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Reviewer#1

Specific comments to authors

The manuscript is valuable as it highlights possible expanding of treatment approach from gastrointestinal vascular malformations in hereditary hemorrhagic telangiectasia (HHT) to small bowel angiodysplasia (SBAD) patients, based on similar clinical features, therapeutic methods and goals but also challenges. The manuscript addresses the key issue of hemorrhagic angiodysplasia in the small intestine that is difficult to treat endoscopically, bringing forward possible pharmacotherapy and presenting current knowledge and available trials results. The main hypothesis of the work is discussing evidence on the use of tranexamic acid in non-HHT patients suffering from bleeding gastrointestinal angiodysplasia, using HHT recent guidelines and relevant publications on the antifibrinolytic use of this drug. Maybe the author could consider if readership would value additional detailing on HHT guidelines (Faughnan ME, et al. Second International Guidelines for the Diagnosis and Management of Hereditary Hemorrhagic Telangiectasia. Ann Intern Med. 2020 Dec 15;173(12):989-1001. https://doi.org/10.7326/M20-1443) recommending that "clinicians consider treatment of mild HHT-related GI bleeding with oral antifibrinolytics" and "treatment of moderate to severe HHT-related GI bleeding with intravenous bevacizumab or other systemic antiangiogenic therapy"- so that similar approach would be evaluated in hemorrhagic angiodysplasia in the small bowel. The limitations of current knowledge are presented in a well-balanced manner, coming from scarcity of strong evidence and weak guidelines recommendations regarding specific use of tranexamic acid. Findings presented by the manuscript have the potential to significantly impact clinical practice in the direct benefit of patients suffering from difficult to manage GI hemorrhagic angiodysplasia.

Reply: Thank you for appreciating my paper. I hope that this paper will be useful for drug treatment of small bowel angiodysplasia. As for English, after improving it as much as

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possible, I received another native check.

Reviewer#2

Specific comments to authors

Small bowel angiodysplasia (SBAD) is one of the common causes of gastrointestinal bleeding, and there are no recommended drugs to treat it now. The paper reports the pharmacological treatments of endoscopic difficult-to-treat SBAD, including the drug mechanism and side effects of them. The application of tranexamic acid in SBAD is also reported. Meanwhile, it is suggested to add more research reports in related fields to enhance the credibility and strength of the viewpoints. The paper was written concisely and clearly, providing drug therapy program support for patients with difficulty in endoscopic treatment of SBAD. The paper is of novel topic and is recommended to be accepted.

Reply: Thank you for appreciating my paper. I hope that this paper will be useful for drug treatment of small bowel angiodysplasia. As far as I can find out at present, I think that it covers not only important papers but also the latest papers on the five drugs shown in the paper. I would like to avoid adding more information so that the meaning of the sentence can be understood concisely. As for English, after improving it as much as possible, I received another native check.

Reviewer#3

Specific comments to authors

First, tranexamic acid is recommended for patients with gastrointestinal angiodysplasias in hereditary hemorrhagic telangiectasia who are difficult to treat endoscopically. Investigation of the use of tranexamic acid for small intestinal angiodysplasia is desired. Second, there are several reports that hormone therapy, somatostatin analogs,

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thalidomide and VEGF-neutralizing antibodies are useful for SBAD for which endoscopic treatment is difficult. Third, although there are concerns about the risk of thrombosis and embolism, tranexamic acid is expected to reduce the amount of gastrointestinal bleeding in patients with SBAD in whom endoscopic treatment is difficult. Future reports are expected, as tranexamic acid could be a first-line drug for patients with SBAD.

Reply: Thank you for evaluating the paper. I hope that this paper will be useful for drug treatment of small bowel angiodysplasia. As for English, after improving it as much as possible, I received another native check.

Reviewer#4

Specific comments to authors

Small bowel angiodysplasia is common disease and also common cause leading to small bowel bleeding. Indeed, the bleeding resulting from small bowel angiodysplasia is difficult to endoscopic treatment. This article reviews the drug treatment of small bowel angiodysplasia bleeding, especially reviewing the efficacy and safety of tranexamic acid, a traditional antifibrinolytic agent, which provides a valuable reference for treatment of small bowel angiodysplasia bleeding. I think it can be published in this journal. My question: 1.The title is long, and did not reflect the main subject of the manuscript, suggesting revision. 2.English is not good, needing improvement.

Reply: Thank you for evaluating the paper. I hope that this paper will be useful for drug treatment of small bowel angiodysplasia.

1. Thank you for your advice. Changed the title as follows. “Tranexamic acid may be a useful pharmacotherapy for endoscopically resistant small bowel angiodysplasia”.
2. As for English, after improving it as much as possible, I received another native check.