

374

To: The Editor,  
World Journal of Dermatology

Internal postal code 374  
P.O. Box 9101  
6500 HB Nijmegen  
The Netherlands

UMC St Radboud West, route 374  
René Descartesdreef 1

Date 18-10-2015  
Your reference  
Our reference Carine van der Vleuten  
Concerning Submission of revised manuscript for publication in World  
Journal of Dermatology

www.umcn.nl

Chairman:  
prof.dr. P.C.M. van de Kerkhof

Dear Editor,

Thank you for your invitation to submit a revised version of our paper entitled **Propranolol for infantile hemangioma: current state of affairs**'.

We thank all reviewers for their fruitful comments. Please find below our responses to all points raised.

We hope this revised version is in agreement with your expectations. Please do not hesitate to contact us, should you have any further questions or comments.

Yours sincerely,  
On behalf of all co-authors,

Carine van der Vleuten, dermatologist  
Radboud University Nijmegen Medical Centre

Reviewer: 3088280

---

This is a timely review of the clinical and basic science literature and the current knowledge that is pointing us towards an understanding of the pathophysiology, presentation, and treatment of infantile hemangioma. The authors are thorough in covering nearly all of the published literature, and provide an appropriate level of rigor in their analyses of the results.

I have several suggestions for improvement.

1. In the introduction, it would be good to include the recent data regarding the propranolol treatment in the multifocal and diffuse hepatic hemangiomas.

**These data have been added to the introduction (Page 4, line 61-63 and line 74-76). Three new references (7, 14 and 15) have been added.**

2. Please check and confirm the year, volume no. and page range in reference #15:

**Reference #15 has become #18. The year and volume number have been changed. These changes have also been made in the manuscript text (line 348).**

3. In the Management section, it should be noted that although propranolol has been a breakthrough drug for IH, many children still require plastic surgery at the end of the involuting/involved phase to correct disfigurement from the lesion.

This information has been added in line 399-401 of the management section.

4. In the section of propranolol treatment (Page 12), citation #92 is not relevant to the potential mechanism "dysregulation of the renin-angiotensin system". It would be good to add the recent publication by Ji et al. Br J Dermatol 2015 (The use of propranolol in the treatment of infantile haemangiomas: an update on potential mechanisms of action).

This publication has been added (reference #96).

For discussing only: The propranolol regime of 3 mg/kg/day may not be suitable for all IH populations. We have known for many years that Chinese individuals have a greater sensitivity and lower tolerance to propranolol compared with people of White race. In contrast, black subjects in South Africa were less sensitive to propranolol than were white subjects. These data emphasize the importance of assessing propranolol efficacy in different IH populations in order to detect desired dose in different racial or ethnic groups.

Reviewer: 2441746

---

Very good and updated hemangioma review according to the ISSVA guidelines.