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Vaping-associated mechanisms in the development of gastroesophageal reflux disease

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ABSTRACT

BACKGROUND: There is compelling evidence of the negative impact of vaping on the respiratory and cardiovascular systems. However, its effects on the gastrointestinal tract remain understudied.

AIM: The study aimed to assess the impact of vaping on the functional state of the gastroesophageal zone in healthy individuals compared with patients with gastroesophageal reflux disease (GERD).

METHODS: The study included 90 participants divided into three groups of 30 individuals each. Group 1 consisted of individuals with no gastrointestinal disorders who had been regularly vaping for more than 12 months. Group 2 included patients with GERD. Group 3 (control group) comprised healthy individuals with no harmful habits. Clinical manifestations of reflux syndrome were assessed using validated questionnaires. Participants underwent 24-hour impedance-pH monitoring, and serum levels of gastrin and motilin were measured. Statistical analysis was performed using the Kruskal–Wallis test and Dunn test. Fisher exact test was used for comparing qualitative variables, whereas Spearman correlation coefficient was applied for dependency assessment. The significance threshold was set at $p < 0.05$.

RESULTS: In Group 2 (GERD), a low pH level in the lower esophagus and a high daily frequency of all types of reflux episodes were recorded. Compared with the control group, patients in group 2 had lower serum motilin levels (83.2 [56.9; 99.3] pg/mL vs 189.7 [117.6; 362.3] pg/mL, $p = 0.001$). Vapers had a more pronounced reflux syndrome compared with healthy individuals, with an increased daily number of acidic (54 [39.5; 71] vs 21.5 [18; 28.8], $p = 0.001$) and weakly acidic (7.5 [4.3; 9.8] vs 2 [1; 3], $p = 0.001$) reflux episodes, along with a decrease in esophageal pH levels (4.7 [4.1; 5.9] vs 6.7 [6.2; 6.8], $p = 0.001$).

CONCLUSION: Vaping is associated with an increased number of gastroesophageal reflux episodes, likely due to the suppression of lower esophageal sphincter motility, and may contribute to the development of GERD.

Keywords: vaping; 24-hour impedance-pH monitoring; motilin; gastrin.

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Вейпинг-ассоциированные механизмы развития гастроэзофагеальной рефлюксной болезни

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АННОТАЦИЯ

Актуальность. Имеются убедительные доказательства негативного влиянии вейпинга на состояние дыхательной и сердечно-сосудистой систем. Кроме того, целесообразна оценка гастроэнтерологических аспектов курения электронных сигарет.

Цель. Оценить влияние вейпинга на функциональное состояние гастроэзофагеальной зоны у здоровых людей по сравнению с пациентами, страдающими гастроэзофагеальной рефлюксной болезнью.

Материал и методы. В исследование включены 90 пациентов, которые разделены на три группы по 30 человек. Первую группу составили лица без заболеваний желудочно-кишечного тракта, регулярно (более 12 мес) курящие вейпы. Пациенты 2-й группы страдали гастроэзофагеальной рефлюксной болезнью. В 3-ю группу (контрольную) вошли здоровые лица без вредных привычек. С помощью валидизированных опросников оценивали клинические проявления рефлюкс-синдрома, выполняли суточную pH-импедансометрию, исследование сывороточных уровней гастрина и мотилина. Статистическую обработку проводили с использованием критерия Краскела–Уоллиса и теста Данна. Для сравнения качественных признаков применяли точный критерий Фишера, для оценки зависимостей — коэффициент корреляции Спирмена. В исследовании установлен критерий значимости p <0,05.

Результаты. Во 2-й группе, наряду с симптомами рефлюксной болезни, зарегистрировали низкий уровень pH нижней трети пищевода, высокое суточное число всех типов рефлюксов. В данной группе, в сравнении с контрольной, выявили низкий уровень мотилина в крови (83,2 [56,9; 99,3] пг/мл и 189,7 [117,6; 362,3] пг/мл соответственно, p=0,001).

В группе вейперов, в сравнении со здоровыми, зафиксировали большую выраженность рефлюкс-синдрома и увеличение суточного количества кислых (54 [39,5; 71] и 21,5 [18; 28,8] соответственно, p=0,001) и слабокислых (7,5 [4,3; 9,8] и 2 [1; 3] соответственно, p=0,001) рефлюксов, на фоне снижения уровня pH в пищеводе (4,7 [4,1; 5,9] и 6,7 [6,2; 6,8] соответственно, p=0,001).

Заключение. Вейпинг сопровождается увеличением числа гастроэзофагеальных рефлюксов, вероятно, вследствие угнетения моторики нижнего пищеводного сфинктера и может способствовать развитию гастроэзофагеальной рефлюксной болезни.

Ключевые слова: вейпинг; суточная pH-импедансометрия; мотилин; гастрин.

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BACKGROUND

In recent years, vaping, which is the process of using electronic cigarettes (ECs), vaporizers, and other similar devices, has become widespread [1]. ECs (vapes) encompass a diverse group of battery-powered devices that allow users to inhale aerosolized substances. The vaping process generates an aerosol cloud that contains nicotine and various toxic substances [2]. The growing use of ECs is becoming an increasingly significant medical and social concern due to their exceptionally high prevalence and negative impact on users' health [3, 4]. Previous studies have confirmed the negative effects of vaping on the respiratory and cardiovascular systems [5, 6]. Furthermore, some studies have explored the effects of EC liquids on the digestive system, particularly the possible development of erosive esophagitis. The pathogenesis of vaping-associated esophagitis may be attributed to the effects of nicotine [7]. Given the widespread use of ECs in the population, further studies into the gastroenterological consequences of vaping is warranted.

"Traditional" cigarette smoking is a key factor in the development of gastroesophageal reflux disease (GERD) and its complications [8, 9]. The prevalence of GERD is high, and it significantly impairs patients' quality of life [10]. Furthermore, its pathogenesis is multifactorial, accounting for the inadequate symptom control even with the most advanced pharmacotherapy [11]. Thus, vaping may contribute to GERD development as well as GERD treatment resistance.

This study aimed to assess the impact of vaping on the functional state of the gastroesophageal zone in healthy individuals and compare it to that of patients with GERD.

METHODS

The study was conducted from 2023 to 2024 at the Republican Clinical Hospital No. 1, Izhevsk, Russia. The study included 90 participants who were divided equally into three groups. All patients had undergone esophagogastroduodenoscopy within 2 weeks before being included in the study.

The study protocol and consent form were approved by the Ethics Committee of the Izhevsk State Medical Academy, Ministry of Health of Russia (No: 761; dated September 26, 2023).

The following were the inclusion criteria for Group 1 (Vapers):

- written consent for study participation;
- age between 18 and 50 years;
- regular (daily) vaping EC for >1 year.

The median vaping duration in this group was 18 months (range, 15–24.75), and the median patient age was 23 years (range, 22.3–24). The group included 9 men and 21 women.

The following were the inclusion criteria for Group 2 (GERD patients):

- written consent for study participation;
- age between 18 and 50 years;
- GERD that was clinically confirmed by a gastroenterologist and who had a GerdQ questionnaire score of ⩾8 [12].

The median disease duration in Group 2 was 5 years (range, 4–7), and the median patient age was 41 years (range 37.3–45). The group included 22 women and 8 men. At the time of inclusion, 5 (17%) patients were being regularly administered proton pump inhibitors (PPIs), 14 (46%) patients were intermittently ("as needed") being administered PPIs (mainly omeprazole), and 11 (36%) were not being administered any maintenance therapy.

The following were the inclusion criteria for Group 3 (Control group):

- written consent for study participation;
- age between 18 and 50 years.

The median age in the control group was 26 years (range, 24–29), which included 9 men and 21 women. The three groups were comparable in terms of sex distribution ($p = 0.742$).

The following were the exclusion criteria for all groups:

- Current or past history of smoking conventional cigarettes (participants who vaped ECs were also excluded from the GERD and control groups);
- Evidence of upper gastrointestinal pathology (including erosive esophagitis) on esophagogastroduodenoscopy;
- Severe or uncontrolled arterial hypertension;
- Ischemic heart disease;
- Nasal passage obstruction;
- Coagulopathies; and
- Psychiatric or oncological diseases.

At the start of the study, patients in all three groups underwent the following assessments: GerdQ and GSRS questionnaires (to assess reflux syndrome severity); blood tests (serum levels of gastrin and motilin); and 24-h esophageal pH-impedance monitoring using the Gastroscan-IAM device. The probe was positioned in such a way that the pH sensors were located as follows: one in the cardia of the stomach and two in the esophagus. The level of the lower esophageal sphincter (LES) was determined as the Z-line level on esophagogastroduodenoscopy +5 cm. The study results were analyzed using the Gastroscan software. The pH levels in the lower third of the esophagus were measured, and the total number of gastroesophageal reflux (GER) episodes over 24 h were recorded. Furthermore, the GER type was categorized on the basis of the pH level (acidic, weakly acidic, or weakly alkaline).

Quantitative data are presented as medians and interquartile ranges (25%–75%). Multiple group comparisons were performed using the Kruskal–Wallis test. If significant differences were detected, pairwise comparisons were conducted using the Dunn's test. Fisher's exact test was used to compare the qualitative characteristics of the independent samples. Spearman's rank correlation coefficient was calculated to assess the dependencies. Differences were considered statistically significant if the p-value was <0.05.

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Table 1. The results of the examination of patients smoking electronic cigarettes in comparison with patients with gastroesophageal reflux disease and practically healthy individuals

Parameter	Group 1 (Vapers) (n = 30)	Group 2 (GERD) (n = 30)	Group 3 (Control) (n = 30)	*p* 1–2	*p* 1–3	*p* 2–3
GerdQ score	5.5 (4–7)	12 (11–14)	0 (0–1)	*p* = 0.001	*p* = 0.001	*p* = 0
GSRS reflux syndrome score	4 (2–5)	9 (8–10.6)	0 (0–1)	*p* = 0,001	*p* = 0.001	*p* = 0
pH in the lower third of the esophagus	4.7 (4.1–5.9)	3.5 (2.25–3.9)	6.7 (6.2–6.8)	*p* = 0.001	*p* = 0.001	*p* = 0
Number of acidic reflux episodes (24 h)	54 (39.5–71)	94 (82.3–100.5)	21.5 (18–28.8)	*p* = 0.001	*p* = 0.001	*p* = 0
Number of weakly acidic reflux episodes (24 h)	7.5 (4.3–9.8)	17.5 (12–21)	2 (1–3)	*p* = 0.001	*p* = 0.001	*p* = 0.001
Number of weakly alkaline reflux episodes (24 h)	0.5 (0–1)	3 (1–4)	0 (0–0)	*p* = 0.001	*p* = 0.003	*p* = 0.001
Serum motilin concentration, pg/ml	184.1 (99.1–184.1)	83.2 (56.9–99.3)	189.7 (117.6–362.3)	*p* = 0.001	*p* = 1	*p* = 0.001
Serum gastrin concentration, pg/ml	70.8 (29.8–92.2)	159.8 (135.9–199.9)	76.9 (58.2–97.4)	*p* = 0.001	*p* = 0.361	*p* = 0.001

Note: n, number of patients; *p*, statistical significance for the null hypothesis of no difference between the compared groups; GERD, gastroesophageal reflux disease

RESULTS

The comparative study results of the three patient groups are presented in Table 1.

Patients in Group 2 (nonerosive GERD) exhibited the most pronounced reflux syndrome symptoms (GSRS questionnaire) and highest GerdQ scores. Furthermore, the patients in Group 2 exhibited a significant shift in esophageal pH toward acidity and markedly higher number of acidic, weakly acidic, and weakly alkaline GER episodes over the 24-h observation period than the patients in Groups 1 and 3. The patients in Group 2 had significantly lower serum motilin levels and significantly higher serum gastrin levels than patients in Groups 1 and 3. Furthermore, in Group 2, there were weak negative correlations between the serum motilin concentration and the daily number of acidic reflux episodes (r_s = –0.41; *p* = 0.024) as well as weakly acidic reflux episodes (r_s = –0.40; *p* = 0.027). A weak correlation refers to a coefficient between 0.2 and 0.5.

As per the primary aim of the study, special attention was given to the clinical and functional characteristics of patients in Group 1. Individuals who had been vaping for > 1 year exhibited significantly more frequent and pronounced symptoms of reflux (GSRS and GerdQ scores) than the controls, in whom these symptoms were almost entirely absent (Table 1). These clinical differences were further supported by the 24-h pH-impedance monitoring data. Vapers exhibited a significant shift in esophageal pH toward acidity, whereas the controls had pH values within the normal range. Furthermore, vapers experienced significantly more acidic, weakly acidic, and weakly alkaline GER episodes than the controls. Moreover, 9 (30%) vapers had a total daily GER episode count exceeding 80, which is classified as pathological [13]. None of the controls exhibited a pathological daily GER episode count (*p* = 0.002). Furthermore, the vapers were slightly younger than the controls (*p* = 0.006).

Although the serum hormone levels did not significantly differ between Groups 1 and 3, negative correlations were observed between the serum motilin levels and the GerdQ scores (r_s = –0.36; *p* = 0.049), as well as between the serum motilin levels and the daily number of acidic (r_s = –0.41; *p* = 0.025), weakly acidic (r_s = –0.51; *p* = 0.0037), and weakly alkaline (r_s = –0.57; *p* = 0.0009) GER episodes.

DISCUSSION

The results of this study indicate that, both in terms of clinical symptoms and 24-h esophageal pH-impedance monitoring findings, vapers occupy an “intermediate” position between healthy individuals and patients with GERD. The more pronounced reflux symptoms and significantly higher number of acidic, weakly acidic, and weakly alkaline GER episodes in vapers than in controls suggest a heightened predisposition to GERD in the future in vapers. The pathogenesis of GERD is complex and multifactorial, with disruptions in the humoral regulation of upper gastrointestinal motility playing a significant role. GERD symptoms, which result from the reflux of gastric contents, including hydrochloric acid and pepsin, into the lower third of the esophagus, are largely attributed to LES dysfunction. Thus, nicotine-induced relaxation of the LES in vapers may contribute to the observed effects [14].

Motilin, a polypeptide hormone, plays a crucial role in regulating the LES tone [15]. Previous studies have demonstrated that individuals with lower LES pressure exhibit lower motilin levels than those with normal LES function. This is consistent with our finding of weak negative correlations between the serum motilin levels and the daily number of acidic and weakly acidic GER episodes in patients with GERD [16, 17]. Similar weak negative correlations in Group 1 patients (between the serum motilin levels and the GerdQ scores as well as daily number of liquid GER episodes) indicate that there may be a similarity in LES motility dysregulation between vapers and patients with GERD. However, the normal serum motilin levels in vapers, compared with the lower concentration in patients with GERD, may be attributed to a shorter vaping history. The low motilin levels in patients with GERD may indicate "exhaustion" of the humoral regulatory mechanisms of gastrointestinal motility due to the chronic nature of the disease. The elevated serum gastrin levels in patients with GERD may be partially attributed to the prior use of acid suppressants and antacids, which may have influenced the study findings. Additionally, the presence of concomitant reflux gastritis in patients with GERD (with duodenogastric reflux-induced hypergastrinemia) cannot be ruled out.

CONCLUSION

Vaping is associated with a pathological increase in GER episodes and a shift toward an acidic esophageal environment, which are most likely due to impaired LES motility. These factors contribute to an increased risk of GERD development.

ADDITIONAL INFORMATION

Authors' contribution. Sh.A.E. — conceptualization, methodology, supervision; D.V.M. — investigation, formal analysis, writing — review and editing; P.A.S. — investigation, project administration; G.Yu.I. — investigation, writing — original draft. Thereby, all authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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