Author's response to reviews

Title: The efficacy of a comprehensive lifestyle modification programme based on yoga in the management of bronchial asthma: a randomized controlled trial

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Author's response to reviews: see over
Reviewer's report - 1

Title: The efficacy of a comprehensive lifestyle modification programme based on yoga in the management of bronchial asthma: a randomized controlled trial

Version: 4 Date: 2 December 2008
Reviewer: Cheryl M Salome

Reviewer's report:

General comments:
This paper reports the effect of a substantial yoga-based intervention on objective and subjective measures of asthma, and has shown small but clinically meaningful changes in quality of life and peak expiratory flow in the active treatment group. The study was appropriately designed as a randomized controlled trial, and the outcome measures were performed using standard techniques. The improvements in PEFR and quality of life are consistent with effects described in earlier studies. The attempt to examine the effects of yoga on biochemical markers of asthma is novel, but the high degree of variability in the biochemical markers means that the findings in this respect are inconclusive. Thus, it is not clear what this paper adds to what is already known. Furthermore, additional information about the subjects and the interventions is essential in order to interpret the findings.

Major compulsory revisions:

1. The hypothesis underpinning the selection of biochemical markers should be clearly stated. What was the rationale for measuring ECP and urinary PGF2a metabolites? How would changes in either of these markers be interpreted in relation to the mechanisms by which yoga affects asthma?

   Sufficient detail has been given.

2. Further information about the baseline characteristics of the subjects should be included. What treatment were the subjects taking at entry into the study? How was mild and moderate asthma defined?

   Sufficient detail has been given.

   Mild and moderate asthma you have said, on p.4, were based on Reference 12. You may consult reference 12, and add the criteria for mild and moderate asthma. Another feature would be that none of the patients was on corticosteroid therapy.

   Sufficient detail has been given.

3. Information should be given about the control intervention. What constituted the conventional treatment in both the control and intervention groups?
Sufficient detail has been given.

Was there any attempt to optimize the level of conventional treatment before introduction of the yoga intervention?

No, because we did not interfere directly with the drug treatment, the subjects were enrolled who had a stable medication dosing for the past one month.

How frequently were the control group subjects seen during the first two weeks of the study, when the yoga group was undergoing intensive training?

During the first 8 wk, the control group was offered a session on health education relevant to their illness and after the end of the trial at 8 wk, the intervention based on yoga. Also at 2 wk, 4 wk and 8 wk when they come for study measurements, they also got an appointment with their treating physician.

Since there is a considerable evidence for the efficacy of yoga in bronchial asthma already exists, it is unethical to deny yoga even to the control group. Hence the same yoga program was offered to the control group at the end of 8 wk study period.

Was the control group asked to keep a diary of medication use?
Yes

Were they telephoned regularly during the follow up period?
Yes

Could any of the differences between the groups be attributable to differences in exposure to the researchers or health care practitioners?

Yes, but negligible because all the subjects from both groups have exposed to the same treating physicians. In yoga group, all the subjects had undergone yoga training under one yoga therapist with an equal amount of exposure.

4. Was the yoga intervention group given any advice about medication use in relation to yogic practice? For example, were they encouraged to delay or reduce their use of rescue medication?

No, but were told to consult their treating physician to make changes in their rescue medication use, if required.

5. What was required of the yoga intervention group during the follow-up period?

To continue with the practice of yoga

How many hours per day did they need to spend on their yogic practice?
About one and half hours, at least 5 days a week

How was compliance monitored?

By a diary

Was adherence with the dietary advice included in the measure of compliance?

Yes

What level of compliance was considered acceptable, and how many of the subjects achieved this?

Yogic practices at least 5 days a week and almost all the subjects achieved this (as reported in their diary).

6. The generalized linear model used for the data analysis is appropriate for this study design, but has not been used appropriately to determine if there are differences between treatment groups. The analysis has primarily determined if there are significant within-group changes from baseline, and the post-hoc tests have been used for multiple between-group comparisons at different time points. A more powerful approach would be to use the GLM to determine whether the time trends in the outcome variables over the period of the study differs significantly between treatment groups (ie a single p value for each variable).

We also did GLM analysis for Within-Group & Between-Groups for all the variables. Between Group-analysis was between yoga and control groups mean differences by considering all study visits over 8 wk period which is reported in Tables.

7. The conclusions are overstated, and need to be qualified. Non-significant trends in the data, such as changes in FVC and response to exercise are incorrectly claimed to be significant in the discussion or conclusions of the study.

Corrected as appropriate.

The statement that yoga could improve physical work capacity is speculative and should be labeled as such.

Corrected as appropriate.

The claim that only yoga can bring about a genuine improvement in physical capabilities is incorrect and should be removed.

Corrected as appropriate.
8. The authors argue strongly that previous studies have failed to deliver a complete and holistic yoga intervention, which they argue is required to adequately test the therapeutic effect of yoga. However, the effects induced by their study are similar to those of previous studies, showing modest gains in various markers of asthma, using components of yogic practice such as breathing exercises or meditation. The claim that a yoga practice can only be effective if it becomes “a component of the yogic way and view of life” is surely a testable hypothesis, and in the absence of specific data should be labeled as speculation.

It is not truly a speculation. Because there was couple of studies conducted by our group to show efficacy of the similar type of yogic intervention reduces the risk factors for cardiovascular disease and diabetes mellitus and improves in subjective well being, and reduces anxiety levels. This can happen more with a holistic treatment than with one limited to physical practices of yoga.

References quoted...

9. The conclusion that yoga has additional benefits over conventional therapy because it gives additional improvements in pulmonary function is incorrect, and should be removed. Although the authors failed to provide any description of the conventional therapy used in this study, there is substantial published evidence that standard therapy for asthma (bronchodilators and inhaled corticosteroids) have substantial effects on pulmonary function. The present study did not examine the effect of conventional therapy on pulmonary function.

The question is that of a sustained improvement in pulmonary function. That happens much more with yoga than with conventional treatment alone. That is what the comparison between the yoga and control groups in our study shows.

10. The applicability of these findings in a general population of asthmatic patients is not clear. The magnitude of the time commitment required by the subjects is large relative to the magnitude of the benefits, suggests that this approach is unlikely to be widely applicable. Although the authors have made some discussion of the limited application of the results, they also need to consider whether

The time commitment required is considerable, but in view of the sustained improvement in pulmonary function, reduced need for medication, and improvement in general sense of well-being, many patients may be willing to invest their time. Moreover, this is one time investment in their life for getting oriented to a yogic way of life.
**Minor essential revisions**

11. Add units (puffs / 2 weeks??) for rescue medication use to table 8 or table legend.

Included as appropriate

**Discretionary revisions**

12. The data presentation would be more effective as figures rather than tables

Since tables are more informative, and therefore have been retained. However, we are also supplying some figures which give the most important results.
**Reviewer's report - 2**

**Title:** The efficacy of a comprehensive lifestyle modification programme based on yoga in the management of bronchial asthma: a randomized controlled trial

**Version:** 4 **Date:** 28 November 2008  
**Reviewer:** Sat Bir Khalsa

**Reviewer's report:**
In general, this is a well-designed and well-executed study that provides support for the efficacy of a yoga-based lifestyle intervention for asthma and deserves to be published. Although the use of a randomized controlled trial design is a strength of the study, the use of a wait-list control is not particularly effective at controlling for the non-specific effects of the extensive intervention, and therefore the potential significance of the positive outcomes must be tempered by this fact. There are a number of mostly minor weaknesses and errors in the manuscript itself which need to be adequately addressed before this paper can be accepted.

**Major Compulsory Revisions**

1) In the Discussion the authors claim that "Since the only built-in difference between the two groups was the yogic intervention during 8 wk of the study, any difference in the outcome during this period may be reasonably attributed to yoga." This sentence is not completely accurate and needs to be revised. The control condition in this study controlled only for the effects of participation in the study (Hawthorne effect), regression to the mean and changes due to natural history of the disease. A wait-list control group does not control for non-specific effects of the treatment including expectation, belief, subject investment in time and effort, change in the subjects' daily routine (particularly in this extensive intervention), investigator interaction, social interaction and support, and placebo effect all of which could be substantial in this intervention. The more extensive the intervention, the more that non-specific effects could be involved, and the weaker the interpretation of the study and the attribution of benefit to the yoga practices themselves. This appears to be discussed somewhat in subsequent text in the Discussion but should be rewritten and acknowledged more cohesively and more explicitly given that this is the most serious weakness of the study.

*Changed as appropriate.*

2) The fact that the subjects underwent 4 hours per day of intervention for 2 week requires elaboration. How were the subjects able to devote this degree of time daily? Were they unemployed or disabled? This could be important information if the subjects were atypical from normal asthmatic patients is some way. If this is due to a cultural difference between India and Western countries this should be addressed, because many of the readers will be Western scientists. It would be a challenge for most asthma patients in Western countries to be able devote 4 hours per day for 2 weeks unless they were unemployed, disabled or retired.
The sessions were conducted from 8 am to 12 noon. The subjects were not all unemployed or disabled. Their ability to spend that much time in the clinic might be due to ‘cultural differences’.

3) Who instructed the yoga sessions; was it by a qualified yoga instructor?

The yoga practice sessions were conducted by a qualified yoga instructor who is a doctorate degree holder in yogic sciences.

How long were the yoga practice sessions during the 2 week training period and during the 6 week home practice?

The yoga practice sessions were about one and a half hour during the 2 wk training period and also during the 6 wk home practice. This included one hour of asanas (physical postures) and pranayamas (breathing practices), 10 min of relaxation and 20 min of meditation.

What was the proportion of content of the 4-hour sessions to the different components of the intervention?

The components were: asanas and pranayamas, 1 hour; breakfast and building up of group support, 30 min; Lecture and discussion, 2 hours; Meditation, 30 min.

Were the subjects required to do the home practice daily? If so, this should be explicitly stated.

Yes, they were expected to do it daily.

What was the content of the daily home practice sessions?

Same as during the 2-wk training, i.e. one hour of asanas and pranayama, 10 min of relaxation and 20 min of meditation.

Were these sessions the same every day?

Yes, they were the same everyday.

The characteristics of the "session of individualized counseling" need to be described in detail as to the content, duration, and therapist. How frequent was the telephonic support?

During the individualized counseling session, the patient’s questions regarding yogic practices, diet, prognosis, test results etc. were answered, family and social history taken in some detail to establish a good rapport, and to discover any major mental stress, real or perceived, which might be aggravating the disease. In case of mental stress, some counseling, primarily in the form of cognitive restructuring based on the spiritual philosophy underlying yoga, was attempted. Each patient received at least one session of
about one hour of counseling; more sessions were arranged if felt necessary. The counseling was done by medical doctors with special interest in yoga and mind-body medicine. Telephonic support was given weekly once also when it was required by the subject.

4) Please check the calculations of the probability of difference in gender between groups; should the p-values not be the same for both men and women?

Yes, it was not same. Chi-square analysis was used to check any significant differences in the categorical variables present between both the groups and the p-values would depict the same (NS - not significant).

5) Is there any adjustment necessary to the between-subjects statistical comparisons of improvements in the 3 variables that were shown to be different between groups at baseline (e.g. if ANOVA was the statistical method then an ANCOVA would be used to correct for this)? There should be a statement of how this was or was not handled statistically.

Incorporated in Results section as follows:

In PEFR, since there is a significant baseline difference, baseline was considered as a constant covariate for between-group comparisons.

6) In the Discussion the authors state: "Thirdly, in a disorder which impairs respiratory function, using only a technique which primarily silences the mind in the absence of any breathing exercises is inappropriate." This is overstated. It is well-known that meditation practices alone (such as Transcendental Meditation and Vipassana) can have significant effect on central nervous system activity, autonomic nervous system activity and physiology and therefore may well have utility in asthma. The authors should either delete this argument or substantially rephrase it to account for this.

Rephrased as follows: "Thirdly, in a disorder which impairs respiratory function, using only a technique which primarily silences the mind in the absence of any breathing exercises seems to be inadequate."

**Minor Essential Revisions**

1) In the Abstract the authors state: “The present RCT has demonstrated that adding the mind-body approach of yoga to the predominantly physical approach of conventional care results in measurable improvement in subjective as well as objective outcomes in bronchial asthma.” This is too strongly worded given that not all of the outcomes measured showed improvement. It would be better to state that there was improvement in "some" subjective and objective outcomes.

Rephrased as follows: “The present RCT has demonstrated that adding the mind-body approach of yoga to the predominantly physical approach of conventional care results in
measurable improvement in some subjective as well as objective outcomes in bronchial asthma.”

2) The incorporation of dietary recommendations, counseling sessions, lectures and health education into this intervention distinguish it substantially from what is more commonly viewed as "yoga" in most yoga research studies, i.e. postures, breathing techniques and meditation. Although the title of this manuscript "comprehensive lifestyle modification programme based on yoga" accurately reflects this, most of the text in this manuscript describes the intervention as simply "yoga". This is potentially misleading. The authors should adopt another more accurate term (e.g. yoga-based mind-body intervention, yoga-base lifestyle intervention, etc.) throughout the manuscript to avoid this.

First, this would be cumbersome. Secondly, yoga does include everything that we have done (as per original yoga text books). If a watered-down version is “commonly viewed as” yoga, that is deplorable, but we cannot do anything about it. We have described what we have done, what we have done is yoga, and that should suffice.

3) The authors have chosen to present all of the data in a large number of tables - this makes reading the manuscript somewhat tedious. The authors should present some of the more compelling results in a few graphs (and perhaps replace some of the tables) to make the paper more readable. Perhaps some tables could be combined, or some of the tables with insignificant results can simply be described in the text in the Results section.

Changed as appropriate

4) There appears to be inconsistency in the reporting of statistical significance in Tables 3 to 8. Either within-group statistics (repeated measures; over time) are presented or between-group statistics or no statistics are included. Tables 3 and 4 appear to within-group statistics but not between-group statistics, Tables 5 and 6 have no statistics, and Tables 7 and 8 appear to have between-group statistics but not within-group statistics.

Corrected as appropriate

5) In the Discussion the authors state "However, in practice the drop-outs increase steeply, particularly from the control group, as the duration of the study increases." What is the justification for this statement? Are there supporting data for this in previous studies?

Changed the sentence as appropriate

6) In general, the language in the Discussion is often too strong. For example, the authors argue that "…in the process of testing a holistic treatment using a design which is ideal for testing a drug, the holistic treatment should not be reduced to one of its components" but later on state "…it would help to integrate mind-body approaches like yoga into the practice of scientific medicine if the trials not only show that these approaches work, but also how they work in terms of measurable basic mechanisms.”. These are inherently
contradictory; determining mechanism requires dismantling of the therapy to determine which are the effective components (e.g. meditation, postures, breathing, etc.). The authors should tone down the strength of these kinds of arguments or rephrase them in the Discussion.

We do not see any contradiction. Working out the mechanism could mean, e.g. whether the patient’s immune system becomes healthier as a result of the intervention. That does not require dismantling the therapy.

7) The Conclusion is somewhat poorly constructed and written and has a number of grammatical errors and should be revised.

Revised the conclusion in the manuscript.

8) There are many spelling, grammatical and formatting errors. The authors should proofread their manuscript more carefully. Below are examples of some of the errors followed by corrections.

The word “yoga” is sometimes capitalized and sometimes not; it should be used consistently throughout.

Corrected as appropriate

The acronym for the quality of life questionnaire is AQOL in the Abstract and Tables but AQLQ in much of the text; there should be consistent use of only one of these.

Corrected as appropriate

“There is substantial body of evidence on yoga and…”
“There is a substantial body of evidence on yoga and…”

Corrected as appropriate

“However, none of these studies has investigated…”
“However, none of these studies have investigated…”

“None of these studies” means “not even one of these studies”, which is singular. Therefore, “has” is the correct word to use.

“…done on 57 adult patients having mild or moderate bronchial asthma…”

“having bronchial asthma” is standard English – it is not wrong.

“…done on 57 adult patients with mild or moderate bronchial asthma…”
“…in addition to conventional care, also an intervention based on yoga”
“…in addition to conventional care, also received an intervention based on yoga”
“…the change being statistically significant in case of forced vital capacity…”
“…the change being statistically significant for forced vital capacity…”
“…referred to the Integral Health Clinic (IHC) by physicians of All India Institute of Medical Sciences (AIIMS) or came to IHC in response to posters in AIIMS or newspaper advertisements.”
“…referred to the Integral Health Clinic (IHC) of the All India Institute of Medical Sciences (AIIMS) by AIIMS physicians or came to the IHC in response to posters at AIIMS or newspaper advertisements.”
“…at the beginning of the study to summon up how many times they had used an inhaler or bronchodilator during preceding 2 wk…”
“…at the beginning of the study to add up how many times they had used an inhaler or bronchodilator during the preceding 2 wk…”
"…had at least one session of individualized counselling."
"…had at least one session of individualized counseling." 
"…previous RCTs on the efficacy of yoga which are arrived at similar conclusions." 
"…previous RCTs on the efficacy of yoga which have arrived at similar conclusions." 
"…some of the recent studies are overlooked some basic features of yoga." 
"…some of the recent studies have overlooked some basic features of yoga."

Incorporated all the above corrections.