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The Effect of Phosphoric Acid on the Development of Neural Tube Defects in Chick Embryos

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Introduction: Neural tube defects (NTDs) are among the most common congenital malformations and arise from disruption of early neurulation. Phosphoric acid is a widely used food additive; however, its potential effects on early neural tube development have not previously been evaluated in experimental neurulation models. This proof-of-concept study aimed to investigate the embryotoxic and teratogenic effects of phosphoric acid on neural tube development in a chick-embryo model of neurulation, at a single tested concentration.

Material/Methods: Fertilized pathogen-free chicken eggs (n=30) were randomly allocated into 2 groups. Control embryos (n=15) received no injection, whereas embryos in the experimental group (n=15) were injected beneath the embryonic disc with 0.25 mM phosphoric acid, at Hamburger-Hamilton stage 9. Embryos were incubated for 72 hours, after which survival was recorded and neural tube development was evaluated macroscopically and histopathologically. Statistical comparisons were performed using Fisher's exact test.

Results: All control embryos survived (15/15, 100%) and exhibited normal neural tube closure. In the phosphoric acid–treated group, survival was significantly reduced (10/15, 66.7%; P=0.0421). Among surviving treated embryos, 80% (8/10) demonstrated NTDs, including cranial and caudal closure abnormalities (P<0.001). Histopathological examination confirmed incomplete neural fold closure, irregular notochord morphology, and disrupted somite organization in affected embryos.

Conclusions: Phosphoric acid exposure at the tested concentration and developmental stage markedly reduced embryo survival and induced a high incidence of neural tube closure defects in a chick-embryo model. These findings provide the first experimental proof-of-concept evidence that phosphoric acid can directly disrupt early neurulation in a vertebrate neurulation model. However, vehicle-controlled replication, dose–response analyses, and exposure-bridging studies are required to distinguish teratogenic specificity from general embryotoxicity and to assess potential relevance to human embryogenesis.

Keywords: Animal Experimentation • Chick Embryo • Embryology • Food Additives • Neural Tube Defects • Phosphoric Acids • Teratogens

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Introduction

Neural tube defects (NTDs) rank among the most common congenital anomalies worldwide, producing severe lifelong disabilities, significant healthcare expenditures, and high rates of perinatal and childhood mortality [1]. Each year, approximately 300 000 infants are affected worldwide, although prevalence varies widely depending on geography, socioeconomic conditions, and public health interventions, ranging from as low as 0.2 to as high as 11 per 1000 live births. Importantly, epidemiological studies indicate that NTDs are consistently more frequent in female than in male newborns [2,3]. Clinically, the 2 most prominent forms are spina bifida, in which the spinal column remains incompletely closed, and anencephaly, a severe defect characterized by absent or rudimentary brain development due to anterior neural tube closure failure [4].

The etiology of NTDs is complex and multifactorial, with both genetic predispositions and environmental influences contributing to pathogenesis. Among the most recognized risk factors is folic acid deficiency, which disrupts nucleotide biosynthesis and DNA methylation, thereby interfering with normal neurulation. Other maternal conditions such as hyperthermia, obesity, and exposure to teratogenic drugs also increase the risk. For example, antiepileptic medications including valproic acid and carbamazepine are known to antagonize folate metabolism, while cocaine exposure has been linked to vascular compromise and impaired embryonic development. In addition, methylenetetrahydrofolate reductase (MTHFR) polymorphisms can reduce folate bioavailability, further predisposing the embryo to closure defects [5,6]. Experimental teratology studies have provided further evidence, showing that agents such as alcohol, salicylates, clomiphene, insulin, chemotherapeutic drugs, and even certain viral infections, including influenza, are capable of disrupting neural tube formation [7].

Phosphoric acid (H_3PO_4) is a simple inorganic acid composed of phosphorus, oxygen, and hydrogen atoms. It is colorless, odorless, fully soluble in water, and widely applied in diverse industrial sectors including fertilizers, chemical processing, pharmaceuticals, and automotive manufacturing. Within the food industry, it is among the most extensively utilized additives. Phosphoric acid serves multiple functions: it regulates acidity in carbonated beverages, stabilizes and preserves processed meats such as sausages and salami, prolongs shelf life in canned goods, and improves texture and flavor balance in dairy products such as cheese. Although regulatory agencies generally consider phosphoric acid safe at controlled concentrations, evidence has accumulated linking excessive intake to adverse systemic outcomes. These include bone demineralization, calcium-phosphate imbalance, renal impairment, and potential systemic toxicity [8-11]. Particularly concerning is the observation that children, adolescents, and women of reproductive age constitute the largest groups consuming carbonated soft drinks containing phosphoric acid, raising questions about long-term developmental effects.

Despite this widespread dietary exposure, the possible teratogenic effects of phosphoric acid have never been directly examined. Previous investigations into other common food additives have produced conflicting results: for instance, tartrazine was reported to induce NTDs in chick embryos, whereas sodium benzoate did not [12,13]. Notably, phosphoric acid has remained untested in experimental models of vertebrate neurulation, despite decades of extensive dietary exposure. This represents a clear and previously unaddressed gap in experimental teratology.

Based on principles of developmental toxicology, we hypothesized a priori that exposure to phosphoric acid during the critical window of neurulation (Hamburger-Hamilton stage 9) would increase embryotoxicity and disrupt neural tube closure in a chick-embryo model. This hypothesis was biologically motivated by the potential for pH-dependent cellular stress, phosphate-related metabolic perturbations, and interference with tightly regulated processes required for neural fold elevation and closure during early embryogenesis, and potential indirect interference with folate-dependent one-carbon metabolic pathways, which are critical for neural tube closure.

Accordingly, the present study was designed as a proof-of-concept experimental investigation to evaluate the effects of phosphoric acid on embryo survival and neural tube development in a chick-embryo model. This model provides direct access to early developmental stages and allows precise assessment of neurulation, making it a well-established system for investigating environmental and chemical influences on early embryogenesis. Importantly, the scope of this study is limited to experimental teratogenicity within a controlled vertebrate model and does not aim to assess dietary exposure relevance or risk in human pregnancy.

Material and Methods

Study Design

This study was conducted in collaboration with the Department of Histology and Embryology, Hamidiye Faculty of Medicine, University of Health Sciences. In this experimental study, fertilized, pathogen-free chicken eggs were used for incubation and injection (Bornova Veterinary Control and Research Institute, İzmir, Türkiye). Eggs were randomly assigned to groups using a computer-generated random sequence to ensure unbiased distribution. Given the exploratory nature of the study, a formal a priori power analysis was not performed. The sample

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size was determined in line with previous chick-embryo teratology studies using comparable group sizes.
Group A (Control group): No phosphoric acid was administered (n=15).
Group B (Experimental group): 0.25 mM phosphoric acid (approximately 25 µL of 1 M phosphoric acid solution per 1 L) was injected (n=15).

Physiological saline was employed as the vehicle for phosphoric acid administration. However, a saline-injected vehicle control group was not included in the study. Therefore, potential effects related to the injection procedure itself, including needle manipulation and fluid volume, cannot be fully excluded. Accordingly, the findings should be interpreted as reflecting the effects of phosphoric acid exposure within the context of the injection procedure rather than isolating the chemical effect alone.

Phosphoric Acid Dose

The dose was determined based on the range (0.05-0.5 mM) reported in the literature as safe for embryonic cultures. During a preliminary screening phase, low (0.05 mM), medium (0.25 mM), and high (0.5 mM) concentrations were evaluated to assess gross embryonic tolerance and neurulation outcomes. Based on this exploratory screening, 0.25 mM was selected as the lowest concentration associated with consistent neural tube disruption and was therefore used in the main experiment. Phosphoric acid (H_3PO_4 from İPEK-KİMYA, Formula 10.5, CAS No: 7664-38-2, concentration: 85%) was diluted with sterile physiological saline to achieve the desired concentration. This exploratory screening was not powered for formal statistical inference and was used solely to guide selection of a single concentration for proof-of-concept testing.

Incubation and Injection

Eggs (average weight 65±2 g) were incubated at 37.2±0.1°C with 60-70% humidity for 24 hours, reaching stage 9 according to the Hamburger-Hamilton classification [14]. Temperature and humidity were continuously monitored using the incubator's digital sensors and verified daily with an external calibrated thermometer/hygrometer. Deviations were corrected immediately to maintain stable conditions. Under a stereomicroscope at 4×magnification, the eggshells were carefully opened under sterile conditions, and the embryonic discs were identified. To maintain consistency and minimize variability, a volume of 0.1 mL of the prepared solution was injected beneath the embryonic disc using a sterile 24-gauge syringe. Following injection, the eggs were resealed with sterile adhesive tape and returned to the incubator for an additional 72 hours. At the end of this period, embryos were dissected from the surrounding membranes and examined macroscopically and histopathologically for neural tube development.

Histopathological Evaluation

At 72 hours, embryos were fixed in 4% formalin for 24 hours, dehydrated in a graded ethanol series (70%, 95%, 100%), cleared in xylene, and embedded in paraffin. Serial sections of 5 µm thickness were prepared using a rotary microtome. Sections were deparaffinized in xylene, rehydrated through descending ethanol concentrations, and stained with hematoxylin and eosin (H&E). Slides were mounted with Entellan® (Merck) and examined under a Zeiss Axiocam light microscope. NTDs were defined as persistent failure of neural fold closure, the presence of an open neural plate, or abnormal notochord and somite organization. All evaluations were performed in a blinded manner, where the pathologist was unaware of the treatment groups to prevent bias. Group codes were concealed during macroscopic scoring and histopathological assessment.

Statistical Analysis

Data were analyzed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA). Survival rates and the incidence of NTDs were compared between groups using Fisher's exact test. Fisher's exact test was specifically chosen as it is the most robust and accurate method for analyzing categorical data with small sample sizes. A P-value <0.05 was considered statistically significant. Results were expressed as absolute numbers and percentages. No correction for multiple comparisons was required, as only 2 groups were analyzed. All histopathological and statistical evaluations were performed in a blinded manner. Embryolethality (based on survival at 72 hours) and neural tube malformation were predefined and analyzed as distinct experimental endpoints.

Results

Survival

At 72 hours of incubation, all embryos in the control group survived (15/15, 100%). In the phosphoric acid group, survival was significantly reduced, to 10/15 (66.7%) (Fisher's exact test, P=0.0421). Odds ratio (OR) analysis with Haldane-Anscombe correction indicated reduced survival odds in the phosphoric acid group compared with controls (OR 0.062; 95% CI 0.003-1.236).

Neural Tube Defects

No anomalies were observed in the control group. In contrast, among the 10 surviving embryos in the phosphoric acid group, 8 (80%) exhibited NTDs. The difference in incidence was statistically significant (Fisher's exact test, P=0.0000416). The odds of developing NTDs were markedly increased in the phosphoric

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acid group (OR 105.4; 95% CI 4.52-2458.5). When calculated relative to the total number of treated embryos, NTDs were observed in 8 of 15 embryos (53.3%), providing a sensitivity analysis that accounts for embryolethality-related censoring. The magnitude of both survival reduction and neural tube defect incidence observed in this study appears greater than that reported in most prior chick-embryo teratogenicity studies involving food additives or environmental exposures, highlighting the distinct strength of the observed effect. These findings directly support the a priori hypothesis that phosphoric acid disrupts early neurulation within this experimental model.

Histopathological Findings

Control embryos demonstrated intact neural tube morphology with well-formed notochord and somites (**Figure 1A**). In the phosphoric acid group, embryos exhibited neural tube closure defects, irregular notochord morphology, incomplete ectodermal invagination, and disorganized somite development (**Figure 1B-1D**). As shown in **Figure 2**, the high incidence of defects in survivors highlights the strong disruptive effect of the tested dose on neural tube development within this experimental model. NTDs in the phosphoric acid–treated embryos demonstrated heterogeneous phenotypic severity. Defects were classified descriptively as mild (partial neural fold elevation without complete closure), moderate (persistent open neural tube with localized notochord irregularity), or severe (extensive cranial and/or caudal non-closure accompanied by marked notochord and somite disorganization). Anatomically, defects involved the cranial region, caudal region, or both, indicating non-uniform disruption of neurulation rather than nonspecific toxicity.

Statistical Summary

Survival and NTD incidence are presented in **Table 1**. Per-embryo survival status, developmental stage confirmation, anatomical localization of defects, and histopathological scoring were recorded for all embryos and are summarized in the figures and tables presented.

Data are presented as number of embryos and percentages. Survival was recorded at 72 hours, and NTD incidence was calculated among surviving embryos. Fisher's exact test results were: survival (P=0.0421); NTD incidence (P=0.0000416). Odds ratios estimated with Haldane-Anscombe correction were: survival OR 0.062 (95% CI 0.003-1.236); NTD incidence OR 105.4 (95% CI 4.52-2458.5). NTD incidence is presented both among surviving embryos and relative to the total number of treated embryos to distinguish malformation from embryolethality (**Figure 2**).

Discussion

In this study, exposure of chick embryos to 0.25 mM phosphoric acid resulted in reduced survival (66.7% vs 100% in controls) and a markedly increased incidence of NTDs, affecting 80% of surviving embryos. No anomalies were observed in controls. These findings indicate a strong disruptive effect of phosphoric acid on embryo survival and neural tube development within this vertebrate model. However, confidence intervals were wide due to the limited sample size, and effect size precision should therefore be interpreted cautiously. In the absence of a saline-injected vehicle control and dose–response analysis, it is not possible to fully distinguish teratogenic specificity from generalized embryotoxicity in this experimental model.

NTDs are among the most frequently encountered congenital birth defects, and they significantly contribute to lifelong disabilities, impose considerable medical care costs, and play a role in increasing both perinatal and childhood mortality rates (4). NTDs represent the second most common congenital malformation that affects the development of the human central nervous system. The global prevalence of these defects has been estimated at approximately 2 cases per 1000 live births, which corresponds to about 214 000-322 000 affected pregnancies every year around the world. The prevalence as well as the adverse clinical and socioeconomic consequences of NTDs are reported to be particularly higher in developing countries, where access to preventive measures and nutritional supplementation may be more limited [4,15].

NTDs occur during the fourth week of embryonic development due to the failure of fusion of either the anterior or posterior neuropores. This incomplete closure results in the formation of a persistent communication between the amniotic cavity and the spinal canal. When the cranial region of the neural tube does not close properly, a substantial portion of the brain fails to develop, and this severe defect is termed anencephaly. Conversely, when the defect arises from the failure of closure at some level caudal to the cervical region of the neural tube, the condition is defined as spina bifida. Classically, NTDs are divided into 2 major subgroups, open and closed defects, and they present with a highly variable prognosis depending mainly on the anatomical site of the lesion. In addition to the nervous system, NTDs may involve the meninges, bone, muscle, or skin. Typically, these defects emerge during the third or fourth week of embryogenesis, when the neural tube is expected to complete its closure [16].

The exact pathogenesis of NTDs has not yet been completely elucidated. It is generally accepted that there are multiple risk factors, encompassing both genetic predispositions and non-genetic environmental influences, that contribute to the

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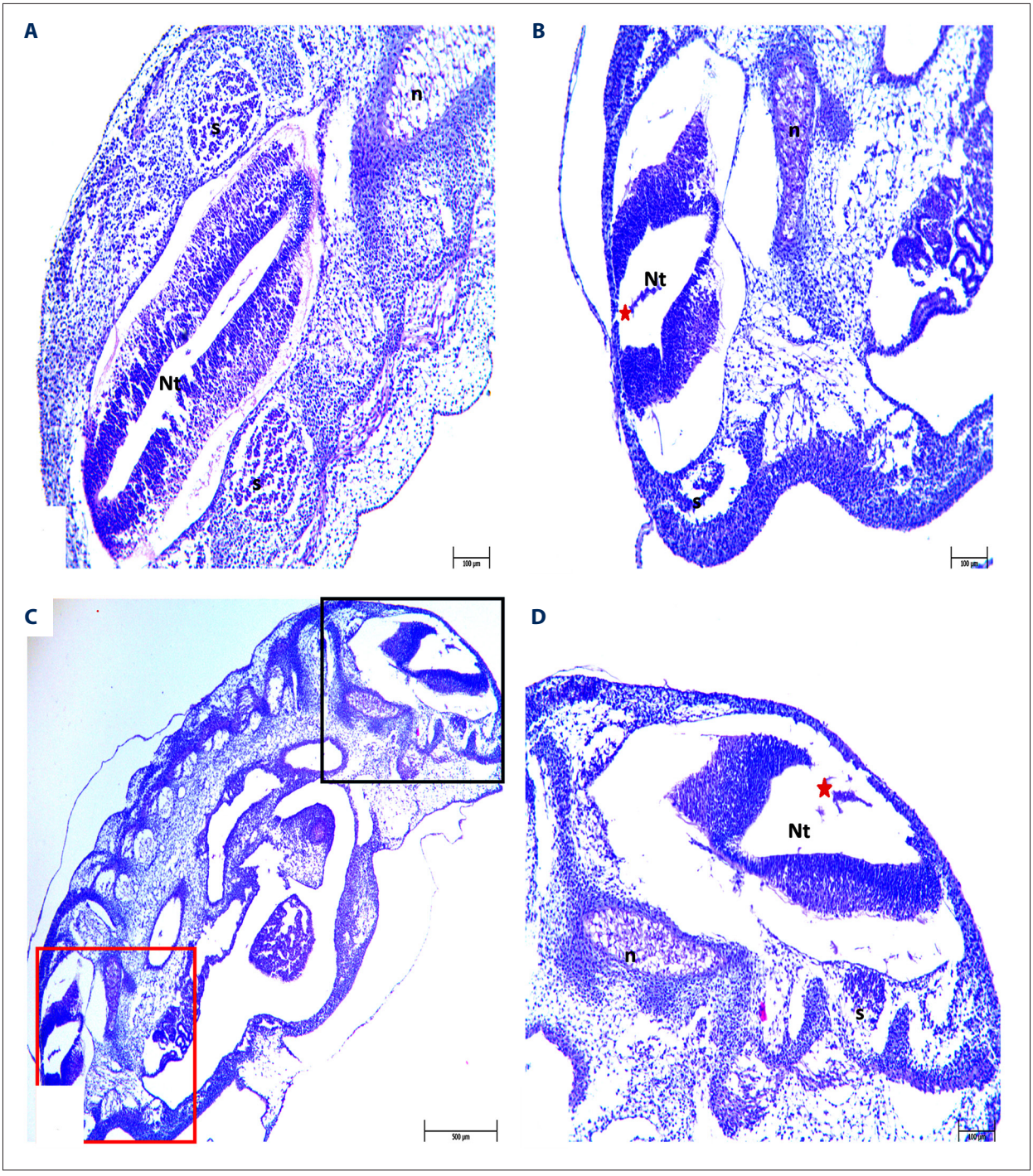

Figure 1. Histopathological evaluation of neural tube development in chick embryos (H&E staining). (**A**) Control embryo showing intact neural tube (Nt), notochord (n), and somites (s). Scale bar=100 µm. (**B**) Caudal region of a phosphoric acid–treated embryo with closure defect (red star). Scale bar=100 µm. (**C**) Treated embryo with multiple closure abnormalities; red rectangle=magnified region in (**B**), black rectangle=magnified region in (**D**). Scale bar=500 µm. (**D**) Cranial region of a treated embryo with a closure defect (red star). Scale bar=100 µm. H&E – hematoxylin and eosin.

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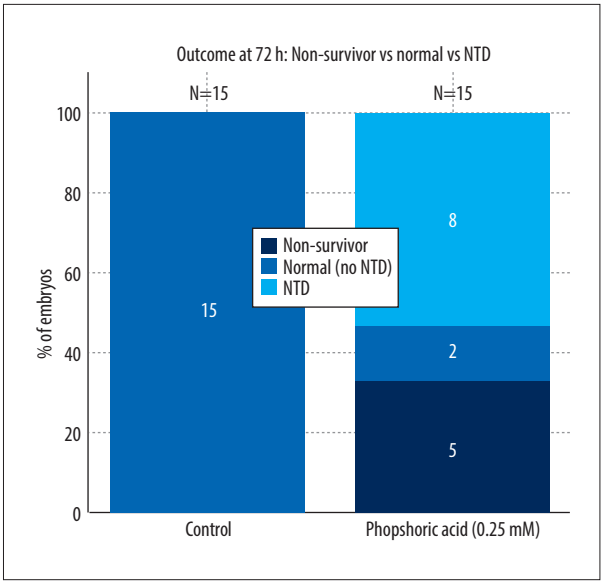

Figure 2. Survival and neural tube defect (NTD) incidence at 72 hours in control (n=15) and phosphoric acid–treated (n=15) chick embryos. Bars indicate percentages of survivors, non-survivors, and NTD-positive embryos among survivors.

occurrence of NTDs. Within the etiology, folic acid deficiency plays a particularly critical role. It has been well established that the early administration of 0.4 mg of folic acid daily during the prenatal period can significantly reduce the risk of NTDs. On the other hand, exposure to high temperatures such as through the use of hot bags, sauna bathing, or febrile illness, maternal intake of valproic acid during pregnancy, maternal obesity, cocaine use, and the administration of folate antagonists (for example carbamazepine) are factors that increase the risk of NTD formation. Moreover, in mothers carrying the 5,10-methylenetetrahydrofolate gene polymorphism, folate levels are typically lower, and this reduction in folate availability further increases the risk of NTDs [6].

Folate (vitamin B9) deficiency is widely recognized as the most important cause leading to an increased incidence of NTDs, although the precise underlying molecular mechanisms remain incompletely understood. Folate deficiency results in DNA hypomethylation, and at the same time interferes with the synthesis of 2'-deoxythymidine-5'-monophosphate (dTMP). This disruption subsequently increases the misincorporation of uracil bases into DNA, which leads to base mismatches, DNA strand breaks, and genomic disorders. To prevent these abnormalities, DNA repair mechanisms are required. Consequently, genomic instability or the absence of adequate DNA repair functions plays a decisive role in the occurrence of NTDs [17].

Folate deficiency, both in the preconception period and during pregnancy, represents the most common preventable risk factor. Folic acid is essential for neural tube formation, particularly during the early stage of pregnancy, approximately 28 days after conception, a period in which the majority of women are still unaware that they are pregnant. In accordance with this, current international guidelines recommend that all women planning pregnancy, or those who may potentially become pregnant, should take a daily supplement containing 400-800 µg of folic acid [15].

Several experimental studies have been conducted using chick embryos to investigate the impact of environmental factors, food additives, and pharmacological agents on the development of NTDs. Nevertheless, the number of studies focusing specifically on the potential effects of food additives commonly found in daily dietary intake remains limited. This lack of data highlights the importance of conducting more experimental work in this area. For instance, Ovalioglu et al demonstrated that tartrazine induced the development of NTDs in chick embryos. In contrast, Emon et al reported that sodium benzoate did not cause NTD development in the same model. When comparing our results with previous literature, phosphoric acid appears to have a more pronounced teratogenic effect than sodium benzoate, which did not induce NTDs in similar chick models. In the present study, we similarly employed the chick embryo model and evaluated the effect of phosphoric acid on the development of NTDs [12,13,18-20]. Although cross-study comparisons are inherently indirect, the high defect rate observed here appears greater than that reported for several other food additives evaluated in similar chick-embryo models.

Table 1. Survival and incidence of neural tube defects in control and phosphoric acid groups.

Group	Eggs incubated	Survived at 72 h, n (%)	Normal (survivors) n (%)	NTD+ (survivors) n (%)
Control	15	15 (100)	15 (100)	0 (0)
Phosphoric acid	15	10 (66.7)	2 (20)	8 (80)
Total	30	25 (83.3)	17 (68)	8 (32)

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Phosphoric acid (H_3PO_4) is an inorganic acid that is colorless, odorless, and exists in either liquid or crystalline form. It is completely soluble in water and possesses a strong acidic nature. Owing to this acidic property, phosphoric acid has a wide range of applications across multiple industrial fields. It is extensively used in the food, agricultural, chemical, pharmaceutical, metal, and automotive industries. Within the food sector, phosphoric acid is especially common as an acidity regulator and preservative. For example, it is utilized to balance taste in carbonated beverages, to prolong shelf life in cheese and other processed food products, and to prevent spoilage by functioning as a preservative. While generally regarded as safe for use in food and beverages under regulated conditions, excessive consumption of phosphoric acid has been associated with potential health problems [8-11].

In this study, we demonstrated for the first time that phosphoric acid, when administered at the tested dose, induced NTDs in chick embryos. This novel finding underscores the importance of further experimental evaluation of widely used food additives in controlled vertebrate models, rather than implying direct relevance to human dietary exposure or pregnancy risk.

Limitations

This study has several limitations. First, only a single concentration of phosphoric acid was administered, which precluded assessment of dose–response relationships. Second, the follow-up period was limited to 72 hours, preventing evaluation of later developmental stages and the persistence of defects over time. Third, although the chick-embryo model is widely used in experimental teratology because of its accessibility and well-characterized stages, it does not fully replicate mammalian embryogenesis. Therefore, extrapolation of these findings to human pregnancy should be made with caution. Finally, although previous reports indicate that saline injections alone do not affect survival or neural tube development in this model [11,12], vehicle-injected controls were not included; therefore, we cannot completely exclude a minor procedural effect of injection. However, the magnitude of the observed differences suggests a treatment-related effect.

Future Directions

Further studies should investigate different phosphoric acid concentrations to establish dose–response relationships. Extending incubation beyond 72 hours would enable evaluation of long-term developmental outcomes and the persistence or resolution of NTDs. Molecular analyses of oxidative stress, DNA damage, and apoptotic pathways may help elucidate the mechanisms by which phosphoric acid disrupts neurulation. Comparative experiments in mammalian models will also be important to clarify the translational relevance of these findings to human pregnancy. Given the widespread use of phosphoric acid in processed foods, future translational research is critical to determine potential risks for human embryonic development.

Conclusions

This study provides the first experimental, proof-of-concept evidence in a vertebrate neurulation model that phosphoric acid can disrupt early neural tube closure when administered during a critical developmental window. The findings demonstrate a strong internal effect at the tested dose and time point, while also highlighting important methodological limitations, including the absence of vehicle-injected controls, dose–response assessment, and exposure-bridging analyses. Accordingly, these results should be interpreted within the context of experimental teratology and do not permit conclusions regarding human dietary exposure or pregnancy risk. Further studies incorporating vehicle-controlled replication, dose–response designs, mechanistic analyses, and translational exposure modeling are required to clarify the biological specificity and broader relevance of these findings.

Ethical Approval

Per Official Gazette No. 28914 (15 Feb 2014), chick-embryo experiments conducted before the last one-third of incubation are exempt from animal ethics approval.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Informed Consent

This type of study does not require informed consent.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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References:

1. Özcan İ, Yücel M, Kahveci H. Retrospective examination of infants with congenital neural tube defect. Cureus. 2023;15:e48886
2. Ravi KS, Hassan SB, Pasi R, et al. Neural tube defects: Different types and brief review of neurulation process and its clinical implication. J Fam Med Prim Care. 2021;10:4383-90
3. Büyükbayrak EE, Akalın M, Dağçınar A, Sakar M. Açık spina bifidalı fetüslerde intrauterin cerrahi tedavi. Maternal-Fetal Tıp ve Rehabilitasyon Derneği Uzman Görüş. Derleme. 2025;1-14; Available from: https://tmftp.org/uploads/acik-spina-bifidali-fetuslerde-intrauterin-cerrahi-tedavi-uzman-gorusu.pdf [in Turkish]
4. Avagliano L, Massa V, George TM, et al. Overview on neural tube defects: From development to physical characteristics. Birth Defects Res. 2019;111:1455-67
5. Au KS, Ashley-Koch A, Northrup H. Epidemiologic and genetic aspects of spina bifida and other neural tube defects. Dev Disabil Res Rev. 2010;16:6-15
6. Greenberg MS. Primer craniospinal anomalies. In: Greenberg MS (ed), Handbook of Neurosurgery, 10th ed. New York: Thieme, 2023;295-316
7. Canbek İ. Spinal disrafizmler-meningosel ve meningomyelosel. In: Karabekir HS (ed), Pediatrik Nöroşirürji – Konjenital Anomaliler, 1st ed. Ankara. Türkiye Klinikleri, 2025;45-51 [in Turkish]
8. Çakmakçı S. Gıda katkı maddesi olarak fosfatlar. Gıda. 1994;19:67-71 [in Turkish]
9. Ünlü D, Bayır AG. Koruyucu gıda katkı maddeleri ve sağlığa etkisi. Akademik Et ve Süt Kurumu Dergisi. 2022;4:55-68 [in Turkish]
10. Ayışkan Ö. Fosfat cevherleri-değerlendirme ve fabrikasyonları. Sci Mining J. 1972;11:53-57 [in Turkish]
11. Berker E. Fosfat kimyası, kullanılış alanları ve süper fosfat. Bilimsel Madencilik Dergisi. 1972;11:59-62 [in Turkish]
12. Ovalioglu AO, Ovalioglu TC, Canaz G, et al. Effects of tartrazine on neural tube development in the early stage of chicken embryos. Turk Neurosurg. 2020;30583-87
13. Emon ST, Orakdogen M, Uslu S, Somay H. Effects of the popular food additive sodium benzoate on neural tube development in the chicken embryo. Turk Neurosurg. 2015;25:294-97
14. Hamburger V, Hamilton HL. A series of normal stages in the development of the chick embryo. J Morphol. 1951;8849-92
15. Kancherla V. Neural tube defects: A review of global prevalence, causes, and primary prevention. Childs Nerv Syst. 2023;39:1703-10
16. Yay A, Önder GÖ. Merkezi sinir sistemi embriyolojisi. In: Avcı E (ed), Temel Nöroşirürji, 1st ed. Ankara: Temel Nöroşirürji Derneği Yayınları, 2023;1783-99 [in Turkish]
17. Wang X, Yu J, Wang J. Neural tube defects and folate deficiency: Is DNA repair defective? Int J Mol Sci. 2023;242220
18. Simsek H, Colak A, Kutlay M, et al. The effects of diesel exhaust particles on neural tube development in the early stage chicken embryo. Turk Neurosurg. 2012;22:77-82
19. Cetinkal A, Cakir A. Does gabapentin affect neural tube development? Experimental study using an early stage chick embryo model. Turk Neurosurg. 2021;31:967-72
20. Temiz C, Temiz P, Demirel A, et al. Effect of sodium phenytoin concentration on neural tube development in the early stages of chicken embryo development. J Clin Neurosci. 2009;16:307-11

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