REVIEW ARTICLE

Camel Milk in the Treatment of Chronic Hepatitis C: A Systematic Review

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ABSTRACT

Background: Hepatitis C virus (HCV) is one of the main reasons of liver that leads to high rate of mortality and morbidity in future. Camel milk (CM) has been considered as a beneficial therapeutic agent which has been widely used.
Methods: The current systematic review was carried out in accordance with the PRISMA guidelines. The aim of this study was to search and evaluate all clinical trials and interventional studies with respect to the effects of camel milk on HCV infection. The search was performed in Scopus, MEDLINE, Cochrane, and Web of Science in June 2018.
Results: A total of 51 articles were obtained in the initial electronic searches. only three interventional studies using camel milk on patients with hepatitis C included in this systematic review. Combination of CM with standard treatment for HCV showed significant improvements in the viral response and decreased adverse effects in the first study ($P < 0.05$).
Conclusion: most studies show a clinical benefit with an intervention of camel milk in combination of standard treatment for chronic hepatitis c (CHC).
Keywords: camel milk, hepatitis C, lactoferrin, hepatoprotective

INTRODUCTION

Hepatitis C virus (HCV) infection is a major public health burden with about 3 % prevalence worldwide estimation[1,2]. The infection can lead to chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). Mortality and morbidity and economic burden of chronic hepatitis C is considerable[2]. Hepatitis C is one of the most common causes of liver transplantation in the world[3].

Many direct acting antiviral therapies have been introduced in recent decades to reduce the complications of the disease, rate of mortality associated with HCV[4]. Although these drugs increase the cure rates from less than 50% to more than 90% in those who reach access to care, but this new anti-HCV drugs are very expensive[3]. Most of them is associated with side effects, including nausea and anemia, which cause nutritional depletion and increase oxidative stress[5].

The unaffordable high cost and associated side effects of medicine are the main reasons for noncompliance of many patients. Therefore, searching for new therapeutic approaches with higher safety and better efficacy is considered[6]. Recent studies established the benefits of certain diets and lifestyle changes on the treatment of chronic hepatitis[1,5,7,8,9]. Camel milk is a good nutritional source with a high energy and vitamin/minerals, which has been widely used for human health. Camel milk has potential pharmaceutical properties with therapeutic effects such as antibacterial, antiviral[10] antidiabetic[11] antioxidant agent[12] anti-allergic[13], antiapoptosis[14], and anticancer properties[15]. The hepatoprotective effects of camel milk in previous studies can highlight its therapeutic role in liver disease such as hepatitis C[16].

The aim of this study was to review all available clinical trials studies and provide a perspective on the use of complementary therapies to treat hepatitis C.

METHODOLOGY

***S*earch strategy and study selection:** The aim of this study was to search and evaluate all clinical trials and interventional studies with respect to the effects of camel milk on HCV infection. The search was performed in Scopus, MEDLINE, Cochrane, and Web of Science in June 2018 for English language human studies. The literature search included the following key words: hepatitis C, viral hepatitis, chronic hepatitis, chronic liver disease, HCV, hepatitis C virus, milk, lactoferrin, camel, camelus, camelini, camelidae and bactrian camel. Keywords relating to clinical trials included randomized controlled trial, randomized clinical trial, RCT, randomized clinical trial allocating, double blind method, single- blind method, single blind, cross over studies, random allocation, placebo, RCT, cross over. Only studies in English were taken into consideration. All reference list of included studies reviewed separately for other eligible trials.
Eligibility criteria: We selected the relevant articles based on the following criteria: participants: HCV-infected patients (all genotypes) with or without cirrhosis. HCV co infected with HBV HIV were excluded. type of study: Both clinical trials and observational studies were reviewed. Intervention: oral administration of camel milk with or without standard regimens therapy were considered. The primary outcomes were early virological response (EVR12), liver enzymes and blood parameters changes, the secondary outcome was sustained virological response (SVR24), and the safety outcomes were (percentage of

adverse events and treatment discontinuation rates due to side effects).

Data extraction: To find relevant articles, an initial screening was done in the title and abstracts. When the articles were identified, the references were imported to the End Note. Two investigators extracted information from the literature individually and controversial cases for inclusion was resolved by consensus**.**

Quality Assessment: The quality and risk of bias of each trial were assessed using the Cochrane Collaboration's tool[17]. Two studies were described as randomized trials and one trial was done without randomization.

RESULTS

A total of 51 articles were obtained in the initial electronic searches by above mentioned key words in the databases. After exclusion of duplicate articles 38 articles remained. In the following after reading titles and abstracts, we eliminated 25 of these due to non-relevance. With a closer inspection at the full texts of these articles, 10 articles were excluded because of 9 articles were cellular study and 1 article had no patients' number. Finally3 clinical trial articles remained with defined criteria.

Overview of Studies: Three clinical trials involving 84 participants were included in this systematic review. Two of these studies were conducted in Egypt and the third study in Iran. One study reported random allocation of participants with hepatitis c to camel milk with Peg-IFN/RBV and Peg-IFN/RBV alone. The other was a before after study compared participants with hepatitis C who received Peg-IFN/RBV interferon before and after receiving camel milk. The last study was a case control, randomized and parallel design investigation, reported effect of camel milk prior and following intervention on hepatitis c patients.

Participants: Eighty four patients were included in these studies aged between 18 to 65 years. Two study were performed on 42 Egyptian patients suffering from chronic hepatitis C infection caused by HCV genotype 4 based on clinical and pathological examination. The other study 45 Iranian patients with chronic hepatitis C infection caused by genotype 2 /3 HCV.

Intervention: The amount of camel milk consumption was varied between studies ranging from 250 ml to 830 ml/day. The duration of intervention was ranged between 2 and 6 months.

Outcomes: El-Fakharany study had measured Liver function tests (ALT and AST); molecular assessments that determined the load of HCV RNA; and serologic tests that detected anti-HCV specific antibodies. Mohamed et al measured serum levels of the proinflammatory markers such as tumor necrosis factor-a, monocyte chemotactic protein-1, hyaluronic acid, and TGF-b1 besides HCV-titre PCR, levels of vitamin D, Bcl2, total antioxidants, and interleukin-10 before and after the addition of camel milk for 60 days to the standard regimen treatment. They also compared liver function tests: AST, ALT, GGT, bilirubin, albumin, PT, and INR AFP at the same time. Hosseini et al evaluated early treatment (EVR12), end-of-treatment (ETR24), sustained virologic responses (SVR24) and biochemical responses (AL,AST) during Treatment and End of Treatment (Week 12, 24, and 48).

Main findings: All study Results revealed a marked decrease in ALT. Hosseini et al study showed significant decrease in ALT between camel milk with Peg-IFN/RBV regimen and Peg-IFN/RBV in 12 weak treatments ($P<0.05$), but no significant decrease was found between them in 24 weeks ($P>0.05$). This study showed no significant difference in EVR12 between groups (60% in intervention group, versus 15% on control group, $P>0.05$) and ETR24 (90% in intervention group, versus 70% on control group, $P>0.05$) but SVR24 rates were significantly different(100% in intervention group, versus 71% on control group, $P<0.05$). EL-Fakharany et al reported marked decrease in ALT in 88.23% of patients and in AST in all 17 patients before and after treatment with camel milk for four months. Their results demonstrated 13 patients (76.47%) had marked decreases in HCV RNA levels. One patient had undetectable viremia (viral load=0) at the end of study. Only 23.53% ofpatients did not respond to the treatment. DespiteA significant decrease of IgG1 in 70-76% of patients following camel milk-treatment ($P<0.05$), notable increases were found in levels of IgG2, 3 and 4 in 52-76, 41-76 and 58-82% of patients.The improving effect of using camel milk in addition of standard treatment PEG for two months in HCV patients was reported. In this before and after prospective study the significant decrease in AST, ALT, GGT, bilirubin, prothrombin time, INR, and alphafetoprotein, the proinflammatory markers,such astumor necrosis factor-a, monocyte chemotactic protein-1,hyaluronic acid, and TGF-b1 and HCV-titre PCR($P<0.05$). In addition, the serum levels of albumin, the antiapoptotic protein BCL-2, the total antioxidant capacity, interleukin-10, and vitamin D elevated significantly ($P < 0.001$).

DISCUSSION

Hepatitis C virus (HCV) is a widespread pathogen and may lead to cirrhosis and hepatocellular carcinoma hence HCV infection is a global concern because of its fundamental effects on morbidity and mortality[18,19,20]. Available drugs for curing hepatitis C besides the side effects, are expensive and may not respond on some patients. So it is essential to introduce new, safe and effective drugs[18]. Camel milk has some health benefits and can help to cure some diseases[21], such as Liver disease[18]. Camel milk is a great source of proteins, unsaturated fatty acids and other compounds, including immunoglobulins such as IgG, lactoferrin, lysozyme, vitamin C and iron[22,23]. High levels of vitamins such as A, B2, C and E lead to antioxidant activity in camel milk and also excessive amounts of magnesium (Mg) may increaseits chelating effects on toxicants. So camel milk play a supreme role in protecting liver tissue against toxic injuries and heavy metals like cadmium, mercury and aluminum[24]. Camel milk also has beneficial effects on cancer, diabetes, tuberculosis, hepatitis B and C, anemia, asthma, piles and high level of cholesterol[23]. Lactoferrin is an important protein in camel milk and plays an important role in antiviral, antibacterial, antifungal, antiparasitic, immunomodulatory and anti-inflammatory activity[23]. It has been shown that camel lactoferrin has immunomodulatory effects and can improve maturation and activation of several immune cells such as macrophages, neutrophils, and lymphocytes[25]. Iron-chelating,

Immunomodulating and antioxidant properties of lactoferrin have an important role in the treatment of HCV infection[26]. Radwan et al incubated human leucocytes with lactoferrin and after that induced HCV infection. Their results showed that lactoferrin prevented the HCV from entering into the leucocytes. They also demonstrated that anti-viral effect of lactoferrin in camel milk is more than bovine and human lactoferrins[27]. EL-Fakharany et al studied antiviral effects of camel milk proteins in vitro. They investigated the effects of IgGs, α-lactalbumin, lactoferrin, and casein of camel milk and also human IgG, against hepatitis C virus in Huh 7.5 and PBMCs cell lines. The results indicated that camel IgGs and lactoferrin inhibited the entry of HCV into PBMCs and Huh7.5 cells. Camel IgGs prevented HCV infection by recognizing the HCV peptides[28]. Another study examined the influences of camel milk on chronic hepatitis B patients. The results of this study showed that consuming camel milk improved cellular immune response and decreased DNA replication of hepatitis B virus[29]. So the antiviral effects of camel milk make it a good remedy for the hepatitis C virus[30]. Camel milk also improves liver function by reducing liver enzymes and globulin levels and elevating the total protein and albumin levels. It also has the ability of increasing lymphocytes and platelets level that were depleted during the infection[31].

All included articles in this systematic review showed the effectiveness of the used camel milk alone or in combination of standard treatment for HCV. However, evidence for suppressing HCV treatment with CM needs to be confirmed in long-term clinical trials with sufficient duration, follow-up, sample size and higher methodological quality.

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