Editorial

What Factors are Related to Death from Intestinal Ischemia in the Patients with Renal Failure Undergoing Continuous Hemodialysis?

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Background and Aim

It has been reported that end-stage renal disease (ESRD) patients on hemodialysis (HD) were at risk for intestinal ischemia (II) [1,2]. II demonstrates clinical manifestations from spontaneous recovery to critical condition causing death [2]. Some cases of II develop transmural gangrenous necrosis of the intestine, resulting in death. Other cases develop ulceration and colitis, and can be treated with conservative management. In this study, we tried to identify factors associated with death from II in patients on HD.

Methods

We used an electronic database at our clinics. Approximately 2,500 patients at our dialysis clinics underwent dialysis three times weekly from January 2009 to October 2013. The diagnosis of II, which includes mesenteric ischemia, non-occlusion mesenteric ischemia, and ischemic colitis, was made from endoscopy, pathology, computed tomography, ultrasound findings, and/or clinical condition. The patients were divided into two groups of the fatal group and the non-fatal group. The former included the patients who died from II, and the latter included the patients who were cured from II, but some of them died from other causes than II. Continuous variables were compared by *t*-test, while qualitative variables by Fishers exact test.

Results

Twenty-six of 2,500 long term hemodialysis patients developed II for the first time from January 2009 to October 2013. The fatal and the non-fatal group consisted of 7 and 19 patients, respectively. Six of the non-fatal group died from the following causes: cerebral hemorrhage, infective endocarditis, heart failure, pneumonia, suicide, and unknown. More than 70% of the 26 patients were male in both of the fatal and non-fatal groups (71.4% and 79.0%, respectively). The mean age (±SD) was higher in the fatal group than in the non-fatal without significance (75.4(±4.42) and 65.9(±14.6), respectively). There was no significant difference in the frequencies of those who had the history of ischemic heart disease (IHD) between

the two groups (57.1% and 47.4%, respectively). The mean durations (months±SD) during which they were on HD before developing II were not significantly different between the two groups (63.9±45.0 and 72.3±49.0, respectively). The frequencies of those who had each of warfarin and laxative were higher in the fatal group than in the non-fatal (57.1% vs 5.26%, respectively, p=0.01). Three of 4 who had warfarin suffered from atrial fibrillation (Af) in the fatal group. In the non-fatal group, 3 had Af but 1 of them took warfarin. There was no significant difference in the frequency of Af between the two groups. The fatal group more frequently underwent laparotomy than the non-fatal (42.9% vs 5.26%, respectively, p=0.05). Regarding the location of II, 71.4% of the fatal group developed the ischemic colitis on the right-sided, while 5.26% of the non-fatalon the right-sided (p<0.01).

Discussion

Our results indicated that having each of laxative and warfarin is related to the fatal II. The patients taking laxative could have constipation, which increases intraluminal pressure leading to ischemia of the intestinal mucosa [3]. Warfarin could cause the fatal II rather than thromboembolism did, because the frequency of Af was not higher in the fatal group. In addition, the patients on HD who have severe ischemia have been reported to be prone to the development of nonocclusive mesenteric ischemia [2]. There was no previous report about the association between warfarin and II as long as we searched PubMed for it using the key words as following; warfarin, and/or ischemia, and/or colitis, and/or end-stage renal disease, and/or hemodialysis. Two fatal cases of the study subjects used both of the drugs. We needed avoid the effect of laxative on II, to focus on the effect of warfarin only. After removal of the two, the corresponding result still remained to be significant (66.7% in the fatal vs 5.56% in the nonfatal, p=0.04). Then, it was possible that 5 (except one suicide case) of 6 who died in the non-fatal group were attributed to II. However, the frequency of having warfarin was higher in the fatal group with significance, even if the 5 were reclassified as the fatal group. The previous studies reported that warfarin provokes calciphylaxis on ESRD, which develops medial calcification of small and medium-sized arteries [4,5]. Therefore, warfarin could facilitate calcification of the arteries, resulting in ischemia based on the loss of the artery blood supply.

The location of II in the fatal group was the right-sided colon, and the fatal undertook laparotomy more frequently. The previous studies reported that the right colon involvement causes severe ischemic colitis, which requires surgical treatment and result in death, and it occurs frequently in patients undergoing hemodialysis [6,7]. The vessels feeding the right colon are so long that they can easily affect the blood supply. Moreover, the right colon has little natural collateral circulation, so that it is more likely to be affected by the change of the

blood supply. Thus, the patients on HD tend to have severe ischemic condition because HD influences the blood perfusion pressure [6,7].

This study had some limitations. The number of the subjects in this study was so small that the results could be affected by the random errors. Therefore, we could not draw the strong conclusions. Some cases were diagnosed as II by imaging procedure without pathological study. So, we could not rule out the possibility that some cases got ulcerative colitis, Crohn's disease and infectious colitis. But according to the fact that they had sudden onset of their symptoms like acute abdominal pain and blood stool after HD, we highly suspected that they have ischemic colitis.

In conclusion, this study showed that there was a possibility that warfarin causes the fatal II by itself, as well as laxative. The fatal group involved the right-sided colon, and undertook laparotomy more frequently as the previous studied reported. Further studies with larger number of the subjects are required to confirm our results.

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