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THERAPEUTIC EFFECTS EVALUATION OF VITAMIN E ALONE AND IN COMBINATION WITH RANITIDINE IN STRESS – INDUCED GASTRIC ULCERS IN RATS

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It is noteworthy to examine the efficacies of vitamin E and its combination with an antagonist of histamine receptor 2 in the treatment of stress gastric ulcers. Animals were divided into 6 groups; group 1 (normal control), group 2 (Cold – restraint stress; CRS), group 3 (ranitidine 20 mg/kg), group 4 (vitamin E 100 mg/kg), group 5 (ranitidine 10 mg/kg + vitamin E 50 mg/kg), group 6 (ranitidine 5 mg/kg + vitamin E 50 mg/kg). Drugs were administered orally for 7 consecutive days 1 hour after induction of the gastric injury. Rats were sacrificed. The assessment of stomach damage was by body weight observation, macroscopic examinations, histological study, and determination of oxidative stress markers (MDA stomach content and SOD enzyme activity). Present findings showed that the using of vitamin E with ranitidine is dose-dependent, and more effective than using vitamin E alone in the management of stress-induced lesions. Vitamin E caused a remarkable body weight decrease.

INTRODUCTION

Gastric ulcer is a defect in the stomach mucosal barrier that can be formed by Helicobacter pylori, alcohol excessive consumption, nonsteroidal anti-inflammatory drugs (NSAIDs), or exposure to stressful events[1]. After years of investigations, the implication of psychologic factors in the pathogenesis of peptic ulcers is still debated[2]. Stress is developed as a response to multiple severe conditions. It leads to stomach ulceration by irritating the secretion of acid and pepsin, and impairing the mucosal defense[3]. Cold restraint stress (CRS) is the most applicable technique which causes certain gastric lesions in experimental animals[4].

CRS stimulates the hypothalamus-pituitary-adrenal (HPA) axis which activates the release of cortisol. In addition, it disrupts the gastric hormones, and aggravates the generation of free radicals. Moreover, Increased catecholamines levels enhance the expression of inflammatory mediators like tumor necrosis factor-α (TNF-α) and interlukin-6 (IL-6)[1]. overproduction of reactive oxygen species (ROS) causes oxidative stress which leads to distorting the biological tissues and mediates their injury[5]. The mechanism of damage of gastrointestinal cells includes peroxidation of cell membrane lipids, associated with release of intracellular components. Consequently, the inflammatory process in the gastric mucosa will start[6].

Vitamin E is known as a powerful antioxidant. It has a beneficial role in preventing oxidation of polyunsaturated fatty acids. In addition, it modulates different mechanisms involved in the origination of gastric lesions[7].

Ranitidine is the safest drug used to treat gastric ulcers. It acts as a reversible antagonist of H2 receptors located on the gastric cells. That appears to decrease the impact of gastric offensives such as pepsin and hypersecretion of stomach acid[8].

The intention was to evaluate the therapeutic effects of vitamin E and its

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combination with ranitidine on experimentally - induced gastric injury and oxidative damage.

MATERIALS AND METHODS

Animals

Male and female wistar albino rats weighing 119-303 g were purchased from the Scientific Research Center, Damascus, Syria. They were acclimatized for one week before any experimental procedures. The animals were kept at controlled environmental conditions (temperature 23 ± 2 °C, humidity 55 ± 15%, under a 12 hrs. light/dark cycle). They had free access to standard rat diet and water. All methods performed in this study were in accordance with the regulatory guidance of the care and use of experimental animals**.**

Drugs

Vitamin E acetate SD 50 (BASF) was used in this study. This product can produce a milky suspension in water.

Ranitidine hydrochloride 99.7% was obtained from ORCHEV PHARMA PVT.LTD, and dissolved in water.

Stock solutions were freshly prepared daily and used for feeding.

Experimental design

Rats were deprived of food for 24 hrs. before the experiment in mesh-bottomed cages to minimize coprophagia, but allowed to free access to water[9]. All animals were put into individual close-fitting tubular restraint cages of wire mesh. They were placed in a refrigerator at 4 C°±1 for 2 hrs.[10]. The door of the refrigerator was opened every 0.5 hour for inspection and follow-up[9].

All experiments were performed during the same time of the day to avoid variations due to diurnal rhythms of putative regulators of gastric functions. All groups -except for the normal control group- were subjected to CRS. After 1 hour, they received either the drugs or vehicles by oral gavage syringe once daily for seven consecutive days.

Treatment Groups

Animals were randomly divided into 6 groups:

- **Group 1.** Normal control (NC): (9 rats) received oral vehicle (water).
- **Group 2**. (CRS): (8 rats) received oral vehicle (water).
- **Group 3**. (R20): (8 rats) received ranitidine (20 mg/kg) [3].
- **Group 4**. (E100): (9 rats) received Vitamin E (100 mg/kg) [11].
- **Group 5**. (R10 + E50): (8 rats) received ranitidine (10 mg/kg) + Vitamin E (50 mg/kg).
- **Group 6**. (R5 + E50): (9 rats) received ranitidine (5 mg/kg) + Vitamin E (50 mg/kg).

Tissue collection and preparation

After seven days of treatment with the appropriate drug for each group, animals were sacrificed. A midline incision was made. Stomachs were isolated and opened along the greater curvature, then washed by saline. Gastric mucosa was examined by naked eye and magnifying lens. A precise evaluation of the lesions was made, then each specimen was fixed in 13% formalin. Stomach tissue samples were stored at −80°C for further analysis.

Clinical findings

Rats were checked daily for body weight, behavioral changes, food intake, rectal bleeding, and stool consistency. Body weight was measured at regular time intervals from day 0 to 7. Changes of body weight (%) were calculated.

Macroscopic scoring

Number and severity of gastric lesions were scored according to the following system[12]: 0 : no lesion, 1 : mucosal edema and petechiae, 2 : (1–5) small lesions (1–2 mm), 3 : > 5 small lesions or 1 intermediate lesion (3–4 mm), 4 : ≥ 2 intermediate lesions or 1 gross lesion (> 4 mm), and 5 : perforated ulcers.

Each lesion was considered as an ulcer to calculate the following parameters:

Degree of ulceration = total ulcer score/ No. of animals ulcerated[13].

ulcer index (UI) = total ulcer score / No. of animals in group.

It was expressed as: UI ± SD (standard deviation)[12].

Curative ratio = [1-(UI treated/UI ulcerated) × 100][13].

Histopathological observations

A portion of the stomach of each rat was fixed in 13% formalin. The specimens were embedded in paraffin wax and cut into sections of 5 mm thickness. The sections were stained with hematoxylin and eosin (H and E) dye for the histopathological examination. The histological sections were assessed by an experienced pathologist who was blinded to the treatment for: grade and type of inflammation (score: 0-4), presence of epithelial erosions (score: 0-2), presence of epithelial ulcers (score: 0-1), edema in the lamina propria (score: 0-1), blood vessels congestion (score: 0-5), epithelial atrophy (score: 0-1), and epithelial hyperplasia (score: 0-1), yielding a maximum total score of 15[14].

Biochemical assays

Precisely weighed tissues of stomach were homogenized in cold phosphate-buffered saline (pH 7.4, 50 mmol) to prepare 10 % tissue homogenate. The resultant suspension was divided into two parts. The first one was used for the determination of malondialdehyde (MDA). The second part was centrifuged for 20 min at 4 °C, and the supernatant was used for SOD activity measurement**.**

Estimation of lipid peroxidation

Detection of malondialdehyde (MDA) (the end product of lipid peroxidation) by a colorimetric reaction with thiobarbituric acid (TBA), is a highly sensitive indicator for evaluating the mucosal injury induced by ROS in gastric tissues exposed to oxidative stress[15]. In brief, 0.5 ml of stomach tissue homogenate was mixed with 2 ml of TBA reagent containing (0.375% TBA, 15% trichloroacetic acid and 0.25 N HCl). Samples were boiled for 15 min, cooled and centrifuged. The absorbance of the supernatant was spectrophotometrically read at 532 nm, using an extinction coefficient of 1.56×10^5 /M cm.

Final Concentration of unknown sample/gram tissue=100×µM LPO equivalent/gram tissue[16].

Estimation of superoxide dismutase (SOD) activity

The procedure is as follows: First, a certain amount of pyrogallol solution (60 mmol in 1 mmol HCl, 37 °C) was well mixed with Tris-HCl buffer (0.05 M, pH 7.4) containing 1 mM Na2EDTA. The volume was adjusted to 3000 µl using the buffer. The A325 nm value of the mixture without a sample was measured every 30 s for 5 min at 37 °C. Second, we repeated the exact previous step with the addition of the sample. Enzyme activity, which matches the amount of enzyme that inhibits the auto-oxidation of pyrogallol by 50%, was calculated and expressed per mg of protein[17].

Statistical analysis

Data analyses were performed using Prism (version 8) statistical package. Data were presented as means ± SEM. Different groups were compared using one-way analysis of variance (ANOVA) followed by Sidak test for multiple comparisons of parametric data, and Kruskal–Wallis test followed by Dunn test for multiple comparisons of non-parametric and parametric data that have shown abnormal distribution. P values < 0.05 were considered statistically significant**.**

RESULTS AND DISCUSSION

Results

Clinical findings, general observation, and body weight changes

After 24 h of exposure to CRS, most animals developed diarrhea and progressively body weight loss, accompanied with weakness and decreased food intake. All these symptoms began to decrease gradually in groups (R20) and (R10 + E50) starting from day 3. However, groups CRS, (E100), and (R5 + E50) did not show any obvious improvement. Some rats died during the experiment. That is likely due to hemorrhagic or perforated stomach lesions.

At the end of the experiment, body weight of CRS group was reduced by (-1.51%) compared to NC group, which revealed body weight increase by (+2.82%) with no statistical significance (p= 0.1654).

Groups (R20) and (R10 + E50) revealed an increase in body weight by (+0.18%, +0.75%, respectively), but with no statistical significance compared to CRS group (p= 0.5942, p= 0.4775 respectively). Meanwhile, body weight of group (R5 + E50) was less by (-1.93%), but with no statistical significance compared to CRS group (p= 0.9399).

Group (E100) revealed a significant decrease in body weight by (-10.76%) compared to CRS group at (p= 0.0078). (figure. 1).

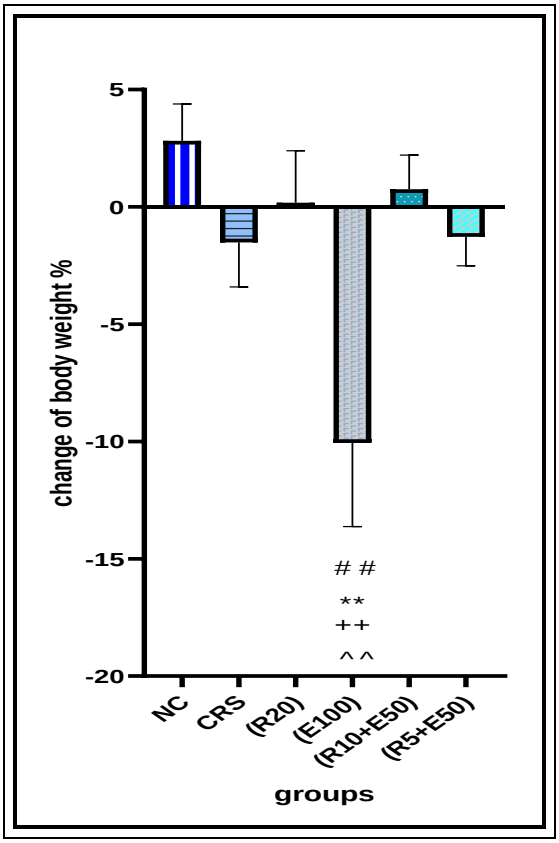

Fig. 1: Effect of ranitidine, vitamin E, and their combination on body weight in CRS exposed rats. Data were expressed as mean ± S.E.M

** P< 0.01 compared to CRS group. ++ P< 0.01 compared to (R20) group. ^^ P< 0.01 compared to (R10 + E50) group. ## P< 0.01 compared to (R5 + E50) group.

Macroscopic scoring

NC group stomachs apparently showed healthy mucosa in most samples, with no swelling or hemorrhage. Two samples showed some tiny pinpoint lesions. In contrast, CRS group showed notable severe injuries in the form of dark reddish hemorrhagic lesions, with variable forms and sizes. Also, there was a generalized hyperemia in the gastric mucosa. CRS significantly increased the ulcer index (P< 0.0001) compared to NC group.

(R20) group stomachs showed fewer ulcers with less marked hyperemia and moderate mucosal injuries, with statistical significance compared to CRS group (P= 0.0056). 59.375 % curative ratio was recorded.

Vitamin E effectively decreased the ulcer index compared to CRS group (P= 0.0006). 66.68% curative ratio was recorded. The combination of ranitidine (5 mg/kg) and vitamin E (100 mg/kg) ameliorated the morphological changes compared to CRS group) P= 0.009). However, this decrease was not significant compared to (R20), (E100), and (R10 + E50) groups (p= 0.0803, P= 0.4258, p= 0.0509 respectively). 69.445 % curative ratio was recorded.

(R10 + E50) group had the best outcome in all measured parameters compared to CRS group) P< 0.0001), but this improvement was not significant compared to (R20), (E100) groups (p= 0.6003, P= 0.23380 respectively). Curative ratio significantly increased compared to (R5 + E50) group (93.75%). (Table. 1, figure. 2, 3)

Table.1: Effect of ranitidine, vitamin E, and their combination on gastric parameters in stress - induced ulcer in rats

Parameter / Group	Ulcer severity	Ulceration Degree	Ulcer index ± SD	Curative ratio
NC	3	1.5	0.333 ± 0.707	-
CRS	32	4	4 ± 0 ****	-
R20	13	2.6	1.625 ± 1.74 ^^	59.375%
E100	12	3	1.333 ± 1.803 ^^^	66.68%
R10+E50	2	1	0.25± ٠.٤٦٣ ^^^^	93.75%@
R5+E50	11	1.2222	1.222 ± 0.667^^	69.445%

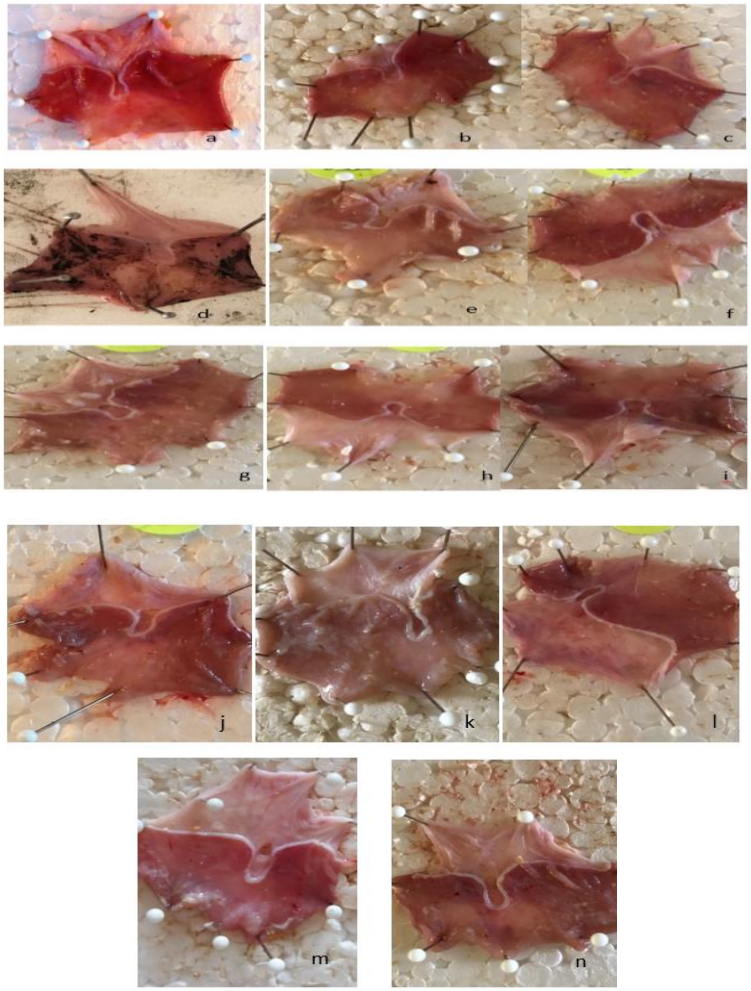

Fig.2: Macroscopic morphology changes in the gastric mucosa. a, NC group (grade0); b, NC group (grade1); c, NC (grade2); d, CRS group (grade 4); e, (R20) group (grade 0); f, (R20) group (grade 1); g, (R20) group (grade 4); h, (E100) group (grade 0); I, (E100) group (grade 1); j, (E100) group (grade 4); k, (R10+E50) group (grade 0); l, (R10+E50) group (grade 1); m, (R5+E50) group (grade 1); n, (R5+E50) group (grade 3).

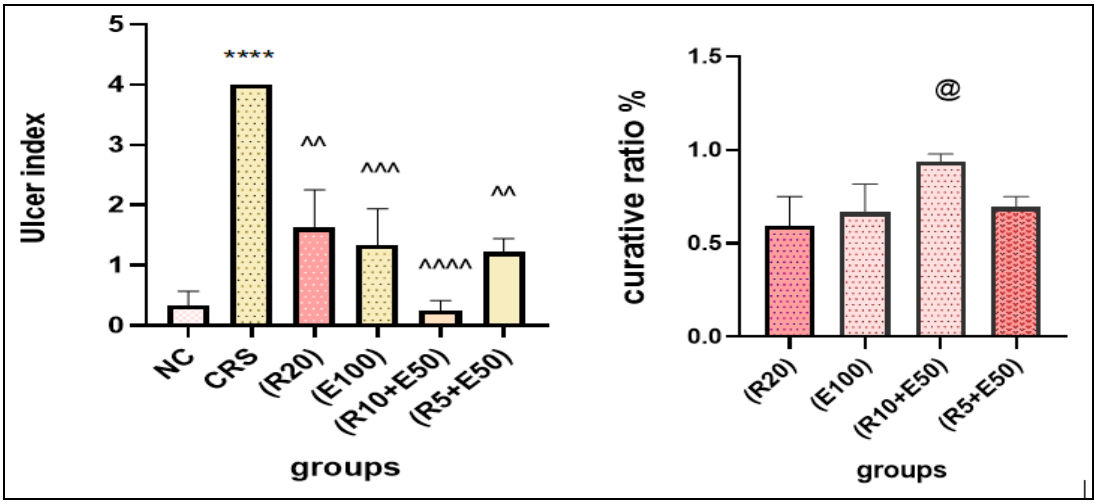

Fig.3: Effect of ranitidine and vitamin E and their combination on UI and curative ratio

**** p<0.0001 compared to NC group. ^^^^ p<0.0001 compared to CRS group. ^^^ p<0.001 compared to CRS group. ^^ p<0.01 compared to CRS group. @ p<0.05 compared to (R5+E50) group.

Histopathological study

Histological evaluation of gastric walls in stress - induced ulcerated rats had manifested an extensive damage to the gastric mucosa (deep erosions and ulcers), severe blood vessels congestion, edema in the lamina propria, inflammatory cells infiltration in the submucosal layer, and disorganized cells (architecture, shape, thickness), with high scores of microscopic damage when compared to NC group ($P< 0.0001$). Administration of ranitidine (20mg/kg) revealed a significant reduction in the severity of mucosal stomach damage when compared to CRS group ($P= 0.0014$). Significant histologic improvement was observed in (E100) group when compared to CRS group ($P= 0.0005$). Meanwhile, rats in (R10 + E50) group showed a significant reduction in the histopathological score when compared to CRS group ($P< 0.0001$). similarly, rats in (R5 + E50) group revealed a significant reduction in the severity of injury when compared to CRS group ($P= 0.0012$). (table. 2, figure. 4)

Table.2: Effect of ranitidine, vitamin E, and their combination on the microscopic score in stress - induced gastric ulcer in rats

group	Edema (score0 -1)	epithelial Hyperplasia (score 0-1)	Blood vessels congestion (score 0-5)	Epithelial erosion (score0-2)	Epithelial ulceration (score 0-1)	Inflammation infiltration (score 0-4)	epithelial Atrophy (score 0-1)	Total Scores 15
NC	0 (0-1)	0 (0-1)	4 (4-4)	0 (0-1)	0 (0-0)	1(0-3)	0(0-0)	6 (5-9)
CRS	1(0-1) ###	1 (0-1)	5(5-5) ##	2(0-2)	0(0-1) ##	3(0-4)	0(0-1) #	11(11-12) ####
R20	1(0-1)	0(0-1)	4(2-4) ***	1(0-2)	0(0-1) *	1(0-2) **	0(0-1) **	7(5-9) **
E100	1(0-1)	0(0-0) **	4(2-4) ****	1(0-1)	0(0-0) **	1.5(0-4)	0(0-1) ***	7(2-8) ***
R10 + E50	0(0-1) *	0.5(0-1)	2(0-4) ****	1(0-1)	0(0-0) **	1(0-3) *	0(0-0) ****	3.5(1-9)****
R5 + E50	1(1-1)+	0(0-1)	4(2-4) ****	1(0-1)	0(0-1)*	2(0-2) ●	0(0-0) **	7(4-9) **

The table shows median values followed by minimum and maximum scores (in brackets). #### p<0.0001 ### p<0.001 ## P<0.01 # P<0.05 compared to NC group. **** p<0.0001 *** P<0.001 ** P<0.01 * P<0.05 compared to CRS group. ● P<0.05 compared to (R20) group. + P<0.05 compared to (R10+E50) group.

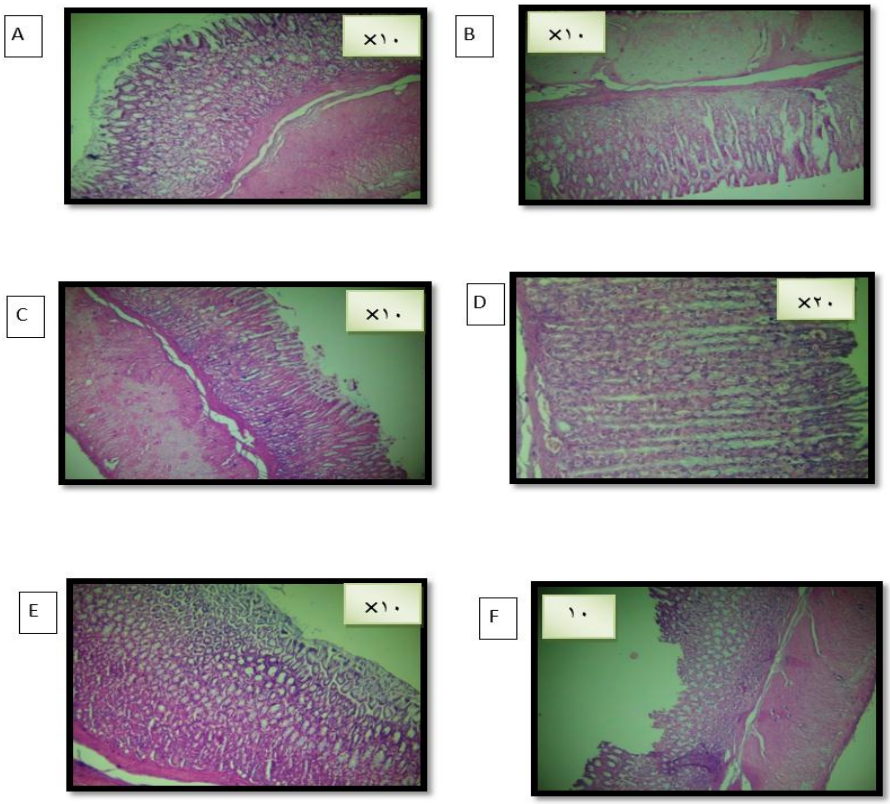

Fig. 4: Histological appearance of stomach tissue sections. A, NC group (grade 5); B, CRS group (grade 10); C, (R20) group (grade 5); D, (E100) group (grade 6); E, (R10+E50) group (grade 3); F, (R5+E50) group (grade 6)

Biochemical Investigations

CRS induced oxidative cascade in rats' stomachs; it was evaluated by lipid peroxides (LPO) levels and SOD activity.

Stomach MDA content

There was a significant elevation in stomach MDA levels in rats exposed to CRS compared to NC group (*P*< 0.0001). These levels were significantly lower in groups treated with ranitidine alone (R20) and the 2 combination groups (R10 + E50) and (R5 + E50) compared to CRS group (*P*= 0.0002, P< 0.0001, P= 0.0031 respectively). A statistically significant difference was found when comparing the combination group (R10+E50) (with the higher dose of ranitidine) with single treatment groups (R20), (E100), and the other combination group (R5+E50) (with the lower dose of ranitidine) (*P*= 0.0310, *P*< 0.0001, P=0.0016 respectively). However, rats received vitamin E alone (E100 group) substantially showed decreased MDA levels compared to (R20) group (*P*= 0.0397), but with no statistical significance compared to CRS group (*P*= 0.0558). These results are shown in (figure. 4).

Stomach superoxide dismutase (SOD) activity

Exposure to stress significantly decreased SOD activity in stomach tissues compared to NC group (*P*< 0.0001). Administration of vitamin E alone or in combination with ranitidine (E100, R10 + E50, and R5 + E50 groups) substantially increased the enzyme activity compared to CRS group (*P*< 0.0001, P< 0.0001, P= 0.0031 respectively). Meanwhile, administration of ranitidine alone (R20 group) elevated the enzyme activity, but not in a significant manner compared to CRS group) P= 0.0850) . A statistically significant difference was found when comparing the combination group (R10 + E50) with (R20) and (R5 + E50) groups (*P*< 0.0001, *P*= 0.0017 respectively), but there was no statistical significance when compared to (E100) group (*P*= 0.9252). on the other hand, we recognized a significant difference when comparing (R5 + E50) group with (R20), (E100) groups (*P*<0.0001, *P*= 0.0009 respectively). These results are shown in (figure.4).

Discussion

One common health problem related to stress is the formation of acute gastric lesions, better known as stress ulcers[5]. Cheng et al, and Perez et al. demonstrated that the pathogenesis of stress ulcers is multifactorial and includes high inflammatory and oxidative damage, reduced gastric prostaglandin synthesis, and inhibition of mucosal growth and proliferation[18]. Pattanaprateep et al. declared that different models of acute and chronic cellular insults are mediated by free radicals. Hence, they promote the degradation of the mucosal epithelial basement membrane, and cause further tissue harm[19].

Various experimental models of ulceration mimicking the disease in human have been developed to test the potential beneficial effects of various drugs. One of the common employed methods is CRS synergistically with fasting in rats[20]. Therefore, we applied this technique in our study.

Our results confirmed that CRS produces oxidative stress status associated with severe inflammatory response in rats. That was evidenced by body weight loss, reduction in food intake, gastric mucosal injury, and changes in biomarkers which include elevation in MDA levels, and depleted antioxidant enzymes activities, such as SOD. There was a reduction in body weight of CRS group by 154% compared to NC group which exhibited a slight increase in body weight. Macroscopic results revealed characteristic acute gastric lesions such as mucosal edema, patchy hemorrhagic ulcers and erosions. That appeared by a significant increase in ulceration parameters, which is in agreement with many studies, i.e. the study of Bahadir et al[21]. Furthermore, the lesions are associated with a significant increase in lipid peroxides levels by 155%, and a significant depletion in SOD activity by 81% compared to NC group. That was in harmony with the findings of Elsaed et al. They attributed the decreased SOD activity and LPO levels increase to the formation of ROS which mediate the cascade of stress-induced mucosal injury [22].

Previous data indicated that antioxidants like vitamin E healed some, but not all of the inflammatory stimuli in this model.

Gastric acid exacerbates the damage of gastric mucosa induced by other agents. Furthermore, it can convert superficial erosions into deeper necrosis, and inactivates some of the growth factors that are vital for the repair of mucosal cells. Ranitidine was shown to inhibit histamine and decrease gastric acid secretion[3].

The present study evaluates the magnitude of the participation of vitamin E with other treatments used in gastropathy, such as ranitidine. Biochemical and morphological examinations were undertaken to investigate the therapeutic effects of vitamin E alone and in combination with ranitidine in stress-induced ulcers.

Our study results revealed that administration of vitamin E alone caused a considerable loss of body weight by 613% compared to NC group. That can be explained by the study of Alcalá et al. They demonstrated that vitamin E reduces triglycerides levels, and enhances adipose tissue capability to increase their storage limits. As a result, circulating free fatty acids will not be then redirected to other tissues[23]. Furthermore, treatment with vitamin E markedly reduced gastric mucosal damage that stress induced. This finding gets along with the finding of Nur Azlina et al.[24]. They attributed that to the capacity of vitamin E to inhibit lipid peroxidation and scavenge free radicals. Regarding the anti-oxidant effects of vitamin E, it decreased gastric MDA content by 20%, and significantly improved the activity of SOD by 414% compared to CRS group. That is in concordance with the study of Shah et al[25].

In comparison, rats treated with ranitidine alone showed body weight improvement by 112%, and a significant decrease in lipid peroxides levels by 43%. Also, SOD activity increased by 63% compared to CRS group. Ching et al. showed that H2 blockers are very strong hydroxyl radical scavengers. Also, Ahmadi et al. observed that ranitidine exhibits a strong, dose-dependent antioxidant activity[26]. According to these studies, the therapeutic effects of H2 blockers in peptic ulcers may be correlated to their antiradical capacity. Moreover, we observed a significant improvement in the macroscopic and microscopic scores compared to CRS group; these results are in agreement with the findings of Chandranath et al. They declared that ranitidine has a protective effect against CRS-induced gastric ulcers[3]. Another study represented that ranitidine exerts powerful scavenging effects towards hypochlorous acid and monochloramine, which are released from inflammatory cells such as neutrophils[26].

The effects of the combination ranitidine (10mg/kg) and vitamin E (50mg/kg) on macroscopic injury (lowest UI and best curative ratio), microscopic scores, and oxidative stress were superior to those of every agent alone, or to the other combination group (R5+E50). These values achieved significance

compared to CRS group; SOD activity increased by 410%, and LPO levels decreased by 66%. Rats in the group (R10 + E50) showed an increased body weight by 149%. Whereas, the combination (R5 + E50) decreased rats body weight by 168%, but not in a significant manner compared to CRS and (R20) groups. However, this decrease was significantly less than the effect of vitamin E alone.

Consistently, the rats treated with ranitidine (5mg/kg) and vitamin E (50mg/kg) showed a remarkable improvement in macroscopic scores, microscopic damage, and oxidative stress parameters; SOD activity increased by 284%, and Stomach MDA content reduced by 28% compared to CRS group.

The rates of healing seem to be faster in the presence of ranitidine as evidenced in the results of the two combination groups. So, the drug appears to play a crucial dose- dependent therapeutic role in this issue.

Conclusion

The findings of this study indicate that vitamin E is effective in the management of stress-induced gastric ulcers, alone and combined with ranitidine. However, this combination has shown a greater efficacy than the single treatment. That is possibly imputed to the consequent synergistic effects, through attenuating the inflammatory cascade, inhibition of tissue oxidative stress, and promotion of mucosal barrier repair.

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تقييم التأثيرات العلاجيّة للفيتامين E منفرداً ، وبالمشاركة مع الرانيتيدين في القرحات المعديّة المحدَثة بالشدّة النفسيّة عند الجرذان

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خلفيّة البحث: تُصنّف الاضطرابات المتعلّقة بالشدّة النّفسيّة ضمن المشاكل الصحيّة ذات الاهتمام العالميّ، لاسيما تلك ذات الصلة بالجهاز الهضميّ. وقد أثبت بأنّ الشدّة التّأكسديّة النّاتجة مسؤولة عن تطوّر قرحات ونخور المخاطيّة الهضميّة، مترافقة مع تحرّر وسائط التهابيّة وعوامل أخرى عديدة. الفيتامين E هو فيتامين منحلّ بالدّسم يتميّز بكونه مضاداً للأكسدة كاسحاً للجذور الحرّة، له تأثيرات مضادّة للالتهاب ومعزّزة لغشاء الخليّة، أما الرانيتيدين فهو مثبّط تنافسيّ انتقائيّ لمستقبلات الهيستامين H2 الموجودة في الخلايا المعديّة الجداريّة.

يهدف هذا البحث إلى تقصّي فعاليّة الفيتامين E منفرداً في علاج القرحة المعديّة المحدَثة تجريبياً، وتقييم مشاركته الدّوائية مع الرانيتيدين عند حيوانات التجربة.

المواد والطّرق: قُسّمت حيوانات التجربة إلى ٦ مجموعات: مجموعة شاهدة، ومجموعة مرضيّة، ومجموعة عولجت بالرانيتيدين لوحده، وأخرى بالفيتامين E منفرداً ، ومجموعتي مشاركة بجرعة ثابتة للفيتامين E وجرعتين مختلفتين للرانيتيدين. تمّ إحداث المرض عند الجرذان بطريقة الحجر والبرودة بعد فترة صيام عن الطّعام، أعطي بعدها العلاج الخاص بكلّ مجموعة لمدّة ٧ أيام متواصلة. تمّت التّضحية بالحيوانات في اليوم الثّامن، ليجري بعدها تقييم الأذيّة المعديّة من خلال دراسة تبدّلات وزن الجسم، إضافة للفحوص العيانيّة لعيّنات المعدة، والمعايرات الكيميائيّة الحيويّة لنواتج أكسدة الشّحوم وفعاليّة أنزيم Superoxide dismutase (SOD) في المعدة.

النتائج: أبدت كلّ المجموعات تحسّناً متفاوتاً في درجة الأذيّة المعديّة، ترافق مع تناقص في علائم الشدّة التأكسديّة. وقد تفوّقت مجموعة المشاركة التي عولجت بالفيتامين E والتركيز الأعلى من الرانيتيدين في نتائجها العيانيّة والكيميائيّة على باقي المجموعات بشكل ملحوظ.

الخلاصة: أعطى الفيتامين E تأثيراتٍ جيّدة في علاج القرحات المعديّة المحدثة بالشدّة النفسيّة، لكنّ هذه التأثيرات تحسّنت بشكل صريح عند مشاركته مع حاصر لمستقبلات H2 كالرانيتيدين.