Chronic hepatitis C (CHC) is a communicable disease caused by infection with hepatitis C virus. Over 20 million people in Arab countries were infected with the virus. Good treatment adherence to Ribavirin (RBV) and Pegylated interferon (PegIFN) may play important role in decreasing morbidity, and complications due to CHC. The objective of this randomized controlled trial study to improve treatment adherence, knowledge, self-efficacy, virological response and HRQL among CHC patients in Tripoli Medical Center, Libya. 103 participant patients under therapy with PegIFN and RBV were randomly allocated 51 patients to intervention and 52 patients to control groups. The education material was given to intervention group comprised from a one-day session of power point presentation, discussion, and booklet. The control group received same education material at the end of the study. The data was collected at baseline, 3-months and 6-months post intervention. Descriptive, bivariate and multivariate statistics as Generalized Estimating Equation (GEE) were used for analyzing the data using SPSS version 21. The mean of age was 43.8 years (SD = 14.36), and the male was 58.3% and the female was 41.7%. A majority of patients were genotype 4 consists of 39.8%, followed by genotype 1 consist of 35.9%. The GEE demonstrated significant higher change in RBV treatment adherence post educational intervention (adjusted odds ratio (OR) = 2.220, p = 0.012) for intervention group compared to control, as well significant result found for PegIFN (OR = 1.973, p = 0.037) and total treatment adherence (OR = 2.512, p = 0.002) for intervention compared to control group. In addition, good virologic response was significant higher in intervention compared to control (OR = 2.155, p = 0.038). The result of hepatitis C knowledge and GSE were significantly higher in intervention compared to control, (OR = 5.720, p <0.001) and (OR = 4.169, p = 0.009) respectively. For physical components score (PCS) and mental components score (MCS) of HRQL were found (OR =15.364, p < 0.001) and (OR = 25.699, p< 0.001) respectively, significantly higher in intervention group compared to control. The result of PCS within both groups was not significant while for MCS was significant only within intervention group at 3-months. The result provides evidence of the effectiveness of the educational intervention to changing and sustaining RBV and PegIFN treatment adherence within intervention group over time. As well, the educational intervention was changing hepatitis C knowledge, GSE, virologic response, and HRQL.

**Keyword:** Hepatitis C; Treatment adherence; Educational intervention