Gonadotoxic Effects of Interferon Therapy on Male Fertility

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Abstract

Hepatitis is a viral disease. More than 71 million people are suffering from chronic Hepatitis C virus (HCV) infection. Interferon therapy is the most common therapy to treat HCV. Many medicines are used for its treatment one of them is most common in Pakistan or developing countries which is interferon. Initially, it was considered as good for HCV but later on it is revealed that interferon has many side effects. In this study,80 individuals were studied for different parameters which were divided into two groups. A Group includes 40 individuals having a history of HCV infection and recovered by interferon therapy and the other group have 40 normal individuals. The mean values of these fertility hormones (FSH, LH, Prolactin and testosterone), hemoglobin level,and blood sugar level indicates that interferon does have not any significant effect on their normal level. Other parameters such as sperm count (normal individual = 76.765 and interferon treated individual = 54.3) and no of children (normal individual =2.65 and interferon treated individual = 0.525). These values show that interferon therapy hasa statically significant effect on male fertility.

Keywords: -Interferon, HCV, Sperm count, Fertility hormones.

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Introduction

Hepatitis is a common viral infection in subcontinent especially in Pakistan. More than 350 million people are affected by this disease over the globe. Sometimes it also causes hepatocellular carcinoma. HCV is a blood-borne virus which is the most common types of infection and spread through exposure to small quantities of infected blood. This may happen through unsafe practices of injection, unsafe health care techniques, and unscreened transfusion of

blood and blood products[1-3].

The most virulent among hepatitis viruses is Hepatitis C Virus (HCV). Different global surveys show that the ratio of Hepatitis C Virus has reached 2.8% in 2005, which was 2.5% in 1990. HCV is spreading at very high speed as in 1990; 122 million patients were reported. This number was increased in 2005 and total patient reported in 2005 was 185 million [4]. According to world health organization every year 1.5 million new patient of HCV reported[5]. About 85% patient of HCV developed chronic infection which leads to develop into cirrhosis, hepatocellular carcinoma andextrahepatic manifestations [6].

There are also many ways to exposure to HCV. some of them are shown here like, This may happen through injection drug use, unsafe practices of injection, unsafe health care techniques,unscreened transfusion of bloodand blood products, and unsafe sexual practices that lead to blood exposure. On the international level, an estimated 71 million people are suffering from chronic HCV infection. A significant number of those patients who are chronically infected with HCV have a chance, that they will develop cirrhosis or liver cancer. World Health Organization (WHO) estimated in 2016 that, approximately 399 000 death cases by hepatitis C, most of which were suffering by cirrhosis and hepatocellular carcinoma (primary liver cancer).

The particle of HCV consists of an RNA core, which is its only genetic matter; a protective protein shell is present around it. The geometry of this shell is icosahedral and a further lipid envelope is also present around it, cellular in origin. The lipid envelope contains two viral glycoproteins, which are named E2 and E1 [7]. Two types of glycoproteins E1 and E2 allow entry of viral particles into the cell, which may help in the development of a vaccine that will act against HCV infection [8].

Globally, 2.2%of the prevalence of HCV is observed. The disease is becoming a major health issue in developing countries like Pakistan, India, and Bangladesh where health facilities are not available to the common citizen. HCV infection ranges from 4 –8% in these developing countries. In Pakistan HCV is studied in small group of population restricted in specific area or city. These studies have included persons such as blood donors, doctors, paramedical staff, pharmacists, drug addicts and patients of chronic liver disease[9].

Material and Method

The effect of interferon therapy on 40 male hepatitis C virus (HCV) patients who got treatment in the period from 2013 – 2017 was evaluated. The research work was done at the Department of pathology Sheikh Zaid Medical College and Hospital Rahim Yar Khan (Ryk), Pakistan. A control group of 40 normal married male persons aged between 20 – 50 years was also selected. Sheikh Zaid Medical College and Hospital is a 1000-bedded hospital providing free medical and health care diagnostic treatment to the common public of the Ryk, Dera Bugti andSukkar region. HCV patients received free treatment from this hospital.

Sample collection

A list of maleswho received interferon therapy having age range from 20 – 35 years in the period from 2013 – 2017 was collected from the pathology department of the hospital.A consent form was signed by every participant then samples were collected. The sample collection was divided into two parts. In the first part, blood sampleswere collected and in the second part, semen sampleswere collected [10].

Parameters

Following were the parameters which were studied in this research.

1. Fertility Hormones
2. Hb
3. Sperm count
4. Sperm motility
5. Sperm morphology
6. Active sperm percentage
7. Sperm concentration
8. Quantity of sperm
9. Number of children before and
10. after the interferon therapy
11. Age of the patient
12. Married life in years
13. The gap between children born before and after interferon therapy
14. Family history of hepatitis C (HCV)
15. Diet schedule of the patient during and after the interferon therapy.

Statistical Analysis

Complete experimental work was analysed statistically by statistical package for social sciences (SPSS). The results were presented in means and standard deviation. The t test was applied to the data collected and results were interpret according to the p value.

Results and discussion

Hepatitis C virus infection has become a major and widely spreading health problem, especially in developing and backward countries like Pakistan[11]. Along with its complications in the liver, HCV also affects other organs of the body. These include arthritis due effect on synovial joints, reduced body immunity to infections due to a reduction in white blood cell counts, nervous system abnormalities, loss of memory, dermatitis, and abnormalities in sperm cell maturation included [12].

HCV infection usually causes the production of ROS (reactive oxygen species) by expressing the protein, which is expressed itself as core protein. This can cause mitochondrial

membrane damage. ROS mediates sperm damage as well [13]. Reactive oxygen species include ions of oxygen, free radicals of oxygen, and superoxides. These can damage sperm by two methods. First, these break membrane of the spermatozoa by reducing ions, whichaffects the sperm morphology and motility of sperm. 2ndsuperoxides directly damage deoxyribonucleic acid of the spermatozoa. This affects the capability of sperms for fertilization[14].

This study indicate that interferon therapy affect the quality and quantity of semen content. The parameters which are affected in semen contents are spermatozoa count, sperm motility, and its survival in the fluid medium. It was also observed that interferon treatment has not any adverse effect of fertility hormones[15].

Other researchers found the treatment of HCV with antiviral drugs like interferon cause worsening in the semen parameters and advised the use of contraceptive methods during the period of treatment. They noted a significant difference in spermatozoa morphology, count, and mobility as this study also indicates[16].

Some other researchers also found the worst influence of HCV infection on spermatogenesis or morphology of sperms which augment these results and after treatment note, no improvement in the sperm morphology and level of testosterone in the blood [17].

Some of the results show that there is no effect of HCV treatment by interferon on fertility hormones and other parameters, such as FSH, LH, SGPT, Hb, TLC, and Blood sugar levels. Hormonal patterns after one year generally got better in treated patients than in freshly treated patients [18].

The main effect of all parameters that we have to study and the basic concern of this research is shown in the number of children difference before and after the treatment. The research shows that one year after treatment sperms were not enough strong to fertilize the egg, and this thing also continues year after year forthe next three years. After that, it gets better. All the patients who have children after treatment took three years to revive their fertility [18].

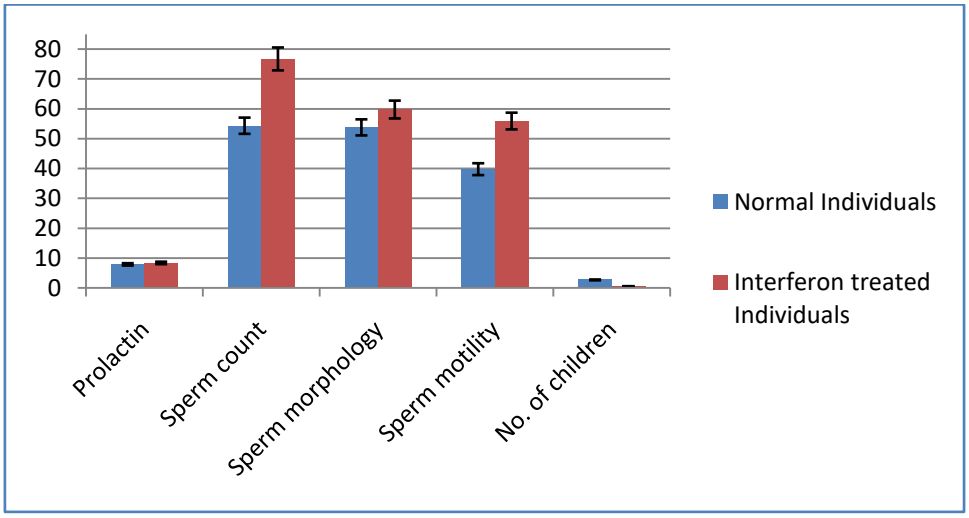

Figure 1: Graphical representation of parameters that are statistically different in normal and interferon-treated persons.

Table 1: Data recorded of different parameters

Sr. #	Test performed	Average value of normal patients	Average value of treated patients	P value	Results
1	FSH	6.09	8.05	0.1788276	Both groups are not statically different from each other
2	LH	6.245	9.6975	0.240603	Both groups are not statically different from each other
3	Testosterone	569.147	992.11	0.000188059	Both groups are statically different from each other
4	Prolactin	7.865	8.342	0.00011265	Both groups are statically different from each other
5	Sperm count	54.3	76.675	0.000462	Both groups are statically different from each other
6	Sperm morphology	53.75	59.725	0.007513	Both groups are statically different from each other
7	Sperm motility	39.75	55.875	0.00649	Both groups are statically different from each other
8	No. of children	2.65	0.525	0.003606	Both groups are statically different from each other
9	Blood sugar	110.025	111.425	0.388	Both groups are not statically different from each other
10	SGPT	38.025	38.725	0.19339	Both groups are not statically different from each other
11	Haemoglobin	12.53	12.72	0.164862	Both groups are not statically different from each other

References

1. Schütte, K., J. Bornschein, and P. Malfertheiner, *Hepatocellular carcinoma–epidemiological trends and risk factors.* Digestive diseases, 2009. **27**(2): p. 80-92.
2. Poynard, T., et al., *Viral hepatitis C.* The Lancet, 2003. **362**(9401): p. 2095-2100.
3. Lavanchy, D., *The global burden of hepatitis C.* Liver International, 2009. **29**(s1): p. 74-81.
4. Mohd Hanafiah, K., et al., *Global epidemiology of hepatitis C virus infection: New estimates of age-specific antibody to HCV seroprevalence.* Hepatology, 2013. **57**(4): p. 1333-1342.
5. Orgnization, W.H. *Hepatitis C.* 2022 [cited 2022 20/06/2022].
6. Chen, S.L. and T.R. Morgan, *The natural history of hepatitis C virus (HCV) infection.* International journal of medical sciences, 2006. **3**(2): p. 47.
7. Op De Beeck, A. and J. Dubuisson, *Topology of hepatitis C virus envelope glycoproteins.* Reviews in medical virology, 2003. **13**(4): p. 233-241.
8. Khan, A.G., et al., *Structure of the core ectodomain of the hepatitis C virus envelope glycoprotein 2.* Nature, 2014. **509**(7500): p. 381.
9. Jiwani, N., *A Silent Storm: Hepatitis C in Pakistan.* 2011.
10. Bukhari, S.A., et al., *Post interferon therapy decreases male fertility through gonadotoxic effect.* 2018. **31**(4 Suppl): p. 1565-1570.
11. Arshad, A. and U.A.J.C.R.i.E.G.E. Ashfaq, *Epidemiology of hepatitis C infection in Pakistan: current estimate and major risk factors.* 2017. **27**(1).
12. Aitken, R.J., M.A. Baker, and D.J.R.b.o. Sawyer, *Oxidative stress in the male germ line and its role in the aetiology of male infertility and genetic disease.* 2003. **7**(1): p. 65-70.
13. Agarwal, A., et al., *Effect of oxidative stress on male reproduction.* 2014. **32**(1): p. 1-17.
14. Zini, A. and J.J.C. Libman, *Sperm DNA damage: clinical significance in the era of assisted reproduction.* 2006. **175**(5): p. 495-500.
15. Lorusso, F., et al., *Impact of chronic viral diseases on semen parameters.* 2010. **42**(2): p. 121-126.
16. Milachich, T. and D. Dyulgerova-Nikolova, *The Sperm: Parameters and Evaluation*, in *Innovations In Assisted Reproduction Technology.* 2020, IntechOpen.
17. Di Guardo, F., et al., *Low testosterone and semen parameters in male partners of infertile couples undergoing ivf with a total sperm count greater than 5 million.* 2020. **9**(12): p. 3824.
18. Durazzo, M., et al., *Alterations of seminal and hormonal parameters: an extrahepatic manifestation of HCV infection?* 2006. **12**(19): p. 3073.