Short Communications

Editorial Process: Submission:05/25/2024 Acceptance:12/07/2024

Serum and Salivary Levels of Phosphate in Gastric and Colorectal Cancer Patients

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Abstract

Objective: Gastrointestinal cancer is one of the most common causes of death worldwide. As there are no clinical symptoms at the beginning of the disease, the diagnosis can be delayed and the stage increased. Timely diagnosis is therefore crucial. Since one of the factors involved in cell division is phosphate, and considering the benefits of using saliva, this study investigated the phosphate concentration in saliva and serum in patients with gastric and colorectal cancer as well as in healthy patients. **Methods:** 26 patients with gastric and colorectal cancer confirmed by pathologic criteria were admitted to the oncology department of Imam Reza Hospital, and 30 healthy individuals participated in this study. Saliva and serum samples were collected in the morning. Phosphate concentration was determined using a photometric method. **Results:** The average phosphate content in serum as well as in stimulated and unstimulated saliva was significantly lower in the patient group. In addition, the results showed that the patients reported more dry mouth than the control group despite increased salivary flow. **Conclusion:** It appears that patients with malignant diseases of the gastrointestinal tract, such as colorectal cancer and gastric cancer, have lower serum and salivary phosphate levels than healthy individuals.

Keywords: Colorectal cancer- gastric cancer- phosphate- serum- saliva

Asian Pac J Cancer Prev, **25 (12)**, 4111-4114

Introduction

Gastrointestinal (GI) cancers are among the most common types of cancer, accounting for approximately 25 percent of cases and having significant death rates. The aging process and environmental factors may create mutations that lead to GI malignancies. In other words, Cell tumor genesis results from the interaction of genetic factors with physical, chemical, and biological factors [1]. Because early-stage GI malignancies do not exhibit typical symptoms, most patients are identified with severe regional lymph node involvement and/or invasion of neighboring tissues in the late stages of the illness. Therefore, early diagnosis is of vital importance for the diagnosis of GI malignancies. A biopsy is the gold diagnostic standard for most tumors, including GI cancers. However, this method has disadvantages such as invasiveness, the need for complex equipment, and incorrect sample evaluation due to the cancerous tissue's different structure. Therefore, the identification and development of a rapid, cost-effective, and non-invasive screening method should be considered [2, 3].

Saliva is a physiologic fluid with the mentioned characteristics that is released by three pairs of salivary glands: parotid, submandibular, and sublingual, or comes from the blood by passive transport [4, 5]. Reduced salivary output may be harmful to the patient since it helps with digestion, moisturizes the oral cavity, and makes speaking easier [6]. Saliva, on the other hand, includes substances such as proteins, antibodies, enzymes, hormones, and metabolites, all of which have been shown in recent research to have promise in the prognosis, diagnosis, and monitoring of patients suffering from various diseases, including cancer [2, 4].

Phosphorus is an extracellular liquid cation that exists in the body in the form of phosphate due to its high reactivity with oxygen. Phosphate is essential for metabolic activities such as cell membrane formation, DNA and RNA molecules, energy metabolism, signal transmission, and pH regulation in the body [7]. Phosphate, like calcium, is regulated by vitamin D3 (vitD) and parathyroid hormone (PTH) and is mostly excreted through the kidneys. Phosphate imbalance is generally induced by one of three factors: low food intake, digestive

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difficulties, or renal excretion disorder which patients with gastrointestinal cancers may have [8]. So, in this study, the phosphate content in serum, unstimulated, and stimulated saliva samples was measured to answer the question of whether phosphate changes in these samples.

Materials and Methods

The ethics committee of Aja University of Medical Sciences (AJAUMS) approved the study protocol (IR.AJUMS.REC.1402.178) and it should be noted that written informed consent was obtained from all participants.

In this cross-sectional study, 26 patients with GI cancer including gastric and colorectal cancer who were referred to Imam Reza Hospital's oncology department in Tehran, Iran in 2023 were included. Patients were chosen using conventional histopathological criteria. In addition, 30 healthy hospital employees participated in the research. Patients with diabetes, hypo or hyperthyroidism, renal disease (chronic kidney disease and/or acute kidney injury), osteoporosis, or periodontal disease were all excluded.

First, all participants answered 11 questions on their dry mouth state (13). The responses to each question were never (scored 1), hardly (2), sometimes (3), fairly often (4), and often (5). The overall score of the dry mouth questionnaire was then computed for each subject to assess the severity of the dry mouth symptoms. The greatest possible score is 55, while the least is 11.

Then unstimulated and stimulated saliva samples were collected from the subjects who were prohibited from eating and drinking one hour before sampling. In non-stimulated saliva sampling, participants were asked to pour their produced saliva into a sterile tube without making mouth movements or sucking. Then, they chewed a piece of natural gum for two minutes and after swallowing the saliva in their mouth, while the gum remained in their mouth, they poured the secreted saliva into the tube. The sample time and volume were properly measured and recorded, and the salivary flow rate was calculated by dividing the saliva volume by the saliva collecting time (ml/min). Then, the nurses took 5 mL of venous blood and put it into the clot tube. All samples were centrifuged at 4000 rpm for 5 minutes, after which the serum and saliva supernatant were carefully transferred into the microtube and frozen at -70°C until the testing time.

Phosphate concentration was determined using a ready-made kit (Biorex, Shiraz, Iran) using the photometric technique specified by the manufacturer. Data was analyzed by unpaired Student's t-test or Mann-Whitney test using SPSS v22.

Results

In this study, 26 patients with gastrointestinal cancer (13 men, 13 women) and 30 healthy people (16 men, 14 women) participated.

There was no significant difference in the unstimulated saliva flow rate between patients and the control group but the stimulated saliva flow rate was significantly higher in patients. However, the xerostomia inventory score in the patient group was significantly higher than the healthy (Table 1).

The mean serum phosphate concentration was significantly lower in the patients (3.29 ± 0.2) than in the healthy group (3.93 ± 0.14) ($p = 0.013$). The mean unstimulated salivary phosphate level was significantly lower in the cancer patients (14.07 ± 1.39) than in the control group (17.94 ± 1.03) ($p = 0.031$). The stimulated salivary phosphate concentration in saliva was also lower in the gastrointestinal malignancies (11.37 ± 0.62) than in the healthy group (13.67 ± 0.9) ($p = 0.048$) (Figure 1)

Discussion

Gastric and colorectal cancers are two prevalent malignancies with a high death rate and growing incidence rates across the world. They have a significant impact on patients' quality of life, thus early detection is advantageous [1, 2]. Phosphate has a function in the construction of cell membranes, DNA, and RNA molecules, and because cancer cells turnover rapidly, it may alter. As a result, measuring the quantity of serum and saliva can aid in the diagnosis and management of the condition [7]. The purpose of this study was to investigate phosphate levels in saliva and serum in patients with gastric and colorectal cancer.

Our investigation found that patients' serum phosphate levels were lower than those of healthy people, which is consistent with the findings of Adhikari et al about malignancies [9].

Also, the current investigation found that patients' phosphate levels in stimulated and unstimulated saliva were significantly lower than those of control volunteers. Azeez et al.'s research on salivary biomarkers in breast cancer showed a significant increase in phosphate levels in patients compared to healthy subjects, which contradicts our findings [10]. The reason for this difference could be

Table 1. Type of Cancer, Stimulated and Unstimulated Salivary Flow Rate, and Xerostomia Inventory Score in Patients with Gastric and Colorectal Cancer and Control Group.

Variable	Control n=30	Patients n=26	p-value
Type of cancer	-	13 gastric cancer 13 colorectal cancer	-
Unstimulated saliva flow rate (ml/min)	0.82 ±0.08	0.98 ±0.07	0.179[a]
Stimulated saliva flow rate (ml/min)	1.79 ± 0.21	2.53 ± 0.28	0.040[a]
xerostomia inventory score	16 ± 4.25	19.5 ± 13.5	0.046[b]

Data are expressed as [a] mean ±s.e.m analyzed by unpaired student t-test, [b] Median ±inter quartile range (IQR), analyzed by Mann-Whitney test.

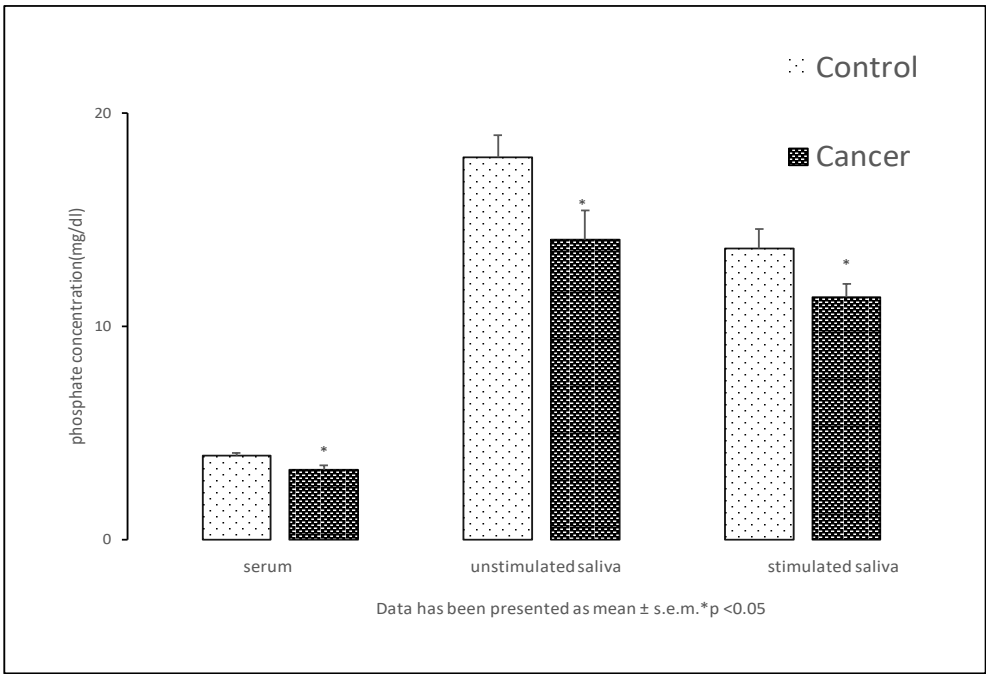

Figure 1. Concentrations of Phosphate in Serum, Unstimulated and Stimulated Saliva of Patients with Gastric and Colorectal Cancer and Control Individuals.

that only women participated in the study by Azeez et al., but both men and women were present in the present study, and studies have proven that the male hormone testosterone can reduce phosphate levels [11].

Most phosphate metabolism is done by PTH and vitD [8]. Studies have shown that PTH levels increase and vitD levels decrease in gastrointestinal cancers [12, 13]. Since the increase of PTH and deficiency of vitD causes a decrease in the absorption of phosphate in the intestines and an increase in its excretion from the kidneys, this can be a reason for the decrease in the serum level of phosphate in gastric and colorectal cancers [9]. On the other hand, as mentioned, the components of saliva originate either from the blood or from the salivary gland cells. As the phosphate concentration in patients' saliva is higher than in serum, it is reasonable to assume that secretion in saliva, like urine, is a way of excreting waste products [4, 5].

An examination of the unstimulated flow of saliva revealed that, despite a small increase in cancer patients, there was no significant difference between the groups. However, stimulated salivary flow was significantly higher in patients. The neurotransmitter acetylcholine regulates the gastrointestinal system by parasympathetic innervation, and studies have indicated that cholinesterase levels are decreased in colon and stomach cancer. As a result, their acetylcholine levels rise, and the salivary glands generate more saliva [14, 15].

This study had limitations, such as not measuring the level of PTH, VitD and cholinesterase in saliva. Therefore, it is suggested that researchers should investigate their levels in patients with gastric and colorectal malignancies by categorizing cancers separately in the future.

In conclusion, it seems that in gastrointestinal malignancies, the concentration of phosphate in serum, unstimulated, and stimulated saliva decreases significantly. Despite the increase in salivary flow, cancer patients feel more dry mouth compared to the healthy group.

Author Contribution Statement

Conceptualization: Mohammad Hossein Hajali, Hamidreza Karbalaei-Musa, Mohammad Arbaghaei; Data curation: Mohammad Hossein Hajali, Hamidreza Karbalaei-Musa; Formal analysis: Iraj Mirzaii-Dizgah, Mohammad Arbaghaei; Investigation: Mohsen Rajaeinejad, Peyman Aslani; Methodology: Iraj Mirzaii-Dizgah, Mohammad Arbaghaei; Validation: Mohsen Rajaeinejad, Peyman Aslani; Writing – original draft: Mohammad Hossein Hajali, Mohammad Arbaghaei; Writing – review & editing: Hamidreza Karbalaei-Musa, Iraj Mirzaii-Dizgah, Peyman Aslani.

Acknowledgements

We are grateful to the staff and patients of Imam Reza Hospital in Tehran for their necessary cooperation.

Ethical approval

Written informed consent was obtained from all subjects involved in the study and the research was conducted in accordance with the principles of the Declaration of Helsinki. In addition, the study protocol was approved by the Ethics Committee of the Aja University of Medical Sciences. The ethical approval code is (IR.AJUMS.REC.1402.178).

Availability of data

The datasets generated and/or analyzed in the present study are available upon reasonable request to the

corresponding author.

Conflicts of interest

The authors declare that they have no conflict of interest.

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