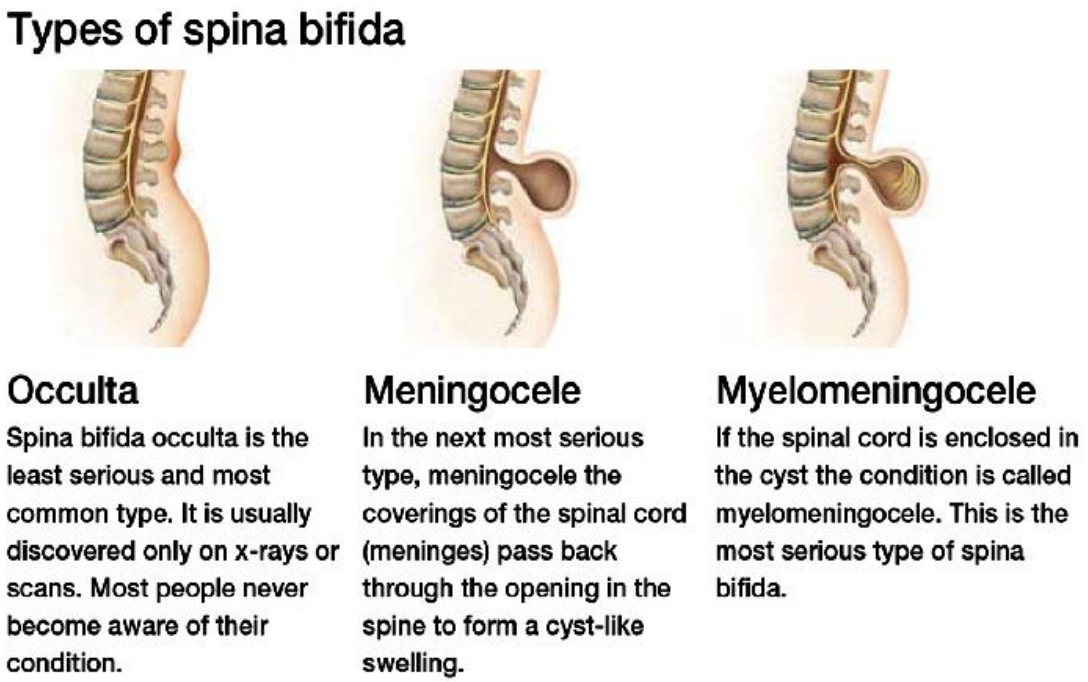

Fig. 1. Types of spaina bifida(23).

3.1. Spina bifida and folic acid deficiency

The embryo's aberrant Defects in the neural tube's creation are caused by the central nervous system's development. The trio of germ layers within an embryo are created by the process of gastrulation during the third fortnight of development of an embryo. Ectoderm development results in the formation of the neural plate. one of these germ layers through the processes of primary and secondary neurulation, this neural plate continues to develop, enabling the neural tube to develop from the neuronal layer [22]. The brainstem gives rise to the The neural tube's cranial segment, which houses the brain and spinal cord, during primary neurulation. The sacral and coccygeal regions of the neural tube comprise the caudal portion. develops during the 26th day of gestation, and is aided in its development by mesenchymal stem cell differentiation during secondary neurulation [21]. The notochord and surrounding tissue include signaling channels that control this neural tube formation process. These signaling pathways cause the neural tube to close, bringing together several regions at once in a manner akin to a zipper [22]. The two main types of NTDs, which are failures in the neural tube formation process, are closed and open

defects. The latter is characterized by the exposure of neural tissue and the leakage of CSF fluid [23].

4. PREVENTION

Spina bifida cannot be fully prevented in a single method. Conversely, however, supplementing with the vitamin folic acid has been linked to a lower risk of of spina bifida. Fruits, green vegetables, whole grains, dry beans, and cereals are common sources of folic acid [24]. In the United States, grain products have required folic acid enrichment since 1998. The U.S. Before and after three months, women ought to consume 0.4 mg of folic acid every day,according to the Food and Drug Administration of pregnancy [25]. Canadian Public Health Agency [26] and United Kingdom [24]. On the other hand, According 0.4–0.8 mg/day, according to the US Preventive Services Task Force. Approximately 0.1 mg should be taken daily by women who are of reproductive age [27]. Folic acid supplementation should be increased for women on anticonvulsant medication if they having previously delivered a child (4–5 mg/day) with spina bifida [24].

5. EXAMINATION AND PROGNOSIS

- Pregnancy and the postpartum period both require screening tests for congenital anomalies such as spina bifida and antenatal evaluation.
- Test for MSAFP stands for maternal serum alpha-fetal protein.

The examination referred to as maternal serum alpha-fetoprotein, or MSAFP helps detect The myelomeningocele [28]. Abnormally elevated AFP levels in the blood suggest that the infant may have spina bifida [28], which calls for two additional tests: an amniocentesis using the amniotic fluid of the mother and a fetal spine ultrasound to check for acetylcholinesterase and alpha-fetoprotein. AFP testing in California is already required by state law [29].

5.1. Ultrasound

In this examination, on a computer screen, Images of bodily tissue in black and white are produced. using high-frequency sound wave bounce. The information in these pictures can be used to determine gestational age and the impact of several pregnancies on AFP levels. Ultrasound is a useful tool for

diagnosing and evaluating spina bifida in skilled hands these days. Mother and child can both safely use ultrasound [28].

5.2. Amniocentesis

A needle is used to extract amniotic fluid from the amniotic sac that surrounds the fetus during this process. Traces of AFP are commonly found in amniotic fluid. However, in an open neural tube lesion, AFP leaks into the amniotic sac and increases the AFP levels in the fluid because the baby's spine lacks skin. In general, this screening is recommended when the blood AFP level is elevated but the ultrasound report is normal [28].

6. High Line Studies Regarding the Management of Spina Bifida

Aijun Wang and the head of the Veterinary Institute for Regenerative Cures at the University of California, Dori Borjesson, developed a novel therapy in 2017 that combines surgery, which is a significant step for both humans and dogs, with cellular therapy with mesenchymal stromal cells (MSCs) obtained from the placenta of dogs. This therapy was applied to two English bulldog puppies that had spina bifida. With the exception of incontinence issues, spina bifida was successfully healed by them. Later, Diana Farmer used human PMSCs in conjunction with prenatal surgery to effectively treat a lamb that had been diagnosed with walking issues;. The lamb appeared to be healthy at birth. Therefore, they anticipate that the findings of their investigation will to the near-term eradication of spina bifida in humans and dogs(30].

CONCLUSIONS

Although there is currently no cure for spina bifida, there are a few methods that can be used to control the disease's severity. Since spina bifida occulta is the least severe type, children with it do not need to be treated. When treating children with spina bifida meningocele, surgery is typically the best option because untreated cases can result in hydrocephalus, bladder issues, or even an overabundance of fluid in the brain, which can lead to mental retardation or mobility abnormalities. Myelomeningocele, spina bifida's most severe variation, can induce hydrocephalus and spinal cord tethering, which can impair The capacity of a youngster to use their legs, bladder, and bowel muscles. In this instance, regaining function might need surgery. Urine draining catheterization is a treatment option for children with bladder function issues [3]. Treatment is therefore based on the diseases' symptoms, signs, and severity.

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