

## Risk Factors for Migraine Attacks in Patients Undergoing Treatment for Hepatitis C

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### Dear Editor,

Migraine, defined as a recurrent unilateral pulsatile headache, which is usually accompanied by nausea, vomiting, phonophobia, and photophobia, is a major cause of chronic headaches. It has been ranked the eight most disabling disorder, and its prevalence is higher in females (17% vs. 6%) (1).

Hepatitis C virus (HCV) infection infects more than 170-million individuals worldwide and is as an important healthcare problem. According to published studies, the prevalence of HCV is less than 1% in the general population. A combination of ribavirin, an antiviral nucleoside analogue, and interferon is the most common treatment for chronic hepatitis C (2-5). This method of treatment is also used in occult hepatitis C infections, which is a chronic form (6).

HCV treatment was reported to be associated with severe migraine attacks, with the source of the attacks attributed to ribavirin-related hemolytic anemia. Hemolytic anemia is a common and reversible side effect of ribavirin therapy, caused by the hemoglobin (Hb) level decreasing by at least 30 g/L in more than 50% of patients treated with this drug. About 7-10% of ribavirin-treated patients develop severe anemia, with a Hb level of < 100 g/L. Treatment has to be withdrawn in some cases (i.e., when the Hb level is < 8.5 g/dL), and the ribavirin dose has to be reduced in others. It is important to determine the factors associated with ribavirin-induced anemia to prevent or decrease the reduction in Hb levels (7).

The dose reduction of ribavirin is related to various factors, such as pretreatment Hb levels of < 14 g/dL. The dose is more likely to have to be reduced in patients with pretreatment Hb levels of < 14 g/dL than in those with pretreatment Hb levels of  $\geq$  14 g/dL. In one study, the ribavirin dose had to be reduced in more than half of the patients with pretreatment Hb levels < 13 g/dL (2). Patients with a decrease of > 2 mg/dL or more in the Hb level 2 weeks af-

ter the start of treatment require special care (8). The ribavirin dose has to be reduced significantly more often in females than in males. Normally, females have lower baseline Hb levels. This may explain why females have a higher risk of hemolytic anemia than males. Older patients ( $\geq$  55 years) are much more likely than younger patients ( $\leq$  55 years) to require a dose reduction of ribavirin. The underlying reason for the increased prevalence of dose reductions among elderly people is unknown, but it may be associated with the presence of erythrocyte membrane anomalies and renal dysfunction among the elderly. A low baseline platelet count was reported to be another risk factor for the development of more severe ribavirin-induced anemia (2). A significant relationship was reported between the ribavirin dose per kilogram and the incidence of anemia. Anemia was observed to be more common in patients receiving > 12 mg/kg than in those receiving < 12 mg/kg (32% vs. 10%) (8). During the continuation of treatment, erythrocyte transfusions and injections of erythropoietin were found to be effective in preventing migraine attacks in patients receiving HCV treatment with ribavirin-related anemia (9, 10).

In conclusion, the risk factors for migraine attacks in migrainous patients undergoing HCV treatment with ribavirin are as follows: pretreatment Hb levels of < 13 g/dL, a Hb decrease of > 2 g/dL within 2 weeks after starting the treatment, female sex, older age ( $\geq$  55 years), receiving ribavirin of > 12 mg/kg, and a low baseline platelet count. Patients with these risk factors must receive more care for better management and prevention of developing migraine attacks during the treatment.

### References

1. Motaghi M, Haghjooy Javanmard S, Haghdoost F, Tajadini M, Saadatian M, Rafiee L, et al. Relationship between vitamin D receptor gene polymorphisms and migraine without aura in an Iranian population.

- Biomed Res Int.* 2013;**2013**:351942. doi: [10.1155/2013/351942](https://doi.org/10.1155/2013/351942). [PubMed: [23984350](https://pubmed.ncbi.nlm.nih.gov/23984350/)].
2. Takaki S, Tsubota A, Hosaka T, Akuta N, Someya T, Kobayashi M, et al. Factors contributing to ribavirin dose reduction due to anemia during interferon alfa2b and ribavirin combination therapy for chronic hepatitis C. *J Gastroenterol.* 2004;**39**(7):668-73. doi: [10.1007/s00535-003-1363-9](https://doi.org/10.1007/s00535-003-1363-9). [PubMed: [15293138](https://pubmed.ncbi.nlm.nih.gov/15293138/)].
  3. Namazee N, Sali S, Asadi S, Shafiei M, Behnava B, Alavian SM. Real response to therapy in chronic hepatitis C virus patients: a study from Iran. *Hepat Mon.* 2012;**12**(9):ee6151. doi: [10.5812/hepatmon.6151](https://doi.org/10.5812/hepatmon.6151). [PubMed: [23087759](https://pubmed.ncbi.nlm.nih.gov/23087759/)].
  4. Sarvari J, Norozian H, Fattahi MR, Pirbonnyeh N, Moattari A. The Role of Interferon Gamma Gene Polymorphism (+874A/T, +2109A/G, and -183G/T) in Response to Treatment Among Hepatitis C Infected Patients in Fars Province, Southern Iran. *Hepatitis Monthly.* 2014;**14**(1):ee14476. doi: [10.5812/hepatmon.14476](https://doi.org/10.5812/hepatmon.14476). [PubMed: [PMC3909640](https://pubmed.ncbi.nlm.nih.gov/PMC3909640/)].
  5. Behzadi MA, Ziyaeyan M. Hepatitis C Virus Load in Seropositive Liver and Kidney Transplant Recipients by Quantitative Real-Time PCR Before and After Transplantation. *Jundishapur J Microbiol.* 2013;**6**(8):ee7365. doi: [10.5812/jjm.7365](https://doi.org/10.5812/jjm.7365).
  6. Rezaee-Zavareh MS, Einollahi B. Treatment of Occult Hepatitis C Virus Infection: Does It Need Special Attention?. *Hepatitis Monthly.* 2014;**14**(7):ee16665. doi: [10.5812/hepatmon.16665](https://doi.org/10.5812/hepatmon.16665). [PubMed: [PMC4101422](https://pubmed.ncbi.nlm.nih.gov/PMC4101422/)].
  7. Russmann S, Grattagliano I, Portincasa P, Palmieri VO, Palasciano G. Ribavirin-induced anemia: mechanisms, risk factors and related targets for future research. *Curr Med Chem.* 2006;**13**(27):3351-7. [PubMed: [17168855](https://pubmed.ncbi.nlm.nih.gov/17168855/)].
  8. Nomura H, Tanimoto H, Kajiwara E, Shimono J, Maruyama T, Yamashita N, et al. Factors contributing to ribavirin-induced anemia. *J Gastroenterol Hepatol.* 2004;**19**(11):1312-7. doi: [10.1111/j.1440-1746.2004.03459.x](https://doi.org/10.1111/j.1440-1746.2004.03459.x). [PubMed: [15482540](https://pubmed.ncbi.nlm.nih.gov/15482540/)].
  9. Kocaman O, Kocaman G, Senturk O. Severe migraine attacks during treatment of chronic hepatitis C. *Eur J Intern Med.* 2009;**20**(3):ee74. doi: [10.1016/j.ejim.2008.09.008](https://doi.org/10.1016/j.ejim.2008.09.008). [PubMed: [19393484](https://pubmed.ncbi.nlm.nih.gov/19393484/)].
  10. Alavian SM, Tabatabaei SV, Behnava B. Impact of erythropoietin on sustained virological response to peginterferon and ribavirin therapy for HCV infection: a systematic review and meta-analysis. *J Viral Hepat.* 2012;**19**(2):88-93. doi: [10.1111/j.1365-2893.2011.01532.x](https://doi.org/10.1111/j.1365-2893.2011.01532.x). [PubMed: [22239498](https://pubmed.ncbi.nlm.nih.gov/22239498/)].