

Clinical Efficacy of LivPro® Herbal Medicine among Hepatitis C Patients Pakistan: Longitudinal Interventional Study

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Abstract

The current study aims to investigate the hepatoprotective effects of LivPro® among hepatitis C patients. An interventional study was performed among n=89 hepatitis C patients. The duration of the study was 3 months and the assessment for liver function, ELISA, and Viral load was performed monthly for the patients recruited in this study. Mean difference was measured and at a Confidence Interval (CI 95%) p-value less than 0.05 was considered statistically significant. This interventional study was comprised of 89 patients who directly participated in this study. Of whom 52 (58.0%) were men and the remaining 42% were women. All the patients were hepatitis C positive at the time of recruitment of study. Overall, it is observed that improvement in ALT at the endpoint assessment was -23.13 [-31.96 - -14.30] in comparison to the baseline ($p < 0.0001$). Similarly, the improvement in AST and ALP was also significant ($p < 0.0006$; $p < 0.0001$). There was a significant decline in the Anti-HCV ELISA however, regardless of the decline the viral load was not found statistically significant at the end of the study. LivPro® is beneficial in improving the hepatic biomarkers of the patients suffering from Hepatitis C.

Keywords: LivPro®, Hepatitis C, Liver, Anti-HCV ELISA

INTRODUCTION

Liver complication amounts a massive economic and societal in developing and developed countries. Literature has shown that liver cirrhosis is the 11th leading cause of mortality in Western regions [1-3]. Chronic viral hepatitis B and C, alcoholic liver disease, non-alcoholic fatty liver disease, and hepatocellular carcinoma are the major entities, and many problems remain unresolved [4]. The use of modern medicines, anti-viral are abundantly practiced however, due to the cost of therapy and affordability, sometimes patients have limited access to modern medicine which is mainly due to the cost of the treatment [5]. In this case, patients with low socioeconomic status might not be able to manage the expenses of therapy.

Therapies developed along the principles of Western medicine are often observed to have limited compliance in developing countries [6]. In addition, in some cases newly developed compounds got limited efficacy and higher risk of side and limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Addressing the situation in Pakistan Chronic hepatitis C got the highest prevalence rates (4.9%) in the world, with 8

million to 11 million individuals with active HCV viremia [7, 8]. There is a huge number of undiagnosed patients in Pakistan, which is perhaps due to the lack of awareness about the disease or due to poor socio-economic status [8]. The main contributors to the HCV in the Pakistani setting are due to unhygienic practices during intravenous injections and due to reuse of the injection equipment in the health care setting [9]. Therefore, treating liver diseases with plant-derived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive.

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Furthermore, despite the advances in conventional medicine in the last decades, professionals and the lay public of developed countries pay increasing attention to phytomedicine. There is a variety of herbal product that is registered by the drug regulatory authority of Pakistan with hepatoprotective claims. The current study aims to explore the clinical benefit of the locally registered products i.e. LivPro® among patients suffering from Hepatitis C.

MATERIALS AND METHODS

An interventional study was performed among the hepatitis C patients who were unable to afford the cost of therapy of hepatitis treatment. All hepatitis C-positive patients were recruited in this study. The duration of the study was 3 months and the assessment for liver function, ELISA, and Viral load was performed monthly for the patients recruited in this study.

Study Location

This study was planned at the welfare clinic of Alkhidmat foundation charity hospital, Sheikhpura. All the treatment regimens and testing were sponsored by Awami Laboratories Pvt. Livpro [10] are one of the herbal regimens proven to improve liver function and contain herbs with anti-viral potential. This product is registered with the drug regulatory authority of Pakistan as a hepatic tonic.

Patients Recruitment

A health campaign was conducted at Alkhidmat foundation charity hospital, Sheikhpura which involve random screening for hepatitis C. Those patients who were observed to be hepatitis C positive and were unable to afford the cost of therapy of hepatitis were approached for their potential participation in this study. At the time of the study, n=89 patients who were hepatitis C positive agreed to avail the free treatment and testing offered by Awami Lab and have given written consent to participate in this study. All the procedures in the recruitment and testing were explained to them before the testing and commencement of therapy. All procedures were in line with the ethics and medical norms and formal approval was also granted by the administration of Alkhidmat foundation to recruit potential patients under the direct supervision of their medical team.

Additional advice was given to the patients telephonically and on their visit about the diet and self-care plan during hepatitis. Moreover, it was also ensured that patients are taking their medication regularly and present for follow-up as scheduled per agreement.

Data Analysis

Data analysis was performed using continuous data which was measured at the baseline and the endpoint of the study. Mean difference was measured and at a Confidence Interval (CI 95%) p-value less than 0.05 was considered statistically significant. MedCalc software ® was used to perform all the required statistics. Standard deviation s was estimated using equation (1).

$$s = \sqrt{\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}} \quad (1)$$

To estimate the standard error and mean the difference between the two means i.e at the baseline assessment and the endpoint assessment equation (2) and (3) were used where s_1 and s_2 are the standard deviations of the two samples with sample sizes n_1 and n_2 . The significance level, or P-value, is calculated using the t -test, with the value t calculated.

$$se(\bar{x}_1 - \bar{x}_2) = s \times \sqrt{\frac{1}{n_1} + \frac{1}{n_2}} \quad (2)$$

$$t = \frac{\bar{x}_1 - \bar{x}_2}{se(\bar{x}_1 - \bar{x}_2)} \quad (3)$$

RESULTS AND DISCUSSION

This interventional study was comprised of 89 patients who directly participated in this study. Of whom 52 (58.0%) were men and the remaining 42% were women. In terms of age, the main population 43 (48.3%) were from the age group of 41-55 years followed by patients from the age group of 18-40 years 40 (44.9%) and 6 (6.7%) were aged 56-70 years. All the patients were hepatitis C positive at the time of recruitment of study. The baseline assessment for the required liver profile, viral load, and ELISA are shown in **Table 1**.

Table 1. Comparison of the Baseline and Endpoint Assessment

Type	Baseline Assessment	SD	End Point Assessment	SD	MD CI	T statistics	p-value
ALT	49.38	27.28	26.25	32.24	-23.13 [-31.96 - -14.30]	-5.167	<0.0001
AST	39.61	21.82	25.64	30.99	-13.97 [-21.89 - -6.04]	-3.477	0.0006
Gamma GT	42.31	57.23	26.45	56.92	-15.86 [-32.74 - 1.025]	-1.854	0.0655
Bilirubin Total	0.69	0.55	0.27	0.34	-0.420 [-0.55 - -0.28]	-6.128	<0.0001
ALP	142.79	58.53	73.25	76.55	-69.540 [-89.70 - -49.38]	-6.808	<0.0001

Anti HCV ELISA	1.55	0.9	0.97	0.98	-0.580 [-0.85 - -0.302]	-4.112	0.0001
Viral Load	1174857.21	10173083.9	89516.85	341044.55	-1085340.360 [- 3214686.3254 to 1044005.6054]	-1.006	0.3158

MD= Mean difference, CI = Confidence interval, p<0.05 was considered significant

Overall, it is observed that improvement in ALT at the endpoint assessment was -23.13 [-31.96 - -14.30] in comparison to the baseline ($p<0.0001$). Similarly, the improvement in AST and ALP was also significant ($p<0.0006$; $p<0.0001$). There was a significant decline in the Anti-HCV ELISA however, regardless of the decline the viral load was not found statistically significant at the end of the study.

Traditional and herbal medicine system has been practiced for centuries and assisted mankind with its benefit. The working mechanism, diagnosis, and treatment philosophy of herbal and traditional medicine is different from modern medicine. However, in current practice the modern medicine is also relying on the herbal system for the exploration and discovery of new salts and regimens in this case it became vital to explore the evidence for herbal medicine using the recommended evidence-based approaches so that cost-effective regimens can be provided for the public use. The current study was one of the similar efforts which aim to establish clinical evidence for the registered herbal products claiming the effectiveness in managing hepatitis C infection. In the regional Asian context, there are plenty of preclinical studies on the anti-HCV effects. However, the majority explore effect in vitro only, and very few clinical trials of good quality have been conducted to provide solid evince of its clinical efficacy. Surprisingly towards the end of this study, there was a massive improvement in liver function and a decline in the viral count and ELISA. Thus, showing the benefit of the use of LivePro among HCV patients.

LivPro is a cocktail of various hepatoprotectants and anti-HCV ingredients that mainly includes Capparis spinosa, Cichorium intybus, Terminalia arjuna, Solanum nigrum, Achillea mille folium, and Cassia occidentalis. Increasing evidence has suggested that the initiation and progression of various liver diseases are caused by oxidative stress-induced cellular damage [11]. Improving liver function by reducing oxidative stress has remained a major challenge in the field of complementary and alternative medicine (CAM), and a lot of efforts have been made to address this challenge in the past [12, 13]. Potential agents such as Silymarin and Quercetin from natural agents are very popular in this regard [14]. Phenolic content in *C. spinosa* is mainly responsible for antioxidant activity and proven by various studies [15]. The decline in transaminase levels can also be attributed to the hepatoprotective effect of *C. spinosa* by strengthening the hepatocellular membrane barrier and reducing the leakage of transaminases into the blood [15]. Moreover, it is also known for its marked antiviral activity in various studies because of the presence of quercetin [16]; however, there is need to conduct more studies on various human and animal models

to assess the isolated response of this compound against hepatitis C virus [17].

Cichoric acid present in *C. intybus* exhibits antioxidant activities, induces cell-mediated immunity and phagocytotic activity against viral infection, inhibits hyaluronidase which is a potent inflammatory agent in any viral infection [18]. The medicinal plant of *S. nigrum* is found to have potential anti-HCV activity in an in-vitro study [19]. The main target for the therapeutic activity of *S. nigrum* is HCV NS3 protease which is an essential enzyme for viral replication and maturation [20]. NS3 not only helps in viral RNA replication but also interferes with the normal functioning of the host cell by inhibition of cell transformation and signal transduction that is normally mediated by protein kinases [21, 22]. One study on the rat model showed significant improvement of baseline liver biomarkers by the use of *C. intybus* and *S. nigrum* in combination [23]. Although *C. intybus* showed various hepatoprotective and antiviral activities after its combination with other ingredients in our drug, its exact pharmacological mechanism of action is yet to be known.

The presence of naringenin and quercetin in *T. arjuna* and *A. mellifolium* has made them potential anti-HCV candidates [24, 25]. Apart from their activity at NS3 proteases, both these herbs have shown potential activity at NS2 proteases which are also a key player in viral replication [25]. *C. occidentalis* is also known for its hepatoprotective antioxidant activities as has been proven by various studies [26-28]. These findings give scientific support for the inclusion of *C. occidentalis* in combination with other herbs in the treatment of HCV.

The beneficial outcomes of all these ingredients against hepatitis C in this cocktail can be mainly attributed to their inhibitory action on cytotoxic cascades and inflammatory actions induced by viral infection. Moreover, these ingredients may have also helped in the synthesis of liver essential proteins that would have helped in the normalization of the liver enzymatic activity by improving the membrane resilience as discussed above. Additionally, these proteins may have helped in the liver regeneration process that can be observed by the improvement of liver markers in the participants [29]. Based on the results presented in our study, we can conclude that LivPro® plays a very important role in hepatoprotection and viral cell load clearance during an HCV infection. Our study also suggests that LivPro® represents an alternative and cost-effective approach to the treatment of chronic HCV and it provides room for further investigations on isolated ingredients for the development of more targeted oral anti-HCV agents.

CONCLUSION

Results from this study have shown the beneficial effect of LivPro® in improving the hepatic biomarkers of the patients suffering from Hepatitis C. Future studies using experimental study design are required to explore the comparative effect of LivPro®.

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ETHICS STATEMENT: None

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