

THE EFFECT OF ACUTE CONSUMPTION OF PARAOXON ON BASAL AND PENTAGASTRIN-STIMULATED GASTRIC ACID AND PEPSIN SECRETION IN RATS

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Background: Paraoxon is an organophosphate. Organophosphates inhibit acetylcholinesterase enzyme and cause nicotinic and muscarinic signs. There is no study, on our knowledge, regarding the effect of these substances on gastric acid and pepsin secretion. In the present study, the effect of acute consumption of paraoxon on gastric acid and pepsin secretion has been investigated. **Methods:** In the present study 30 female N-mari rats weighing 200-250gr were used. The first group (paraoxon) received 0.5mg/kg paraoxon intraperitoneally. The second group (alcohol) received the doses of ethyl alcohol (96%) and the third group (control) received no drug. Animals were anesthetized by intraperitoneal injection of 50mg/kg Sodium thiopental. After tracheostomy and laparotomy gastric secretions were collected with a tube via duodenum. Pentagastrin (25µg/kg, ip) was used as gastric stimulator. Acid and pepsin secretions were measured by titration and Anson methods respectively. Stages of measurement were basal, stimulated, and re-basal. **Results:** The basal acid secretion in control, alcohol and paraoxon groups was 7.6 ± 0.26 , 7.46 ± 0.4 and $7.03 \pm 0.28 \mu\text{mol}/15\text{min}$ respectively that shows no significant difference among three groups. Although following pentagastrin-stimulation acid secretion was significantly more than basal stage in all groups, but there was significantly more secretion in control than alcohol subjects. But there was no difference between control and paraoxon or alcohol and paraoxon groups in this regard. Regarding pepsin secretion, there was significantly more secretion in alcohol subjects than others in all measured stages. **Conclusion:** in comparison to control group, acute paraoxon has no effect on basal acid/pepsin secretion, while acute alcohol caused a significant increase in basal acid/pepsin secretion.

Key words: Paraoxon, Gastric secretion, Acute, Rat

INTRODUCTION

Organophosphate chemicals are toxic esters of phosphoric acid. Insecticides, pesticides and nerve agents are in this group. Among these compounds nerve agents have the most toxicity.¹ Organophosphates are absorbed by various ways: via derm, mucosal membranes, respiratory and digestive systems. After entering the blood stream, they are spread in all the body.² Organophosphates inhibit acetylcholine esterase enzyme and cause nicotinic and muscarinic signs, such as salivation, lacrimation, vomiting, urinary and fecal incontinence, severe muscle pain, neurological and respiratory disorders.³ Previous studies about the effects of organophosphates on heart and visual system have shown that they decrease acetylcholine receptors in heart and disturb the visual system.³⁻⁴ Moreover, it has been observed that organophosphates poisoning leads to acute pancreatitis and delayed neuropathy.⁵

To the best of our knowledge, there is no study about the effect of organophosphate compounds on digestive system, except some limited reports of nausea and vomiting after exposure to these chemicals³ without clarifying whether this is

via affecting the Central Nervous System (CNS) or digestive system itself. It is hoped the findings of this study will clarify the effects of paraoxon on gastric acid and pepsin secretion and pave the way for further researches about the effects of organophosphate compounds on digestive system.

MATERIAL AND METHODS

In the present study 30 N-Mari rats weighing 200-250 gr were used. Animals were kept in 12 hours dark / 12 hours light cycle and at the temperature of $25 \pm 2^\circ \text{C}$. All animals were fed with standard food and were classified into the following three groups (n= 12):

- A. Control group: received no drug.
- B. Acute experimental group: received one dosage of 0.5 mg/kg paraoxon dissolved in ethyle alcohol (96%) intraperitoneally (10).
- C. Acute group: received one dosage of 0.5 mg/kg ethyl alcohol(96%) intraperitoneally (as paraoxon solvent).

Twenty-four hours before the experiments, animals were deprived of food but had free access to water (4,12). After having been weighed, animals were anaesthetized by intraperitoneal injection of sodium

thiopental (50 mg/kg b.w). Following tracheostomy, their esophagus was closed by a tie in neck region^{6,7} subsequently, laparotomy was performed, and a silicon tube with the external diameter of 2.5 mm entered into the stomach via duodenum and was fixed with a tie. In order to empty stomach, it was washed with 1 ml normal saline for several times (T= 37° C) and 30 minutes was passed to arrive at a stable state.⁸ In all groups basal gastric secretion was collected with an interval of 15 minutes by the washout technique. Then 25 µg/kg pentagastrin (Sigma Co.) was administered intraperitoneal as a gastric stimulant. After 15 minutes gastric secretion was collected in the presence of pentagastrin. After stimulant withdrawal and returning to the basal state, gastric secretion was collected an interval of 15 minutes. In all states (basal, stimulation and returning to the basal) 1 ml normal saline was entered into the stomach and after 15 minutes another 1 ml was added and then gastric contents were emptied. Acid output was determined by titrator instrument (DIN, Germany, 0.02ml), using sodium hydroxide 0.01 N.

Pepsin output was determined by the modified Anson method⁹ using hemoglobin as substrate.¹⁰ All data are expressed as the Mean±SE. ANOVA was used for statistical analysis of data. Multiple comparisons were made using Tukey procedure with P<0.05 considered statistically significant.

RESULTS

The basal acid secretions in control, alcohol and paraoxon groups were 7.6 ±0.26, 7.46 ±0.4 and 7.03 ±0.28 µmol/15min, respectively, that shows no significant difference.

Fifteen minutes after the use of pentagastrin as a stimulator of gastric secretion, acid secretions in control, alcohol and paraoxon groups were 16.48 ±0.53, 13.75 ±0.59 and 15.11 ±0.32 µmol/15 min respectively. That in all three groups show significant increase in comparison to the basal state (P=0.0000). While pentagastrin-stimulated acid secretion in control group had significant increased comparing to alcohol group (0.001), it showed no significant difference with paraoxon group. There was also no significant difference between alcohol and paraoxon groups in regard to the pentagastrin-stimulated acid secretion (fig.1)

After stimulant withdrawal and 15minutes of returning to the basal state, acid output secretion showed no significant difference in subjects (fig.1).

The basal pepsin secretion in control group was 0.55 ± 0.06 µg/15 min., while in alcohol group it was 2.48 ± 0.26 µmol/15 min. that shows a significant difference (P=0.000)(fig. 2). In paraoxon group, the basal pepsin secretion was 0.62 ± 0.04

µg/15 min. that shows no significant difference with control group, but is significantly less than alcohol group (P=0.000). In fact in the basal state, the amount of pepsin secretion in alcohol group was significantly more than the other two groups (P=0.000) (fig. 2).

Fifteen minutes after the administration of pentagastrin, pepsin secretions in control, alcohol and paraoxon groups were 1.09 ±0.06, 2.42 ±0.29 and 1.05 ±0.06 µg/15 min, respectively, that is more in alcohol group than control and paraoxon groups(P=0.000). But in the presense of pentagastrin, pepsin output was not significantly more than the basal state in this group (fig. 2).

After pentagastrin withdrawal and 15 minutes of returning to the basal state, pepsin output in the in alcohol group was significantly greater than control and paraoxon groups (P=0.000) (fig. 2).

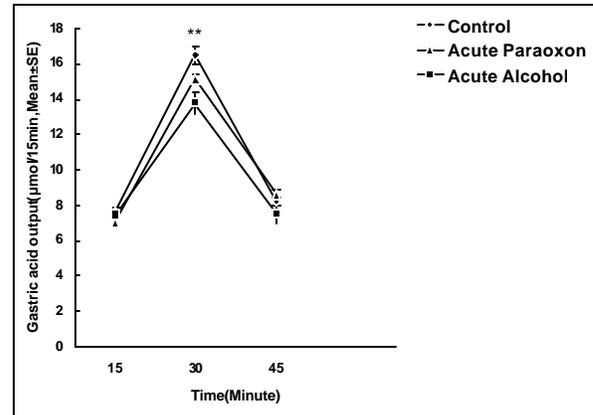


Fig.1: Comparison of the acid secretion between the control, alcohol and paraoxon groups (n= 10 in each group) **P< 0.05 ***P< 0.001 R.Basal= Reverse Basal

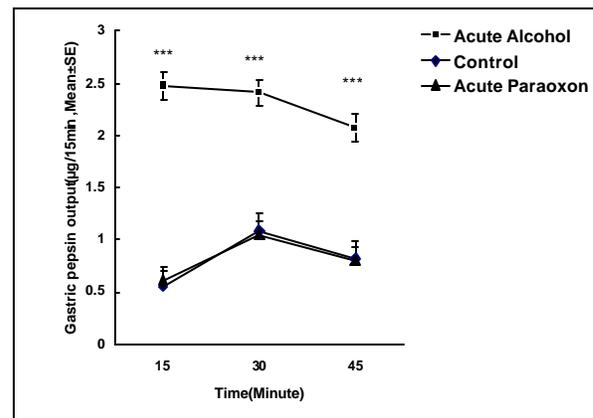


Fig.2: Comparison of the pepsin secretion between the control, alcohol and paraoxon groups (n = 10 in each group)

DISCUSSION

This study showed that acute exposure to paraoxon, although it is an acetylcholine esterase inhibitor, can not alter basal acid secretion.

After the administration of pentagastrin, acid secretion in all groups showed significant increase in comparison to the basal state which was expectable since pentagastrin is the synthetic form of gastrin that increases acid secretion directly via its effect on parietal cells and consequently increasing Ca^{++} influx into the cells,¹¹ but in this study, after the use of pentagastrin, acid secretion in control group was significantly more than alcohol group, while there was no significant difference between control and paraoxon or alcohol and paraoxon groups. It seems that pentagastrin can exert its effect more efficiently in the absence of alcohol. This point requires more precise studies.

Pepsin secretions in all of the states (basal, stimulation, and returning to the basal) were significantly greater in alcohol group than paraoxon and control groups ($P=0.000$) (fig.1), but there was no significant difference in this regard between control and paraoxon groups. It seems that acute exposure to paraoxon can not alter the activity of chief cells, and thus pepsin secretion. But alcohol can increase the activity of pepsin producing cells and consequently leads to an increase in pepsin secretion in all states. All these assumption require further studies.

After administration of pentagastrin, pepsin secretion in control and paraoxon groups showed significant increase in comparison to the basal state which was expectable. It is probable that pentagastrin increases pepsin secretion directly on chief cells and consequently increasing Ca^{+2} influx into the cells via its receptors.¹¹ Although, in alcohol group after using pentagastrin, pepsin output was more than control and paraoxon groups, but can not increase comparison to the basal state in this group. Further studies are required to find the mechanisms in this regard.

As we did not find other study about the effect of acute exposure to paraoxon on gastric acid/pepsin secretions in the literature, the results of the present study could not be compared with any other study. Further studies are recommended in order to understand the involved mechanisms.

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