Author's response to reviews

Title: Evaluation of pulse-oximetry oxygen saturation taken through a skin protective covering

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Author's response to reviews: see over
To

The Editor

BMC Pediatrics

The reviewers have asked about ethics committee approval of our study looking at oxygen saturation in neonates.

We wanted to test if saturation readings taken through a protective covering were less accurate than readings taken directly. In essence this was a test on the instruments capability to read through the protective covering.

The guidelines for ethical approval for biomedical research on human subjects in India were enunciated by the Indian Council of Medical Research (ICMR) and are known as the ICMR Code as revised in 2000. Under the heading ‘Statement of specific principals for clinical evaluation of devices’ it defines a ‘Non critical device’ as an investigational device that does not present significant risk to patients like a thermometer, BP apparatus. The Saturation monitor we tested comes in this category. A phase 4 trial is defined as one undertaken after the approval of the drug or device for marketing, so as to obtain additional information about the risks, benefits and optimal use. Paragraph 8 of ‘Specific Principles’ states clearly that phase 4 study are outside the purview of the ethical committee but adverse reactions should be brought to the notice of the Ethics Committee. As such we have not sought Ethical Committee approval of our study protocol using a pulse oximeter saturation monitor to take saturations in newborn babies (being a standard instrument approved for marketing and clearly a ‘non-critical devise’).
However on receiving the comments of the reviewer the authors placed the paper for consideration of the Hospital Research Ethics Committee on 10/12/05. The committee cannot give approval for a study retrospectively. With regard to the reference made by the referees they were willing to say they have examined the study and found no ethical problems with the study and they could approve of the study prospectively.

There is however an ethical principal (Selection of special groups as research subjects/children/ICMR Code 2000) that states that children must be used only in experiments where the same readings cannot be had from adults. If the monitor could read saturations in an adult through the protective covering, it can be assumed it would do the same in the case of infants. We therefore did this study of taking saturation readings from consenting adults – many hospital staff doctors and nurses. The reviewer of BMC rejected the paper saying, “as pulse oximetry is not invasive and side effects are negligible, it is crucial to have data from infants.’ (The reviewers also asked for analysis using Bland Altman method.) The Editor BMC rejected the submission but left us the option of resubmitting the paper after making the changes suggested by the reviewers.

The authors reviewed the matter and concluded that the reviewers were right in suggesting there was no clinical risk to neonates in taking their saturation reading. It was after this that we repeated the study in neonates.

The Editor and Reviewers need to decide if the paper merits publication in the Journal in the absence of prior ethic committee approval, given the guidelines for seeking ethical consent of the Indian Council of Medical Research. In any case we thank the reviewers for their help in improving the paper.
Reviewer 1
(Amir Kugelman)

1. The reference for comparing two methods (one of which is an established standard method) with another new method, without using 'gold standard' was described by Bland & Altman (Reference 2 in the article).

The references for use of adult probes in neonates are Reference 1 and 5 in the article.

2. The details of the neonates are now given in the article. The exact weight age and diagnosis of each neonate has not been noted but the text now says “The neonates, were all babies born in the hospital less than a week old, and admitted on the post-natal ward. No effort was made to select babies – so as to get a wide range of readings. Babies with low saturation were treated as per hospital protocol”

3. The reviewer asks why we “did not choose to compare measurements simultaneously with same pulse oximeter”

We suspect there is a typing error in the reviewers comment. It is not possible to get 2 simultaneous measurements on 1 oximeter

We had two options

a) We could use the same instrument and take readings one after the other

b) We could take readings on 2 instruments simultaneously but we would introduce the error due to differences in the instrument.

We chose option 1, of using the same instrument

This has been added to the text in Discussion

4. Change has been added - We have used the phrase “may prevent injury”

5. Title has been changed as suggested
6. Oxygen pulse oximetry saturation replaces saturation reading

7. Reference 1 and 5 refer to use of adult probes in neonates

8. Abstract now has study population – number, age etc

9. Methods

We have added this sentence to Methods

‘The neonates, were all babies born in the hospital less than a week old, and admitted on the post-natal ward. No effort was made to select babies – so as to get a wide range of readings. Babies with low saturation were treated as per hospital protocol.’

Ethical approval (please see above)

We took readings only once – not the mean of 3 readings. This again was how Bland & Altman did their study on oximeters

We did not count pulse to check accuracy of the pulse monitor

The reviewer asks, "Can we compare readings 10 and 15 minutes apart".

Our feeling is that that there is variation in saturation all the time. But there is little reason why (in a stable baby) readings 10 and 15 minutes apart must be more varied than readings taken a minute apart

10. The figures have been redrawn. The 3 cases with low saturation showed correlation between methods but the number is too small to do a statistical analysis

11. 12. Last line deleted.

12. US $ is quoted for prices
Reviewer 2

Alex Dullenkopf

1. The text has been revised and a UK Consultant Physician has checked language
2. Figures are redrawn
3. Micropore & gauze specifications given
4. Ethics committee approval: Please see above
5. Can tests done on opposite limb be called a test of repeatability?
We agree that the reviewer that this is a pertinent point. However there is little reason for there to be a real difference in saturation between right and left lower limbs and so we decided, while planning the study protocol, to use two limbs for the repeatability test. It is true that we could have used another protocol. We hold that the method we used does not invalidate the findings.
6. Sample size: A 0.05 two-sided Fisher's z test of the null hypothesis that the Pearson correlation coefficient $r = 0.50$, will have 90% power to detect an $r$ of 0.0 when the sample size is 38. We used a sample size of 50 for greater confidence in the findings.
Answer to Define bias: If there is a lack of agreement between methods, bias can be calculated by the mean difference d and standard deviation of the difference. If there is a consistent bias this can be adjusted for by subtracting d from the new method. (Bland & Altman). However as there was no difference between the methods we have deleted the statement about bias from the article
7. Last sentence of Methods changed as suggested
8. Results now only to 2 decimal places. Use of 1 decimal place would involve too much of rounding off.
9. What does ‘the absorbance was 1.97’ mean
We have changed the sentence and hope the meaning is clearer now.
“With Micropore, the absorbance was 1.97 for red light and for infrared light it was 1.99.’ This suggests that both light are absorbed to about the same degree. If one light were absorbed excessively compared to the other, it would result in errors in readings of saturation

10. The discussion has been reorganized.

11. As the other reviewer has also suggested, we have now changed the sentence that suggests that the study found that pressure necrosis is less with the protective covering.

12. Table 1 legend has been changed. Spectrometer readings do not have units and so none have been used

13. Figures have been redone. To make the figures the figures self explanatory the SD have been retained