A Case Series Investigation between Transaminitis and the Improvement in Body Mass Index Trend among Patients with Anorexia Nervosa and Eating Disorder not Otherwise Specified of the Anorexia Nervosa Type

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Received date: December 07, 2015; Accepted date: December 23, 2015; Published date: December 28, 2015

Citation: Goh Kye Hock Robin (2015) A Case Series Investigation between Transaminitis and the Improvement in Body Mass Index Trend among Patients with Anorexia Nervosa and Eating Disorder not Otherwise Specified of the Anorexia Nervosa Type. J Obes Eat Disord 2: 1. doi: 10.21767/2471-8203.100011

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Abstract

Introduction: Anorexia nervosa and eating disorder not otherwise specified are eating disorders on a rising trend in Singapore. Apart from psychological aspects of the disease, many such patients suffer from serious medical complications. Liver function tests abnormalities, usually in the form of elevation of the transaminases, have been reported to occur in up to 12.2% of patients with anorexia nervosa. The paper aims to investigate the correlation of transaminitis with the improvement of body mass index (BMI) in these patients.

Method: A retrospective cohort analysis of 373 patients with anorexia and eating disorder not otherwise specified at a tertiary hospital was done. The clinical course of transaminitis was correlated with the body mass index.

Results: There were 32 complete data of patients with BMI with transaminitis and their corresponding BMI on resolution of transaminitis. The mean BMI on resolution of transaminitis was BMI 15.8 for these 32 patients. The statistical analysis showed that there was no significant association between BMI group and resolution of transaminitis, \( \chi^2 = 1.32, p=0.73 \).

Conclusion: There is no significant association between improving BMI and resolution of transaminitis. Tracking of BMI is inadequate to monitor the recovery of the liver function. There is need for routine liver function test to determine improvement of the liver function.

Introduction

People with anorexia nervosa are 18 times more likely to die early compared with people of similar age in the general population [1]. The reasons for the high morbidity can be related to the medical complications, or the co-morbid psychiatric disorders, or the eating disorder alone. It could be even due to a combination of the various risk factors highlighted. Eating, food, and weight control became obsessions. People with anorexia nervosa typically weigh themselves repeatedly, portion food carefully, count calories rigorously, and eat very small quantities of only certain foods. Some people with anorexia nervosa may also engage in binge-eating followed by extreme dieting, excessive exercise, self-induced vomiting and/or misuse of laxatives, diuretics, or enemas. Liver function tests abnormalities, usually in the form of elevation of the transaminases, have been reported to occur in up to 12.2% of patients with anorexia nervosa in the community, and up to 60% in hospitalized patients [2,3]. There are case reports of fatalities due to liver failure among patients with anorexia, but these are rare occurrences [4-6]. The severity of hepatocellular injury has been reported to be inversely related to the body-mass index of the patients, and usually reverses with nutritional intervention. Case studies showed that brief elevation of hepatic enzymes occur secondary to liver ischemia in anorexia nervosa [7-9]. The mechanisms for this complication are unclear. Liver cell glycogen depletion is common findings under electron microscopy together with increase in serum alanine aminotransferase in the absence of significant hepatocyte necrosis in histology. Starvation induced autophagy in the human liver may be involved in the liver cell death during anorexia nervosa, even though other mechanisms of liver cell damage could also play a role [7]. Many such patients also have hepatic steatosis on imaging of the liver, which is thought to be related to the protein-energy malnutrition [10,11]. The acute rise in liver enzymes which result from ischemic hepatitis secondary to liver hypoperfusion usually resolves with therapeutic intervention comprising of fluid support and gradual nutritional support [12,13]. The aim of the study looks into the phenomenon of resolution of transaminitis with nutritional rehabilitation to ascertain if improving body mass index and directly correlate with resolution of transaminitis among patients with anorexia nervosa and eating disorder not otherwise specified* (Not fulfilling Anorexia Nervosa DSM IV criteria).
Methodology

The study design was a retrospective cohort study of patients with eating disorders under the care of Department of Psychiatry, Singapore General Hospital from 01 January 2003 to 31 December 2010. Inclusion criteria included inpatients and outpatients with the age range of 12 years old to 40 years old fulfilling the DSMIV criteria for anorexia nervosa and patients with the diagnosis of eating disorder not otherwise specified (without fulfilling the criteria of amenorrhea i.e. absence of at least 3 menstrual cycles) [14-15] with liver function tests done. The age limit was set from 12 years old to 40 years old because patients less than 12 years old would be treated in a hospital specializing in pediatric care and would not be transferred to Singapore General Hospital. The upper limit of 40 years old was set because the epidemiology of first onset eating disorders usually occurred in the younger age group and the catchment for eating disorder patients above 40 years old was small. The period of study was limited from Jan 2003 to Dec 2010 because Singapore General Hospital Eating Disorder service was only set up in 2003. The cut off of Dec 2010 was an arbitrary cut off to facilitate completion of the thesis. Information from only the first consultation was used for the analysis as the patients’ clinical presentation often changed with disease progression. Data mining was done by 2 independent doctors from Apr 2012 to Mar 2013. Both doctors were trained together to ensure consistency in the data collection. Patients with existing liver diseases, drug overdoses (intentional and accidental) during the first consultation or had history of substance abuses e.g. alcohol; opiates were excluded from the study as they might cause liver function abnormalities with their pre-existing medical conditions. Patients on slimming pills, diuretics or laxatives to lose weight were also included. The study was cleared by the Singhealth Centralised Institutional Review Board (CIRB) which operated in accordance with the International Conference on Harmonisation (ICH) / Singapore Guideline for Good Clinical Practices (SGGCCP). The case notes of eligible patients were reviewed and information on the presence and absence of liver function abnormalities, and body mass index during initial presentation and on resolution of transaminitis was collected. The liver function abnormalities were determined by looking at elevations of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and also alkaline phosphatase (ALP) in the liver panel during the initial consult. Any results which were above the stipulated range for the respective liver enzymes were considered as having liver function abnormalities or transaminitis. The patients’ abnormal liver function tests were recorded all the way until they were normalized and the corresponding body mass index with the normalization of results was recorded. 373 patients were identified for the study of which only 32 were included. The selected number is small because there were only a total of 63 patients who developed transaminitis on initial presentation. Of which, 20 does not have documented body mass index when their transaminitis were resolved and hence have to be excluded from the analysis. 11 of the patients have a chronic transaminitis picture. They also have a chronic eating disorder course and their body mass index did not improve to the normal range.

Statistical analysis

Statistical analysis was done using the Statistical Package for Social Sciences Version 21.0 (SPSS v21.0 for Windows XP). Parametric variables were analyzed using T-test and Chi-square test while nonparametric variables were analyzed using Kruskal Wallis and Man-Whitney U tests for continuous and categorical variables respectively. Statistical significance was set at 0.05. The data analyst was blinded to the data collection.

Results

There were 32 complete data of patients with BMI with transaminitis and their corresponding BMI on resolution of transaminitis. Patients with incomplete data were not included in the calculation. The mean BMI on resolution of transaminitis was BMI 15.8 for these 32 patients. The statistical analysis showed that there was no significant association between BMI group and resolution of transaminitis, $\chi^2=1.32$, $p=0.73$. I.e. there was no correlation of the initial BMI in the clinic with the course of recovery of transaminitis with treatment. One observation noted was that some patients with eating disorders took a very long duration for treatment and recovery. Their transaminitis might improve with improvement of the body mass index and then they would relapse again. These patients did not completely recover from the eating disorder (i.e. at least achieve the body mass index of 18.5) and their body were constantly under insults and they presented with chronic mild transaminitis. There were also patients who defaulted follow ups before the complete resolution of their eating disorder and their underlying transaminitis. Their data were analyzed using the worst case scenario, i.e., there was no resolution of their transaminitis.

Discussion

During times of starvation, the hepatocytes may first undergo reduction in size and gradual cessation of metabolic activities. During extreme starvation, the complete cessation of core metabolic activities may bring about cell death or apoptosis. The breakdown of the cellular membranes will lead to leakage of the liver enzymes and present with the phenomenon of transaminitis. It is important to establish which patients have transaminitis early as refeeding syndrome may set in following nutritional rehabilitation and cause more insults to the hepatocytes. There is a need for early referral to the Gastroenterology colleagues to seek their professional opinions to co-manage these eating disorder patients with liver dysfunctions. Fortunately the number of patients with transaminitis during initial consultation is low. (63 out of 373 patients) As a result of the small initial numbers, the eventual catchment number of 32 is small. With the small number, it was inevitable that there was no significant association between BMI group and resolution of transaminitis, $\chi^2=1.32$, $p=0.73$. There is room for more research with a larger patient pool to evaluate the relationship of BMI with evolution of
transaminitis. This case series of 32 patients however showed that there must still be the rigor to actively check the liver function tests of patients with anorexia nervosa with an initial presentation of transaminitis. The improvement of body mass index from nutritional rehabilitation does not directly correlate with the resolution of transaminitis.

Limitations

This was retrospective analysis and it was difficult to draw a direct causal link between the low BMI and transaminitis. However, the evidence which was obtained from the analysis was adequate to infer the possible linkage to each other. There was also limitation in the quality of the data collected as this was a retrospective study using an available eating disorder registry. There was no control over the completeness of data as well. For example, when we were trying to get the actual BMI during the resolution of the liver function tests, we were unable to do so as the BMI might be recorded during an earlier consult. We had to record the BMI based on the last observation carried forward. It would be ideal if BMI was directly recorded down onto the case notes when the transaminitis resolved should there be an extension to this study.

Conclusion

Patients with anorexia nervosa and eating disorders not otherwise specified* were at increased risks of having transaminitis. However, improvement of body mass index from nutritional rehabilitation does not correlate with improvement of liver function tests and there is need for follow up liver function tests till complete resolution of transaminitis.

Conflict of Interest

None of the authors have any actual or potential conflict of interest related to the submitted manuscript. There was no sponsorship from pharmaceutical companies for the thesis.

Acknowledgement

I would like to thank Lee Ee Lian for her advice and Dr Andrew Green for his assistance in data collection for the study. The authors also thank Jason Chang and Tay Hiang Keat from Department of Gastroenterology, Singapore General Hospital for assistance in queries in liver function abnormalities and Miss Pearlene Lim, research assistant from Department of Psychiatry, Singapore General Hospital, for helping with the data analysis.

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