

Safety And Efficacy of Unani Compound Drug in Helicobacter Pylori Positive Antral Gastritis (Warm-E-Meda Patients): A Controlled Study

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Abstract: Warm-e-meda/gastritis is the prime concern in unani medicine and unani physicians emphasized on better functioning of stomach/meda. Acute gastritis, chronic gastritis, peptic ulcer disease, atrophic gastritis, gastric carcinoma, primary gastric B-cell lymphoma are some of the manifestation of H. pylori infection. An appreciable number of unani mufrad (single) and murakkab (compound) drugs are used to treat them. In this study we evaluate the efficacy of a unani compound drug in endoscopically proved H.pylori positive antral gastritis. This was a double blind randomised clinical trial, on 160 patients. All the patients were divided into three groups. Test group comprising of 110 patients, control group comprised of 20 patients and placebo group comprising 30 patients. Patients of control group were given tab Pantoprazole (40 mg). All the drugs were given for a period of 3 months and weekly follow up was done and repeat endoscopy was carried out after completion of treatment. In 84.5% patients H. Pylori positive antral gastritis was found in group A (test group), 66.7% in group B (Placebo group) and 100% in group C (control group). Antral gastritis was cured in 89.1% patients in group A (test group), only 3.3% in group B and 40% in group C. 90% patients became H. Pylori negative after receiving test drug for 3 months, only 6.7% patients became negative in group B while in group C all the patients remained H. Pylori positive after treatment.

In our study we found the Unani polyherbal formulation was found to be effective in treating antral gastritis and eradicating H. Pylori bacteria.

Keywords: Antral gastritis, Endoscopy, H. pylori.

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I. Introduction

Antral gastritis (warm-e-meda) is one of the commonest problem among different culture and civilizations. Unani physicians have mentioned the disease by different names e.g Hurqat-e-Meda, Sozish-e-Meda, Warm-e-Meda, and Iltehab-e-Meda. They described gastritis on the basis of clinical features (Warm-e-meda har, Warm-e meda barid), causative factors and humor (Warm-e-meda damvi, Warm-e-meda safravi, Warm-e-meda balghami, Warm-e-meda saudavi), duration (Warm-e-meda falghamuni, Warm-e-meda hamratemedi, Warm-e-meda rekhu, Warm-e-meda sulb) and gross pathological changes (Warm-e-meda ha'ad (acute gastritis), Warm-e-meda muzmin (chronic gastritis). There is a close relationship between chronic gastritis and H. Pylori infection was reported and about 75% patients with chronic gastritis have H. Pylori infection compared to 10% in those without gastritis.⁽¹⁾ Dr Berry and Warren discovered H. Pylori in 1882 in patients having gastritis and gastric ulcers, since then H. Pylori has been the focus of researchers.⁽²⁾ H. Pylori infection once established persists throughout life and generally remains asymptomatic in many cases. The rate of infection increases with age and its prevalence is related to the stage of social development of the people.⁽³⁾ More than 50% of world's population harbours H. Pylori in the GIT. The infection is more prevalent in developing countries like India (80%) as compared to western countries.^(4,5) Infection of H. Pylori spread either by eatables, fomite, through direct contact or by vectors, exact route of transmission is not known but it may be transmitted through Oro-oral route, Gastro-oral route, Faeco-oral route and also transmits from one patient to another by inadequately disinfected endoscope.⁽⁶⁾ Chief complaints of patient includes abdominal pain, dyspepsia, indigestion, nausea or vomiting, heart burn, loss of appetite. Initially the disease starts as superficial gastritis, eventually it may progress to atrophic gastritis or gastric carcinoma. Other infestations caused by H. Pylori infection includes peptic ulcer disease, Primary gastric B cell lymphoma, iron deficiency anaemia and B12 deficiency.⁽⁷⁻¹⁰⁾

In spite of tremendous advancement, no effective drug is available to treat gastritis. In Modern system of medicine, the treatment regimens for H. Pylori positive antral gastritis are available with minimum of 2 antibiotics like amoxicillin, tinidazole or clarithromycin in combination with gastric acid inhibitor but the results are not satisfactory.⁽¹¹⁻¹²⁾ There were hundreds of herbal drugs used for the eradication of H. Pylori and to treat gastritis.⁽¹³⁻²¹⁾

Some of the unani drugs are used since ancient times for the treatment of gastritis. Single drugs (Mufrad advia) are Althaea officinalis Linn. (Khatmi), Alpinia galangal (Khulanjan), Aloe barbadensis (Elva), Anchusa Strigosa (Gaozaban), Glycyrhiza glabra (Asl-us-soos), Withania somnifera (Asgand), Zingiber officinale (Adrak), Andrographis paniculata wall (Bhui neem), Embelica officinale (Amla), Picrorhiza kurroa (Kutki), Nigela sativa Linn.(Kalonji), Curcuma longa (Haldi), Berberis aristata (Dar hald), Momordica charantia Linn. (Karela), Aegle marmelos correa (Bael), Asparagus racemosus (Satawar), Acacia arabica (Samagh-e-arabi), Myristica fragrans Houtt (Jaiphal), Plantago ovate (Aspghol), Bambusa arundinacea (Tabasheer), Pistacia lentiscus Linn (Mastagi).⁽²²⁻⁵⁷⁾

Compound drugs (Murakkab advia) are Majoon Dabeedulward, Qurs e Satawari, Qurs e Tabasheer, Jawarish e Tabasheer, Majoon e Zanjabeel, Jawarish e Anarain, Jawarish e Mastagi, Khameera Sandal, Itrifal Aftimoon, Sharbat e Neelofar, Sharbat e Anar, Sharbat e Unnab.^(37-46, 58-70) In the present study, we tried to establish the safety and efficacy of a unani compound drug in endoscopically proved H. Pylori +ve antral gastritis patients.

Table 1 Constituents of the unani formulation

Unani Drugs	Botanical Names	Part Used	Ratio in each Capsule (each capsule of 500 mg)
Asl-us-soos	Glycyrhiza glabra	Stem and bark	1 part
Aspaghool Musallam	Plantago ovate	Seeds	2 part
Samagh-e-arabi	Acacia arabica	Dry exudates	2 part
Mastagi	Pistacia lentiscus	Resin	1 part

II. Material And Methods

The study entitled “Safety And Efficacy Of Unani Compound Drug In Helicobacter Pylori Positive Antral Gastritis (Warm-E-Meda Patients): A Controlled Study” was conducted in the department of Jarahat (surgery), Ajmal Khan Tibbiya College, Aligarh Muslim University, Aligarh from February 2010 to march 2013 on 274 patients. The patients with upper G.I. symptoms like heart burn, nausea or vomiting, indigestion, abdominal pain, loss of appetite were screened from the Jarahat (surgery) OPD, AKTC, Hospital and the clinical evaluation on a prescribed Performa was carried out, these patients were asked to attend the operation theatre for upper G.I. endoscopy. The patients were called nil orally on the day of endoscopy.

Inclusion criteria: -

- a. Patients having following symptoms for at least 7 days.
 - Heart Burn
 - Nausea
 - Vomiting
 - Indigestion
 - Abdominal Pain
 - Loss of appetite
- b. Patients with H. Pylori +ve antral gastritis confirmed by rapid urease test (RUT).
- c. Patients of either sex between the age of 20-60 years.

Exclusion criteria: -

- a. Patients who had NSAIDS or any antibiotic within the last 4 weeks.
- b. Pregnant and Lactating mothers.
- c. Patients with any systemic disease (hepatorenal and pulmonary malfunctions).
- d. Patients with prior history of pyloric stenosis or gastric resection.
- e. Patients with history of gastric carcinoma.
- f. Patients with active G.I. haemorrhage, obstruction or perforation.
- g. Alcoholic subjects.
- h. Systemic diseases like hypertension, diabetes, CRF etc.
- i. Non-co-operative and non-willingness for follow ups.
- j. Anxiety disorders.
- k. Bleeding disorders.
- l. HIV positive and Hepatitis B/C positive patients.
- m. Patients with H. Pylori -ve antral gastritis confirmed by rapid urease test (RUT).

The total number of 160 H. Pylori +ve patients included in the study, were randomly divided into three groups. Group A- 110 H. Pylori +ve patients were given the coded drug (UNIM 701). Group B- 30 H.Pylori +ve patients were given the coded drug (UNIM 701 P). Group C- 20 H.Pylori +ve patients were given standard drug (Pantoprazole 40 mg).

All the patients were asked to rest for about 5 – 10 minutes on a trolley under care of the nursing staff after the endoscopy. Drinking allowed after 10 minutes of the procedure. After that patients were sent home with the endoscopy report and advice.

Statistical analysis was done by applying Yates Correction Chi Square test.

III. Results And Observations

The study was conducted in the department of Jarahat (Surgery) AKTC Hospital, AMU, Aligarh, India. A total number of 274 patients were enrolled in the present study with the complaints of heart burn, nausea/vomiting, indigestion, loss of appetite and abdominal pain and after the screening 160 patients (58.4%) were found to be H. Pylori positive. The age of the patients ranged from 13-70 years of age and the mean age was 33.4 ± 13.7 years. Maximum number of patients were in the age group of 20-30 years of age. (Table 2)

Table no. 2 According to age

Age (in yrs)	No of Patients	Percentage
10 – 20	33	20.6
20 – 30	44	27.5
30 – 40	41	25.6
40 – 50	21	13.1
50 – 60	14	8.7
60 – 70	7	4.4
Total	160	100
Mean \pm S.D	33.4 \pm 13.7	

Among 160 patients, there were 84 (52.5%) males and 76 (47.5%) females. (Table 3)

Table no. 3 According to sex

Sex	No of Patients	Percentage
Male	84	52.5
Female	76	47.5
Total	160	100

Regarding symptomatology in group A, 82 (74.5%) patients complained of heart burn, 74 (67.3%) had nausea or vomiting. Maximum number of patients, that is, 88 (80%) were complaining of abdominal pain. 62 (56.7%) were having loss of appetite and 63 (57.3%) patients have indigestion. Symptomatic presentation of patients in group B, maximum number of patients 25 (83.3%) were complaining of abdominal pain, 21 (70%) patients had nausea and vomiting, 18 (60%) were having heart burn, 22 (73.3%) were complaining of loss of appetite and 14 (46.7%) were complained of indigestion. Among 20 patients in group C, 16 (80%) patients presented with abdominal pain, 14 (70%) patients had nausea and vomiting, 18 (90%) complained of indigestion, 14 (46.7%) were complaining of heart burn and 6 (30%) were having of loss of appetite. Symptomatic relief of the patients after the eradication therapy was evaluated and summarized. (table. 4)

Table no. 4 Symptomatology

Symptoms	Pre-treatment (N=160)						Post treatment (N=160)					
	Group A (N=110)		Group B (N=30)		Group C (N=20)		Group A (N=110)		Group B (N=30)		Group C (N=20)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Heart burn	82	74.5	18	60.0	14	70.0	8	7.2	12	40.0	0	0.0
Nausea/Vomitting	74	67.3	21	70.0	12	60.0	5	4.5	19	63.3	2	10.0
Indigestion	63	57.3	14	46.7	18	90.0	6	5.4	10	30.0	2	10.0
Abdominal Pain	88	80.0	25	83.3	16	80.0	9	8.2	23	76.7	2	10.0
Loss of appetite	62	56.7	22	73.3	6	30.0	6	5.4	21	70.0	4	20.0

N= number of patients.

160 patients were screened having the complaints of heart burn, nausea and vomiting, abdominal pain, indigestion and loss of appetite. It was observed that among 160 patients, 93 (84.5%) patients had antral gastritis in group A, 20 (66.7%) in group B, 20 (100%) in group C. Generalised gastritis was found to be 8.2%

(9) in group A and only 3.3% (1) in group B. 20 (18.2%) patients had duodenitis in group A, 4 (13.3%) in group B. 29% (32) were found to have Reflux Esophagitis in group A and 3.3% (1) in group B. out of 160 patients, only 2 (1.8%) patients were found to have peptic ulcer disease in group A but not a single patient with peptic ulcer disease was found in group B and group C. There were 8 (7.3%) patients having normal upper G.I. endoscopic finding but they are H. Pylori positive on antral biopsy.

Table no. 5 Endoscopic Findings

Endoscopic Findings	Pre-treatment						Post treatment					
	Group A		Group B		Group C		Group A		Group B		Group C	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Antral Gastritis	93	84.5	20	66.7	20	100.0	3	2.7	19	63.3	12	60.0
Duodenitis	20	18.2	4	13.3	0	0.0	4	3.6	3	10.0	0	0.0
Hiatus Hernia	32	29.1	4	13.3	0	0.0	32	29.1	4	13.3	0	0.0
Reflux Esophagitis	25	22.7	1	3.3	0	0.0	4	3.6	1	3.3	0	0.0
Generalized Gastritis	9	8.2	1	3.3	0	0.0	1	0.9	1	3.3	0	0.0
Peptic Ulcer	2	1.8	0	0.0	0	0.0	2	1.8	0	0.0	0	0.0
Normal Upper GIT	8	7.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Effect of unani polyherbal formulation (test drug), placebo and pantoprazole after 3 months treatment in the eradication of H. Pylori bacteria is shown. (Table. 6)

Table no. 6

Group	No. of patients who became H.Pylori negative after treatment		No. of patients who remained H.Pylori positive after treatment	
	No of Patients	Percentage	No of Patients	Percentage
A	99	90	11	10
B	2	6.7	28	93.3
C	0	0	20	20

Out of 110 patients in group A, 99 (90%) patients became H. Pylori negative and only 11 (10%) remained H. Pylori positive. It shows that unani formulation eradicated H. Pylori bacteria in 90% cases. In group B, among 30 patients only 2 (6.7%) became H. pylori negative after treatment after 3 months therapy and 28 (93.3%) patients remained H. pylori positive. On the other hand, in group C, there is no effect of pantaprazole in eradication of H. pylori bacteria. In group C, all patients 20 (100%) remained H. pylori positive even after 3 months treatment. On applying Yates correction chi square test between group A and group B, its value is 77.36 (d.f = 1, p<0.0001) and between group A and group C, its value is 70.61 (d.f = 1, p<0.0001) the difference is highly significant between both the groups. Table 8 shows endoscopic status of gastritis before and after 3 months of treatment in group A, group B and group C. It was observed that 89.1% patients get cured from gastritis with unani polyherbal formulation in group A and only 3.3% (1) patient got relief in group after taking placebo, while in group C, 8 (40%) get cured with pantaprazole. After applying Yates correction Chi sq test its value between group A and group B is 86.74 (d.f = 1, p<0.0001) which is highly significant. The value of Yates correction Chi sq between group A and group C is 30.82 (d.f = 1, p<0.0001) and there is highly significant difference between the two groups.

Table no. 7

Status of Gastritis (antral/generalised)	Group A		Group B		Group C	
	No. of patients	percentage	No. of patients	percentage	No. of patients	percentage
Cured	98	89.1	1	3.3	8	40
Not Cured	4	3.6	20	66.7	12	60

IV. Discussion

Warm e Meda (Gastritis) has been one of the common problems of people during various periods and among different cultures and civilizations. Health of Meda (Stomach) has been given a prime importance in Unani Medicine. The diseases related to Meda/stomach are well described and well understood in Unani Medicine. Almost all Unani physicians had contributed towards the knowledge of health and disease of Meda/stomach. Hippocrates(460-370 B.C.), Galen (130-210 A.D.), Sabit Bin Qurrah (826-901 A.D.), Ali Bin Rabban Tabri (838-870 A.D.), Abu Bakr Mohammad Ibn Zakariya al-Razi (Rhazes) (865-925 A.D.), Ali Ibn Abbas Majoosi (930-994 A.D.), Abu Ali al-Husayn ibn Abd Allah ibn Sina (Avicenna) (980-1037 A.D.), Zayn al-Din Sayyed Ismail ibn Husayn Gorgani (1040–1136 A.D.) Muhadhib al-Din Abul-Hasan Ali ibn Ahmad Ibn Hubal (1122-1213), Abu-Marwan Abd al-Malik ibn Zuhr (Avenzoar) (1094-1162 A.D.), Abu Mansoor Al

Hasan· *Hakim* Ali ibn Kamal al-Din Muhammad *Gilani*, Hakim Muhammad Azam Khan (d. 1902 AD) are among the prominent Unani Medicine physicians who had discussed the etiopathogenesis and the treatment of the disease in detail.⁽⁷¹⁻⁸³⁾

Unani Physicians have mentioned a wide spectrum treatment for this disease according to the causes, clinical presentations, regions, climates, age, acuteness or chronicity and dietary habits with prime concern on the correction of Mizaj (temperament) and Akhlat (humors) of the patients. A number of medicines and corrective approaches covering all these aspects have been described in Unani Medicine resource books. These medicines have been in use since centuries. The efficacy of these medicines are well established.

In Unani system of medicine plants, animals as well as mineral origin drugs are being used for the treatment of gastritis without any known side effects e.g. some of the commonly used single drugs (Adviya mufrida) are Aloe barbadensis Mill (Elva), *Alpinia galanga* Willd (Khulanjan), *Althaea rosea* Linn (Khatami), *Anchusa strigosa* Labill (Gaozaban), *Glycyrrhiza glabra* Linn (Asl-us-soos), *Withania somnifera* Linn (Asgandh), *Andrographis paniculata* Wall (Bhuineem), *Zingiber officinale* Rosc (Adrak), *Picrorhiza Kurroa* Royle (Kuttki), *Embllica officinalis* (Amla), *Nigella sativa* Linn (Kalonji), *Momordica charantia* Linn (Karela), *Curcuma longa* Linn (Haldi), *Asparagus racemosus* Willd (Satawar), *Aegle marmelos* Correa (Bael), *Myristica fragrans* Houtt (Jaiphal) etc and in the form of compound drugs (Adviya murakkaba) are Majoon Dabidul Ward, Jawarish Anarain, Sharbat Anar, Majoon Zanjbil, Jawarish Mastagi, Qurs Satawari, Itrifal Aftimoon, Sharbat Unnab and Khammeera Sandal have been indicated by Unani physicians for the treatment of chronic gastritis and their efficacy against gastritis has also been tested by in vivo and in vitro studies.^(37,39,43,44,84,65,85-88)

Mode of action of these drugs are both systemic and local. Apart from the correction of altered mizaj (temperament), these drugs produce soothing effect on the inflamed mucosa, provide ground material for healing, removes the factors responsible for inflammation and also provide antiseptic or antibacterial effect. Further these physicians have suggested different medicines in different seasons, regions and mizaj.

The aim of this study was to demonstrate the effect of Unani compound drug containing “*Glycyrrhiza glabra* (Asl-us-soos), *Plantago ovata* (Asapghol musallam), *Acacia arabica* (Samghe arabi) and *Pistacia lentiscus* (Mastagi)” in the treatment of antral and generalized gastritis and eradicating *H. pylori* bacteria from the stomach, which is a major cause.

Aslus-soos (*Glycyrrhiza glabra*)/licorice reduces gastric secretion produces thick mucus which protects the lining of stomach from inflammation, gastritis and peptic ulceration, it contains flavonoids, so it possess anti-inflammatory and anti-bacterial effect.^(89,90)

Aspaghool musallam (*Plantago ovata*) is a water soluble seed husk polysaccharides promote proliferation cleaning and wound healing properties in guinea pigs.^(91,92)

Mastagi (*Pistacia lentiscus*) is cytoprotective and has mild anti-secretory effect and is effective for the healing of gastric and duodenal ulcer.^(93,94,95)

Samagh-e-arabi (*Acacia arabica*) contains tannins, saponins, glycosides, phenols, terpenes and flavonoids which can be easily hydrolysed, this property of samagh-e-arabi attributes to anti-bacterial and anti-inflammatory effect.⁽⁹⁶⁾

Krausse R et al, Marjan R et al, and Fukai T et al found licorice extract had potent eradication effect against *H. Pylori* strain.^(89,97,98)

Castillo J. et al and Nabati et al reported anti *H. Pylori* activity of *Plantago ovate*.^(99,100)

Omayma K.H., and M. Amin et al conducted in vitro studies and found anti-bacterial and anti-*H. Pylori* activity of *acacia arabica*.^(100,101)

Mastagi showed anti- *H. Pylori* effect not only in vitro but in clinical trial as well.^(102,103,104)

In 1999 Gharzouli K et al found gastro-protective effect of tannic acid and the aqueous extract of from *Quercus ilex* L. root bark, *Punica granatum* L. fruit peel and *Artemisia herba-alba* Asso leaves in rats against ethanol-induced gastric damage and suggested that monomeric and polymeric polyphenols can strengthen the gastric mucosal barrier.⁽¹⁰⁵⁾ On the other hand Ajai Kumar K.B., et al in 2005 conducted in vivo study on the inhibition of gastric mucosal injury by methanolic extract of *Punica granatum* and they revealed the gastro-protective effect of the extract through antioxidant mechanism.⁽¹⁰⁶⁾

Jamal et al suggested that Tabasheer and other unani mufrad advia/single drugs are safe and cost effective in gastric ulceration.⁽⁸⁷⁾

In 2010, Shagufta N et al conducted an experimental study on Anti-ulcer effect of hydroalcoholic extract of Tikhme Kishneez (*Coriandrum sativum* Linn.) in stress induced gastric ulceration in albino rats with Ranitidine as the standard drug and demonstrated that Tikhme Kishneez possesses anti-ulcer effect against stress induced gastric ulcer.⁽¹⁰⁷⁾

A study was carried out on 100 patients in the department of Jarahat, Ajmal Khan Tibbiya College and Hospital, AMU, Aligarh to assess the effect of Qurs-e-Tabasheer in endoscopically proved antral gastritis and duodenitis and demonstrate that Qurs-e-Tabasheer not only declines the symptoms of gastritis and duodenitis but it also corrects them as the ingredients of this medicine have been formulated in such a way to cover

maximum aspects of the treatment of gastritis. It contains such drugs which corrects inflammation, reduce gastric secretions, have haemostatic property, remove toxic Material, produce soothing effects and provide material for the healing.^(105,60,108)

V. Conclusion

Health of Meda (Stomach) has been given a prime importance in unani medicine and the disease related to Meda/stomach are described in detail in their literature by various unani physicians and they also emphasised on better functioning of Meda/stomach. Warm-e-Meda / Gastritis is one of the commonest problem among different culture and civilization. The diseases related to Meda/stomach are well described and well understood in Unani Medicine. Almost all Unani physicians have contributed towards the knowledge of health and disease of Meda/stomach. There are various unani drugs of plant, animal and mineral origin are being used for the treatment of gastritis and having H. Pylori effect.

In our study we found the Unani polyherbal formulation containing Glycyrrhiza glabra (Asl-us-soos), Plantago ovata (Asapghol musallam), Acacia Arabica (Samghe arabi) and Pistacia lenticus (Mastagi) to be effective in treating antral gastritis and eradicating H. Pylori bacteria and it is recommended to conduct more clinical trials to prove their efficacy and obtain more conclusive results.

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