

ANSWERING REVIEWERS



Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 22103-Review.doc).

Title: Retinopathy of prematurity: Past, present and future

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The manuscript has been improved according to the suggestions of reviewers:

Reviewer's code: 00505066

This review about the Retinopathy of Prematurity has been done base on all references from 1940 to 2015. Authors present Past, Present and Future of ROP including the role of Oxygen, the pathogenesis, the experimental findings, epidemics, Stages, screening and Treatment. This is a good review for pediatricians and ophthalmologists to have. I suggest to accept it.

Ans: We thank the reviewer for accepting our manuscript.

Reviewer's code: 00505045

1. This review is quite good and well written. I have some suggestion to improve the quality of the article. 1. In the abstract, I suggest "preventable blindness" instead of "needless blindness" as an expression.

Ans: "preventable" changed to "needless"

2. Please correct retolental fibroplasia as retrolental fibroplasia.

Ans: "Retrolental" spelling corrected.

3. Please correct occurring as occurring.

Ans: "occurring" spelling corrected.

4. I suggest 'regions' instead of 'pockets' as a word.

Ans: "pockets" replaced by "regions"

5. I suggest 'since 1951 to...' instead of 'from 1951 to...'

Ans: "from" replaced by "since"

6. Please describe the pathology more clearly in following sentence: This mechanism of vasoconstrictive and obliterative effect of oxygen is not only limited to the eye with an immature retinal vasculature but confined predominantly to the retinal vessels.

Ans: The sentence is changed to "This mechanism of vasoconstrictive and obliterative effect of oxygen is seen predominantly in the developing retinal vessels."

7. In the pathogenesis section, the role of growth factor related to angiogenesis can be included.

Ans: Role of Vascular Endothelial Growth Factor added in pathogenesis section.

8. I suggest a more detailed definition of the terms of threshold retinopathy, pre-threshold retinopathy, type 1 ROP and type 2 ROP in a separate paragraphs under the title of Stage of ROP following subtitle of the pre-plus disease or AP-ROP.

Ans: Detailed definition of the terms of threshold retinopathy, pre-threshold retinopathy, type 1 ROP and type 2 ROP are already included under "Treatment for ROP." We have rearranged it in separate paragraphs, as suggested.

9. The following information is also valid for the developed countries and I think there is no need to express "especially in the developing economies": The initial eye examination should be performed by 31 weeks' postmenstrual age or 4 weeks from birth, whichever is later, in order to detect prethreshold retinopathy in a timely fashion, especially in the developing economies.

Ans: "especially in developing economies" is deleted.

10. Is there any reference for the following information or is the authors own suggestions?: Thus, in developing countries, to enable early identification and treatment of AP-ROP, infants <28 weeks or <1200 g birth weight should be screened relatively earlier at 2-3 weeks of age.

Ans: Reference added as no. 25 (Jalali S, Anand R, Kumar H, Dogra MR, Azad R, Gopal L. Programme planning and screening strategy in retinopathy of prematurity. Indian J Ophthalmol. 2003 Mar;51(1):89-99 [PMID: 12701873]).

11. Please correct this sentence: Alternatively, tropicamide (0.4%) may be used for cyclopentolate.

Ans: Sentence corrected.

12. Diluted cyclopentolate may also be suggested to reduce probable systemic adverse effects.

Ans: This statement added.

13. I think that the effects of diode laser vs others for ROP treatment is not verified and in many institutions a general anesthesia is needed for laser treatment. A wrong message should not be given for pediatricians in term of anesthesia.

Ans: The following statement "However many institutions prefer general anaesthesia for patient comfort" has been added.

14. The following information may be included: In cases in which observation is undertaken, in which intervals an examination is needed?

Ans: Follow up intervals added.

15. There is a need for more precise recommendation related to following information: Retinal examination of infants at risk for ROP using the RetCam digital camera system using wide angle lens with interchangeable high magnification lenses allows photographic documentation permitting remote interpretation of images and is increasingly being used for telemedicine world over.[28-31] However a recent review showed that digital imaging screening cannot replace indirect ophthalmoscopy.[32]

Ans: Precise recommendation made by stating that telescreening is advisable only in places where there is no ophthalmologist available for bed side screening.

16. I think that any message that suggesting superiority of anti-VEGF over the laser treatment should not be given. I think that laser treatment is still gold standard and anti-VEGF therapy should be carry out as an adjunctive and/or in selected cases.

Ans: Statement that “laser is still the gold standard” has been added.

17. I suggest “reduced” instead of “non-exist” in the following sentence: it may be hoped that occurrence of severe retinopathy or severe visual morbidity from ROP may be non-existent in future.

Ans: “non-existent” replaced by “reduced.”

18. ‘focussed monitoring’ should be ‘focused monitoring’

Ans: Spelling corrected.

19. Legal issues related to ROP treatment can also be included in such a review. Because I think that neonatologists or pediatricians as well as ophthalmologist should tell to the parents about prognosis, course and consequences of ROP and ROP treatment.

Ans: Medico legal implications added as a last paragraph.

20. I think that OCT can be omitted from the section of “Newer therapeutic modalities for ROP” It can be mentioned elsewhere in the manuscript

Ans: OCT removed from ‘Newer therapeutic modalities for ROP’ and moved earlier after telescreening.

21. Please correct ‘dialated’ as ‘dilated’ in the following sentence: Figure 7: Fundus picture of right eye showing dialated and tortuous vessels suggestive of plus disease.

Ans: Spelling corrected

22. It would be very useful to insert a demonstrative pictures for threshold retinopathy, examples of type 1 and type 2 ROP

Ans: Images of Threshold ROP, Type 1 and Type 2 ROP inserted and Figures 9, 10 and 11 respectively.

Reviewer’s code: 00505049

This manuscript entitled “Retinopathy of Prematurity-Past, Present and Future” was to review the past, present and future strategies of retinopathy of prematurity (ROP) that include ROP from 1940s and 1950s when seen as retrolental fibroplasias to current screening and treatment guidelines to the future trends. This review would help the pediatricians to update their current knowledge on ROP for preventive monitoring and treatment. This is well written and worth to be published. There are

some suggestions for authors mainly try to make the manuscript more clearly for reader to understand.

1. P7, Classification, line 3. I think it is better to put "However with the advances in retinal imaging techniques,.....of plus disease called 'pre-plus disease'." This paragraph on P9 after the stages section, before Plus disease. Because it is quite hard to understand for pediatrician without hints to know this new classification.

Ans: We have deleted the sentence "...included the more virulent aggressive, posterior ROP and an intermediate level of plus disease called pre-plus disease." APROP and preplus have been described later.

2. P13, Treatment for ROP. I think this title seems same value as the title of "Screening for ROP-Present Concept", thus I suggest it should be revised as "Treatment for ROP-Present Concept".

Ans: "Present Concept" added.

3. P16 and P17, I think the subtitles of "Low weight gain proportion, WINTROP algorithm, ROPScore, IGF-I, Plasma soluble E-selectin (sE-selectin)" should revise as "Low weight gain proportion, WINTROP algorithm, ROPScore, IGF-I, Plasma soluble E-selectin (sE-selectin)".

Ans: Subtitles kept the same...as suggested.

4. P21, 3rd paragraph, "Optical Coherence Tomography (OCT).....its long-term sequelae." I think this paragraph not belong to the new therapeutic modality for ROP, I suggest move to the P18 "Telescreening" section.

Ans: OCT moved to Telescreening section.

Minor suggestions:

1. P8, Extent of Retinopathy, line 2, I think it is "30o sectors".

Ans: "300 sectors" deleted.

2. P11, line 10, I suggest to separate another paragraph from "In many developing"

Ans: Separate paragraph started from "In many developing...."

3. P13, Treatment for ROP, I suggest put " .." on the threshold disease, type 1 ROP, and type 2 ROP, revise as "threshold disease", "type 1 ROP", "type 2 ROP".

Ans: "... " put for Type 1 & Type 2 ROP. Not put for threshold ROP as it has been included as a separate point.