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Unani Treatment Decreased Fibrosis and Improved Liver Functions in Decompensated Cirrhosis of Liver: A Case Series

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Abstract

At present, liver transplantation remains the only curative option for the patients with cirrhosis and end-stage liver diseases. The survival rate and recurrent diseases remain the major issues in the patient post-transplantation. Unani medicine is one of the oldest traditional systems of medicine which has been treating chronic liver diseases and cirrhosis (Talayyaful-Kabid) for centuries. The current study aimed to assess the impact of Unani treatment on decompensated cirrhosis and collect data to warrant further clinical trials. Authors conducted a case series on five patients with decompensated cirrhosis and portal hypertension. The disease was confirmed through FibroScan and ultrasound and treated with Unani treatment orally for seven months. Results were evaluated based on FibroScan, liver function test (LFT), EuroQol-5D (EQ5D), Child-Pugh and TTO-TIME (trade-off question). Significant improvements in LFT, fibrosis and quality of life were achieved in the studied patients. The literature related to the herbal constituents of chief medicines used to treat in this case was reviewed. The herbs proved their potential anti-oxidative, anti-inflammatory, hepato-protective, immuno-modulator and antiviral activities, suggesting plausible mechanisms of action in the cases. The preliminary findings indicated the potential therapeutic role of Unani treatment in decompensated cirrhosis. Clinical trials should be conducted to explore further therapeutic potential of Unani treatment in decompensated cirrhosis.

Keywords: Liver Cirrhosis, Unani Medicine, Complementary Medicine, Liver Fibrosis, Chronic Liver Disease, Hepato-Protective, Regenerative Herbs, Liver Diseases, Traditional Medicine, Case Series Cirrhosis

1. Introduction

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic persistent liver injury, which leads to portal hypertension, ascites and end-stage liver disease. Liver fibrosis is a dynamic process resulted from the perpetuation of the normal wound healing response resulting in an abnormal continuation of fibrogenesis (connective tissue production and deposition) (1, 2). Progression of fibrosis occurs at variable rates, depending on the cause of liver disease, environmental and host factors (1). The major clinical consequences of cirrhosis are impaired hepatocyte (liver) function, an increased intrahepatic resistance (portal hypertension), ascites and the development of hepatocellular carcinoma (HCC) (1-3).

Alcoholic liver disease and hepatitis C are the most common etiologies of liver fibrosis in the Western world, while hepatitis B prevails in most parts of Asia and sub-Saharan Africa (1). Alcohol consumption is estimated to cause 20% - 50% of liver cirrhosis (4). After the identification of the hepatitis C virus in 1989 and of non-alcoholic steato-hepatitis (NASH) in cases with obesity and diabetes, the diagnosis of cirrhosis without an apparent cause (cryptogenic cirrhosis) is rarely made. Epidemiological studies identified regular (moderate) alcohol consumption, age above 50 years and male gender as risk factors in chronic hepatitis C, or older age obesity, insulin resistance/type 2 diabetes, hypertension and hyperlipidemia (all features of the metabolic syndrome) in NASH. Approximately 10% - 20% of patients with chronic hepatitis B virus or hepatitis C virus infection have cirrhosis at first clinical presentation, and as many as 20% - 30% of those who do not have cirrhosis will eventually develop this condition and its complications within one or more decades (3).

Liver cirrhosis is a significant cause of global health burden, with more than one million deaths in 2010. Mortality from liver cirrhosis was also comparatively high in countries of Central Asia, particularly Mongolia, Uzbekistan and Kyrgyzstan, and in parts of sub-Saharan Africa (5).

The physicians of Unani system of medicine treat liver cirrhosis and its consequences for centuries. The entity "Warm-e-Jigar Barid Saudawi" / "Taleef-ul-Kabid" in Unani literature, mimic liver cirrhosis and associated constellation of symptoms. A large number of single and compound drug preparation are documented to treat "Taleef-

ul-Kabid". These scientific studies validated the antioxidant, anti-inflammatory, antiviral, immuno-modulatory and hepatoprotective nature of plant-based medicines and their bioactive principle is isolated and characterized. The cases treated in the present series include only the ones advised for liver transplantation. Due to non-availability of donor and certain factors such as restricted and costlier resources in overpopulated India, Unani treatment is given in these such as per Unani paradigms documented in Unani literature for liver cirrhosis. Unani treatment, given in this case series included multiple poly-herbal or compound preparation of Unani medicine. Therefore, the present case series was performed, primarily to explore the antifibrotic and liver regenerating effect of Unani treatment in the five cases of liver cirrhosis.

2. Case Presentation

2.1. Consent

Informed consent was taken from the patients. The human data included in this case series were obtained in compliance with the Declaration of Helsinki.

2.2. Outcome Measures

Results were evaluated based on the clinical manifestations and investigations such as FibroScan, liver function test (LFT) and ultrasonography of abdomen. Assessment of quality of life was also done using EuroQol-5D (EQ5D), Child-Pugh score and TTO-TIME [trade-off question] section 37 of physical health version 2, October 2005, before and after Unani treatment.

Case 1: S.J, 40-year-old non-smoker non-vegetarian Indian male admitted to the in-patient department of Majeedia Unani hospital (MUH) on 13 February 2015 with chief complains of fever, dark yellow coloration of urine, pain in abdomen, constipation, distension of abdomen, loss of appetite and general weakness for one and a half months. Patients complained of chronic weakness and indigestion for two years. No prior history of jaundice was found although patient reported history of blood donation seven years ago. Patient was investigated with haemogram, LFT, kidney function test (KFT), ultrasonography of abdomen, FibroScan of liver and viral hepatitis profile. Patient was diagnosed as a case of chronic hepatitis B complicated-decompensated cirrhosis of liver with portal hypertension, gross ascites and contacted edematous gall bladder with left renal calculus, confirmed by ultrasonography of abdomen and FibroScan. Viral count was 188,115 IU/ mL on 19 February 2015. The serum bilirubin total, alanine transaminase (SGPT), alkaline phosphatase were 17.05 mg/dL, 1271 IU/ L and 407 IU/ L respectively on 13 February 2015. Prothrombin time (PT), activated partial thromboplastin time (APTT) and international normalized ratio (INR) was not deranged. The first FibroScan of liver revealed 'E' median 45.0 kPa and 'CAP' median 148 dB/m on 24 February 2015. Unani treatment (started from 14 February) specific for etiology, given in this case consisted of:

1) Primarily decoction of earth smoke (*Fumaria officinalis*), wasteland weed (*Tephrosia purpurea*), chirata (*Swertia chiraita*), East Indian globe thistle (*Sphaeranthus indicus*), red sandalwood (*Pterocarpus Santalinus*), chicory seed (*Cichorium intybus*), tukhm saddab and black nightshade (*Solanum nigrum*) 5 g each, in the morning before breakfast , started since admission. Henna (*Lawsonia inermis*), Indian globe thistle (*Echinops echinatus*), Indian ebony (*Diospyros ebenum*), rose flower (*Rosa damsecenes*), chicory seed (*Cichorium intybus*), yarrow seed (*Achillea millefolium*) were added to the above decoction formula, 5 g each from 5 March 2015.

2) A mixture of aqueous extracts of black nightshade (*Solanum nigrum*) 50 mL + chicory (*Cichorium intybus*) 50 mL + yarrow (*Achillea millefolium*) 50 mL, twice daily,

3) Wormwood powder (*Artemisia absinthium*), chicory seed (*Cichorium intybus*) and costus (*Saussurea lappa*), 5 g each was started from 5 March 2015,

4) Habbe Kabid Naushadri, two tablets twice daily after meal,

5) Habbe Halteet, two tablets twice daily after meal.

Repeated assessment of liver function test and urine analysis were performed weekly. On 21 March, serum bilirubin total, SGPT, alkaline phosphatase and gamma-glutamyl transferase (GGT) reduced to 10.62 mg/dL, 295.67 IU/L, 463.48 IU/L and 206.9 IU/L respectively. Another analysis of LFT on 31 March 2015 showed further reduction in serum bilirubin total, SGOT, alkaline phosphatase and GGT values to 9.76 mg/ dL, 186.1 IU/L, 358.07 IU/L and 186.31 IU/L respectively. Second ultrasonography of abdomen performed on 25 March 2015 showed a mildly enlarge liver, no free fluid and non-dilated portal vein and left renal calculus. A repeated FibroScan on 25 March 2015 (approx. after six weeks of Unani treatment) revealed a definite reduction in liver fibrosis to 'E' median 27.0 kPa and 'CAP' median 185 dB/m from 'E' median 45.0 kPa and 'CAP' median 148 dB/m. Haemogram and KFT remain normal before and after the Unani treatment. Patient was discharged on 30 March 2015 with the following medicines:

1) Above mentioned decoction,

2) "Sharbat-e-Jigreen", 20 mL, twice daily,

3) A mixture of aqueous extract of black nightshade (*Solanum nigrum*) 50 mL + aqueous extract of chicory (*Cichorium intybus*) 50 mL + Aqueous extract of yarrow (*Achillea millefolium*) 50 mL, twice daily,

4) "Arq-e-Murakkab-e-Musaffiye-e-Khoon", 50 mL, twice daily,

5) "Habbe-e-Halteet" two tablets, SOS in case of acidity and flatulence.

Further follow up on 3 September 2015, analysis of LFT showed normalization of serum bilirubin total, SGOT, alkaline phosphatase and GGT values to 0.63 mg/dL, 25.1 IU/L, 120 IU/L and 57.7 IU/L respectively. Viral count which was 1, 88,115 IU/ mL on 19 February 2015 became undetectable on 3 September 2015 (approximately 28 weeks post-treatment). Hepatitis B surface antibody (HBsAg) was positive with titer value of 13.83 IU/mL (before starting the treatment) became negative (< 0.08 IU/mL) approximately 28 weeks after treatment. Before the treatment, the values of EQ5D, Child-Pugh and trade-time-off (TTO) score were 60%, 10 and 21 respectively, which reduced to 0, 5 and 4 respectively, 28 weeks after Unani treatment.

Case 2: SHN, a 45-year-old non-smoker non-vegetarian Indian female, known case of chronic hepatitis B, admitted in MUH on 17 September 2014 with chief complains of: yellow coloration of sclera and urine, mild continuous fever, general weakness and pain in legs while walking for two months. Patient was investigated with haemogram, LFT, KFT, ultrasonography of abdomen, FibroScan and further HBV profile. After ultrasonography finding of splenomegaly, portal hypertension and provisional cirrhosis were subsequently confirmed by FibroScan as a case of chronic hepatitis B induced liver cirrhosis. HBV DNA quantitative value on 20 September 2014 was 2300 IU/mL, hepatitis B s-antigen (HBsAg) was positive with titer value of 14.76 and HBeAg positive 2.59 S/CO while HBeAb was negative. Her FibroScan showed 'E' median 16.1 kPa and 'CAP' median 180 dB/m on 26 September 2014. The case was treated with the following Unani treatment:

1) Primarily consisted of decoction of earth smoke (*Fumaria officinalis*), wasteland weed (*Tephrosia purpurea*), chirata (*Swertia chiraita*), East Indian globe thistle (*Sphaeranthus indicus*), red sandalwood (*Pterocarpus santalinus*), 5 g of each, before breakfast, in the morning,

2) A mixture of aqueous extract of black nightshade (*Solanum nigrum*) 50 mL + aqueous extract of chicory (*Cichorium intybus*) 50 mL + aqueous extract of yarrow (*Achillea millefolium*) 50 mL, twice daily,

3) "Majoon Dabeed-ul-ward", 10 g twice daily,

4) "Habbe Kabid Naushadri", three tablets three times daily after meal.

Before starting the treatment, LFT showed serum bilirubin total, SGPT and alkaline phosphatase of 8.5 mg/dL, 231 IU/L and 192 IU/L respectively on 17 September 2014 which reduced to 5.0 mg/ dL, 73 IU/L, and 101 IU/L respectively on 22 September 2015, after one week of Unani treatment. HBV DNA which was 2,300 before the treatment became undetectable on 11 December 2014 after Unani treatment. Repeat FibroScan performed on 9th December 2014 revealed reduction in liver fibrosis to 'E' median 13.3 kPa and 'CAP' median 216 dB/m from 16.1 kPa and 'CAP' median 180 dB/m after approximately 12 weeks of treatment. Before starting the treatment, the values of EQ5D, Child-Pugh and TTO score were 40%, 10 and 17, respectively, which reduced to 5%, 5 and 3, respectively, after 12 weeks of Unani treatment.

Case 3: RJV, a 50-year-old smoker non-vegetarian Indian male patient with diabetes and hypertension and a known case of alcoholic liver cirrhosis, portal hypertension referred to out-patient department of MUH on 10 March 2014 with chief complains of: loss of appetite, nausea, distension of abdomen, loss stool 3 - 4/day, general weakness, insomnia, heaviness in epigastrium and frequent giddiness. Serum bilirubin, SGPT, alkaline phosphatase and GGT were 2.10 mg/dL, 54 IU/L, 220 IU/L and 205 IU/L respectively on 3 March 2014. Ultrasonography showed cirrhotic liver with splenomegaly and portal hypertension on 10 March 2014. First, patient's blood sugar was controlled. FibroScan showed 'E' median 49.6 kPa and 'CAP' median 343 dB/m on 4 March 2014. The case was treated with the following Unani treatment started from 10 March 2014.

1) Jigreena, two capsules, twice daily,

2) A mixture of aqueous extract of black nightshade (*Solanum nigrum*) 50 mL + aqueous extract of chicory seed (*Cichorium intybus*) 50 mL + [Aqueous extract of yarrow (*Achillea millefolium*)] 50 mL, twice daily,

3) "Qurs kuliya" two tablets in the morning,

4) "Ajmaloon", two tablets twice daily,

A repeated LFT revealed reduction in serum bilirubin, SGPT, alkaline phosphatase and GGT values from 2.10 mg/dL, 54 IU/L, 220 IU/L and 2004 IU/L, respectively, to 0.9 mg/dL, 16 IU/L, 133 IU/L and 631 IU/L respectively on 28 March 2014. A further repeated observation showed normal LFT pattern with serum bilirubin, SGPT, alkaline phosphatase and GGT values of 0.8 mg/dL, 12 IU/L, 128 IU/L and 148 IU/L on 10 May 2014. FibroScan, showed reduction in liver fibrosis to 'E' median 33,3 kPa and 'CAP' median 292 dB/m from 'E' median 49.6 kPa and 'CAP' median 343 dB/m, repeated on 10 May 2014 after eight weeks of the above mentioned Unani treatment. Haemogram and KFT were normal before and after the treatment. Before starting the treatment, the values of EQ5D, Child-Pugh and TTO score were 25%, 9 and 17, respectively, which reduced to 1%, 5 and 2, respectively, after six weeks of Unani treatment.

Case 4: AQL, a 50 year-old non-smoker non-vegetarian Indian male with diabetes referred to OPD of MUH for Unani treatment on October 17, 2014 with complains of: loss of appetite; distension of abdomen; heaviness in epigastrium; flatulence for two years. He was already treated

in two major tertiary care centers in New Delhi but got no relief in his condition. After excluding viral, autoimmune and other etiologies, he was diagnosed and treated as a case of non-alcoholic fatty liver disease (NAFLD) related cirrhosis of liver with portal hypertension (HTN) with splenomegaly. Patient was allowed to continue the same oral hypoglycemic. The following regimen was advised to this patient:

1) Jigreena, two capsules, twice daily,

2) Triphala Amaltas Ras syrup, 30 mL, twice daily,

3) A mixture of aqueous extract of black nightshade (*Solanum nigrum*) 50 mL + aqueous extract of chicory (*Cichorium intybus*) 50 mL + aqueous extract of yarrow (*Achillea millefolium*) 50 mL, twice daily,

4) Habbe Kabid Naushadri, three tablets twice daily after meal.

Before the treatment, serum bilirubin total, SGPT, and alkaline phosphatase were 0.4 mg/dL, 84 IU/L and 146 IU/L respectively on 15 September 2014 which became 0.7 mg/dL, 48 IU/L, and 46 IU/L respectively on 9th January 2015 post-treatment. TNF-α which was 13.4 IU/mL before the treatment, reduced to 8.41 IU/mL on 17th January 2015, before initiation of Unani treatment. Before starting the treatment, FibroScan showed significant fibrosis with 'E' median 7.3 kPa and 'CAP' median 333 dB/m on 15 September 2014. Repeated FibroScan performed on 9th January 2015 revealed reduction in liver fibrosis to 'E' median 4.3 kPa and 'CAP' median 297 dB/m after approximately 11 weeks of treatment. Before starting the treatment, ultrasonography of abdomen showed mild enlarged liver coarse echo texture, splenomegaly and PHTN. After treatment, liver size was normalized with the presence of coarse echo texture, splenomegaly and PHTN. The values of EQ5D, Child-Pugh and TTO score were 25%, 6 and 14, respectively, which reduced to 0, 5 and 2, respectively, after approximately 11 weeks of Unani treatment.

Case 5: SLU, 35 years old non-smoker non-vegetarian female with diabetes referred to OPD of MUH for Unani management of liver cirrhosis after not being relieved from reputed tertiary care center in New Delhi. She came with complains of pain in abdomen, vomiting after meals, recurrent loose motions, distension of abdomen, heaviness in epigastrium for three years. Patient was diagnosed as liver cirrhosis through portal HTN with splenomegaly after excluding viral, metal, auto-immune and other etiologies. FibroScan before starting the treatment confirmed fibrosis with 'E' median 20.9 kPa and 'CAP' median 123 dB/m on 17 April 2014. Unani treatment (started from 17 April 2015), given in this case consisted of:

1) Jigreena, 20 mL, twice daily,

2) A mixture of aqueous extract of black nightshade (*Solanum nigrum*) 50 mL + aqueous extract of chicory (*Cichorium intybus*) 50 mL + aqueous extract of yarrow (*Achillea millefolium*) 50 mL, twice daily,

3) Majoon Dabeed-ul-ward, two capsules, twice daily,

4) Habbe halteet, three tablets, three times daily after meal,

5) Aqueous extract of woodworm (*Atremisia absinthium*) 10 mL, twice daily.

Serum bilirubin, SGPT, and alkaline phosphatase were 2.3 mg/dL, 88 IU/L, and 319 IU/L respectively on 3 April 2014 which reduced to 1.0 mg/ dL, 30 IU/ mL and 151 IU/ mL, respectively, on 23 September 2015. Ultrasonography of abdomen showed mild enlarged liver with coarse echo texture, splenomegaly, and PHTN before the treatment. After treatment, the liver size was normalized with the presence of coarse echo texture, splenomegaly and PHTN. FibroScan showed reduction in liver fibrosis from 'E' median 21.1 kPa and 'CAP' median 302 dB/m to 'E' median 14.4 kPa and 'CAP' median 201 dB/m, repeated on 10 May 2014 after 20 weeks of the above mentioned Unani treatment. The values of EQ5D, Child-Pugh and TTO score were 60%, 6 and 20, respectively, which reduced to 0, 5 and 2, respectively, after 12 weeks after Unani treatment.

Table 1 provides a summary of the relevant biomarkers and Table 2 provides summary of quality of life assessment in these five cases.

3. Discussion

The ultimate therapy for cirrhosis and end stage liver disease is liver transplantation. The major issues that remain in the care of the patient post liver transplantation are recurrent disease in the transplant, particularly HCV, and long term consequences of immunosuppressive agents such as hypertension, hyperlipidemia and renal disease (1). Even in the developed world, although the organ donors are available, the condition of the potential recipients limit the applicability of this transplantation, and thus validation of traditional therapies to halt or reverse fibrosis are urgently needed.

In the current series, treatment was given with a decoction, including plants such as earth smoke (*Fumaria officinalis*), wasteland weed (*Tephrosia purpurea*), chirata (*Swertia chiraita*), East Indian globe thistle (*Sphaeranthus indicus*), henna (*Lawsonia inermis*), Indian globe thistle (*Echinops echinatus*), Indian ebony (*Diospyros ebenum*), rose flower (*Rosa damsecenes*), chicory seed (*Cichorium intybus*), yarrow seed (*Achillea millefolium*)and red sandalwood (*Pterocarpus santalinus*) or Jigreen along with aqueous extract of black nightshade (*Solanum nigrum*), aqueous extract of chicory (*Cichorium intybus*) and aqueous extract of yarrow (*Achillea millefolium*) and Jigreena capsules used in single

Table 1. Summary of Investigation on Five Cases Following Unani Treatment

Investigation	Case 1		Case 2		Case 3		Case 4		Case 5	
	Before the Treatment	Approx. 28 weeks. of Treatment	Before the Treatment	Approx. 12 weeks. of Treatment	Before the Treatment	Approx. 8 weeks. of Treatment	Before the Treatment	Approx. 11 weeks. of Treatment	Before the Treatment	Approx. 20 weeks. of Treatment
Serum bilirubin total, mg/dL	17.05	0.63	8.5	5.0	2.10	0.8	0.4	0.7	2.3	1.0
SGPT, IU/L	1271	25.1	231	73	54	12	84	48	80	30
Alkaline phosphatase, IU/L	407	120.6	192	101	220	128	146	46	319	151
GGT, IU/L	206.9	57.7	UN	UN	205	148	UN	UN	UN	UN
FibroScan ('E' median and 'CAP' median)	45.0 kPa and 148 dB/ m	27.0 kPa and 185 dB/m	16.1 kPa and 180 dB/ m	13.3 kPa and 216 dB/ m	49.6 kPa and 343 dB/ m	33.3 kPa and 292 dB/ m	10.1 kPa and 333 dB/m	4.3 kPa and 297 dB/m	21.1 kPa and 302 dB/m	14.4 kPa and 201 dB/m
Ultrasonography of abdomen	Liver cirrhosis with PHTN, gross ascites and contacted edematous gall bladder with left renal calculus	Liver normal size with coarse echo texture	Splenomegaly, PHTN and liver cirrhosis	UN	liver Cirrhosis with splenomegaly and PHTN	UN	Mild enlarge liver coarse echo texture, splenomegaly, PHTN	Liver size normal, coarse echo texture, splenomegaly, PHTN	Mild enlarge liver coarse echo texture, splenomegaly, PHTN	Liver size normal, coarse echo texture , splenomegaly, PHTN
Hepatitis B Virus DNA, IU/mL	1, 88,115	< 20 Undetectable	2300	< 20 Undetectable	NA	NA	NA	NA	NA	NA

Abbreviations: NA, not applicable; UN, unavailable; SGPT, alanine amino transferase; GGT, gamma-glutamyl transferase; PHTN, portal hypertension.

Table 2. Effect of Unani Treatment on Quality of Life

Value	EQ5D		Child-Pugh Score		TTO Score	
	Before the Treatment, (%)	After the Treatment, (%)	Before the Treatment, (%)	After the Treatment, (%)	Before the Treatment, (%)	After the Treatment, (%)
Case 1	60	0	10	5	21	4
Case 2	40	5	10	5	17	3
Case 3	25	1	9	5	17	2
Case 4	25	0	6	5	14	2
Case 5	65	0	6	5	20	2

Abbreviations: EQ5D, EuroQol-5D; TTO, time-trade-off.

and poly-herbal form for chronic liver diseases for decades in Unani system of medicine.

The immune system (both the innate and the adaptive immune cells) plays an important role in fibrosis, since persistent inflammation almost always accompanies fibrosis. In the current cases, reduction in fibrosis could be due to immuno-modulatory effect of the constituents in the above mentioned Unani treatment, proven in various animal models (6-8).

Chronic inflammation almost always precedes and accompanies fibrotic changes and the medicines that target the inflammatory cascade typically have antifibrotic activity. Moreover, the vicious cycle of scar formation is initiated by oxidative stress so targeting ROS generation also reduces the inflammatory response, which will attenuate hematopoietic stem cell activity (HSC) and fibrogenesis. Antioxidants can attenuate reactive oxygen species (ROS) effects and hold promise as potential antifibrotic therapies, provided that sufficient antioxidant activity can be delivered to the sites of injury within the liver.

Antioxidants exert a preventive effect on hepatocyte injury but may also be directly antifibrogenic (9). Based on this principle, various constituents of given Unani treatment such as earth smoke (*Fumaria officinalis*), East Indian globe thistle (*Tephrosia purpurea*), chirata (*Swertia chiraita*), Indian globe thistle (*Sphaeranthus indicus*), red sandalwood (*Pterocarpus santalinus*), black nightshade (*Solanum nigrum*), chicory (*Cichorium intybus*) proved as potent antioxidant (inhibiting ROS generation), could be the plausible mechanism of reduction of fibrosis in FibroScan and liver regenerative effect (10-15). Moreover, these drugs proved helpful for their hepatoprotective and

anti-inflammatory activity (15-19) and persistent inflammation that almost always precedes and accompanies fibrosis. Therefore, medicines that target the inflammatory cascade and mitigate further liver injury (hepatoprotective) are typically designated to possess antifibrotic activity and highlight the anti-fibrotic effect of Unani treatment (9). Return of liver function test toward normal and reduction in inflammation could be due to hepato-protective and anti-inflammatory effect of Unani treatment (9). HBV DNA became undetectable in cases 2 and 3, could be due to anti-hepatitis B and antiviral properties of constituents such as Swertia chiraita (15, 20) etc.

Jigreen, for its effects on anorexia, pain in abdomen, nausea and vomiting, is probably the cause for symptomatic relief in the current cases. Jigreen also reduced bilirubin levels and improved other liver biochemical markers (21, 22). Chicory exhibited analgesic activity in mice in hot plate and tail-flick tests (22, 23). Majoon Dabeed-ul-ward is a compound formulation of Unani medicine, which contain Rosa damescene (Rose) as main drug, proven as hepatoprotective in various studies (15, 24).

3.1. Conclusion

The current case series provide a novel direction in which the above mentioned Unani treatment can be used to regenerate liver and halting progression of fibrosis in cirrhosis and alleviate constellation of symptoms. Unani treatment also improved quality of life in these five cases. Therefore further studies should be performed to warrant the anti-fibrotic and regenerative effect along with elucidation of mechanism of action of Unani treatment in cirrhosis of liver.

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Footnote

Authors' Contribution: Study concept, critical revision of the manuscript for important intellectual content, statistical analysis, administrative, technical and material support, study supervision: Mohammad Akhtar Siddiqui; study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis, administrative, technical, and material support: Shabnam Ansari.

References

1. Schuppan D, Afdhal NH. Liver cirrhosis. *Lancet.* 2008;**371**(9615):838–51. doi: 10.1016/S0140-6736(08)60383-9. [PubMed: 18328931].
2. Cohen-Naftaly M, Friedman SL. Current status of novel antifibrotic therapies in patients with chronic liver disease. *Therap Adv Gastroenterol.* 2011;**4**(6):391–417. doi: 10.1177/1756283X11413002. [PubMed: 22043231].
3. Benvegnu L, Gios M, Boccato S, Alberti A. Natural history of compensated viral cirrhosis: a prospective study on the incidence and hierarchy of major complications. *Gut.* 2004;**53**(5):744–9. doi: 10.1136/gut.2003.020263.
4. WHO . Age-standardized death rates of liver cirrhosis Global Health Observatory; 2015. Available from: http://www.who.int/gho/alcohol/harms_consequences/deaths_liver_cirrhosis/en.
5. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC Med.* 2014;**12**:145. doi: 10.1186/s12916-014-0145-y. [PubMed: 25242656].
6. Nancollas MP, Peimer CA, Wheeler DR, Sherwin FS. Long-term results of carpal tunnel release. *J Hand Surg Br.* 1995;**20**(4):470–4. [PubMed: 7594985].
7. Amirghofran Z, Azadbakht M, Karimi MH. Evaluation of the immunomodulatory effects of five herbal plants. *J Ethnopharmacol.* 2000;**72**(1-2):167–72. [PubMed: 10967468].
8. Kumar IV, Paul BN, Asthana R, Saxena A, Mehrotra S, Rajan G. Swertia chirayita mediated modulation of interleukin-1beta, interleukin-6, interleukin-10, interferon-gamma, and tumor necrosis factor-alpha in arthritic mice. *Immunopharmacol Immunotoxicol.* 2003;**25**(4):573–83. doi: 10.1081/IPH-120026442. [PubMed: 14686799].
9. Kawada N, Seki S, Inoue M, Kuroki T. Effect of antioxidants, resveratrol, quercetin, and N-acetylcysteine, on the functions of cultured rat hepatic stellate cells and Kupffer cells. *Hepatology.* 1998;**27**(5):1265–74. doi: 10.1002/hep.510270512. [PubMed: 9581680].
10. Shirwaikar A, Prabhu KS, Punitha IS. In vitro antioxidant studies of Sphaeranthus indicus (Linn). *Indian J Exp Biol.* 2006;**44**(12):993–6. [PubMed: 17176673].
11. Kshirsagar P, Chavan J, Nimbalkar M, Yadav S, Dixit G, Gaikwad N. Phytochemical composition, antioxidant activity and HPLC profiles of Swertia species from Western Ghats. *Nat Prod Res.* 2015;**29**(8):780–4. doi: 10.1080/14786419.2014.986124. [PubMed: 25482162].
12. Miniaev VI, Grabel'nikov SA. The capacity of animals to purposefully alter their respiratory stereotype. *Fiziol Zh.* 1987;**33**(3):42–7. [PubMed: 3609363].
13. Arulmozhi V, Krishnaveni M, Karthishwaran K, Dhamodharan G, Mirunalini S. Antioxidant and antihyperlipidemic effect of Solanum nigrum fruit extract on the experimental model against chronic ethanol toxicity. *Pharmacogn Mag.* 2010;**6**(21):42–50. doi: 10.4103/0973-1296.59965. [PubMed: 20548935].
14. Rafiquzzaman SM, Kim EY, Kim YR, Nam TJ, Kong IS. Antioxidant activity of glycoprotein purified from Undaria pinnatifida measured by an in vitro digestion model. *Int J Biol Macromol.* 2013;**62**:265–72. doi: 10.1016/j.ijbiomac.2013.09.009. [PubMed: 24060280].
15. Akhtar Siddiqui M, Ansari S. Therapeutic effect of a unani formulation on hbsag in chronic hepatitis b: A case series. *Asian J Pharmaceut Clin Res.* 2015;**8**(5).
16. Ali A, Shyum Naqvi SB, Gauhar S, Saeed R. Anti-inflammatory and analgesic activities of ethanolic extract of Sphaeranthus indicus Linn. *Pak J Pharm Sci.* 2011;**24**(3):405–9. [PubMed: 21715276].
17. Ramachandran S. Review on Sphaeranthus indicus Linn. (Kottaikkarantai). *Pharmacogn Rev.* 2013;**7**(14):157–69. doi: 10.4103/0973-7847.120517. [PubMed: 24347924].
18. Mukherjee S, Sur A, Maiti BR. Hepatoprotective effect of Swertia chirata on rat. *Indian J Exp Biol.* 1997;**35**(4):384–8. [PubMed: 9315240].
19. Karan M, Vasisht K, Handa SS. Antihepatotoxic activity of Swertia chirata on paracetamol and galactosamine induced hepatotoxicity in rats. *Phytother Res.* 1999;**13**(2):95–101. doi: 10.1002/(SICI)1099-1573(199903)13:2<95::AID-PTR379>3.0.CO;2-4. [PubMed: 10190179].

20. Zhou NJ, Geng CA, Huang XY, Ma YB, Zhang XM, Wang JL, et al. Anti-hepatitis B virus active constituents from Swertia chirayita. *Fitoterapia.* 2015;**100**:27–34. doi: 10.1016/j.fitote.2014.11.011. [PubMed: 25447162].
21. Tamanna SA. Effect of Jigreen on Patients Suffering from Hepatitis B. Proceeding of the National Seminar on Reasearch Methodology in Unani Medicine. New Delhi,India. .
22. Ansari S, Siddiqui A, Nikhat S, Mushtaq S. Gilbert's syndrome- a case with interpretation and management in unani medicine. *Int J Pharmacognosy.* 2015;**2**(2):98–101. doi: 10.13040/IJPSR.0975-8232.IJP.2.
23. Wesolowska A, Nikiforuk A, Michalska K, Kisiel W, Chojnacka-Wojcik E. Analgesic and sedative activities of lactucin and some lactucin-like guaianolides in mice. *J Ethnopharmacol.* 2006;**107**(2):254–8. doi: 10.1016/j.jep.2006.03.003. [PubMed: 16621374].
24. Saxena M, Shakya AK, Sharma N, Shrivastava S, Shukla S. Therapeutic efficacy of Rosa damascena Mill. on acetaminophen-induced oxidative stress in albino rats. *J Environ Pathol Toxicol Oncol.* 2012;**31**(3):193–201. [PubMed: 23339694].