



**Baishideng  
Publishing  
Group**

7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
**Telephone:** +1-925-223-8242  
**Fax:** +1-925-223-8243  
**E-mail:** bpgoffice@wjgnet.com  
**https://**www.wjgnet.com

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35562

**Title:** The efficacy of thalidomide for pediatric Crohn’s disease coexist with tuberculosis: a case series

**Reviewer’s code:** 00074323

**Reviewer’s country:** Italy

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2017-07-26

**Date reviewed:** 2017-08-02

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

Wang et collaborators presented a retrospective experience with thalidomide to treat children with Crohn’s Disease (CD) who had laboratory evidence of infection from Mycobacterium Tuberculosis. The main drawbacks of the study are its retrospective nature and the lack of a control group. Indeed, it is clinical research and it can offer useful data for the development of future studies. Even if several questions stay unanswered about the relationships and the differential diagnosis between CD and Intestinal Tuberculosis (TB), the results of the study may be relevant for clinicians dealing with CD in countries with high prevalence of TB. The authors adopted practical criteria to differentiate CD from IT, arguing that CD can be diagnosed when intestinal compliant fail to recover after a proper treatment against TB (ATT). In the discussion, they argue that we cannot exclude a role of MTB in triggering CD in such patients and this could be of importance when considering conventional antiinflammatory treatments,



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such as anti-TNFalpha biological therapies, which may affect the response to mycobacteria. I have some comments and questions: - The efficacy of thalidomide in children with CD has already been described. The main information added by Wang et al. regard the safety of the drug in subjects with CD and evidence of latent TB. I suggest to change the title accordingly. For example: "Safety of thalidomide therapy in children with Crohn's Disease and evidence of latent tuberculosis". - A better description of the histological finding would be welcome: in particular, were caseous granulomata found in any patient at any time? - As concern TB, were other signs of TB present, before ATT? - The authors should report if any change in TB status (either AFB or tuberculin skin testing) occurred after long term treatment with thalidomide. - The authors must state if any of the cases described in their 2011 manuscript has been included in the present series. - As concerns the patient with monogenic CD (IL10RA deficiency), how the mutations have been judged as causative? I wasn't able to find ref 12 on the web. - Even if this is a pediatric series, in methods, it could be worth to specify if females in reproductive age were included or not in the research and if contraception was prescribed and controlled in these cases. There are some errors that need correction. For example, "one patient were received nutritional treatment", or "conditions could be coexist in countries". Moreover, I recommend not using the name of the name of the disease as an adjective for the subjects with that disease. Not CD patients, but patients with CD. Not "CD who has been treated for tuberculosis", but "children with CD who have ...".



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**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35562

**Title:** The efficacy of thalidomide for pediatric Crohn’s disease coexist with tuberculosis: a case series

**Reviewer’s code:** 02529364

**Reviewer’s country:** Australia

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2017-07-26

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

This study examined the efficacy of thalidomide in the treatment of children diagnosed with both Crohn’s disease (CD) and tuberculosis. The authors concluded that thalidomide is an effective and safe drug in inducing remission for pediatric patients with CD who have been treated for tuberculosis. The same group in 2010 published a paper reporting the use of thalidomide to treat pediatric refractory CD, of which three children had TB. The current study reported the outcomes of thalidomide treatment in 10 younger children with CD coexist with tuberculosis. The patient numbers included in this study are small. However, this study still provides some useful information for the management of pediatric CD, if more clinical data are included. Please see my comments below. 1. Of the 10 patients included in this study, two children were 2-month and 7-month old at the time of their diagnosis of intestinal TB and CD. CD is rare at this age, although it can occur. Please provide clinical evidence for the diagnosis of CD and



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**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

TB for each individual child included in this study. 2. Table 1. The start dose varied in individual patients. For example, both patient 6 and patient 9 had ileocolonic CD and anal fissure, but the thalidomide starting doses were different. What was the base for choosing the starting dose? Table 1 provided final dose and treatment duration. However there were no details regarding how the doses were changed during the treatment. Please provide a table including detailed changes of doses corresponding to the clinical information of the patients at the time of dose changing including the time when the remission was achieved for each individual patient. Please also provide information whether the thalidomide was ceased in any of the patients, if yes, were other medications used for the maintenance of the remission? For example, there was no final dose for patient 1. Does this mean that this patient was off thalidomide and was free of any other CD treatments? 3. All patients received TB treatments. Was their TB cured at the time starting CD treatment using thalidomide?