Prevention of Traumatic Stress in Mothers With Preterm Infants: A Randomized Controlled Trial

AUTHORS: Richard J. Shaw, MD, Nick St John, PhD, Emily A. Lilo, MPH, Booil Jo, PhD, William Benitz, MD, David K. Stevenson, MD, and Sarah M. Horwitz, PhD

Departments of Psychiatry and Behavioral Sciences and Pediatrics and Stanford Health Policy, and Division of Neonatology, Stanford University School of Medicine, Palo Alto, California; and Department of Child and Adolescent Psychiatry, New York University Medical School, New York, New York

KEY WORDS
intervention, neonatal intensive care, premature infants, posttraumatic stress disorder

ABBREVIATIONS
ASD—acute stress disorder
BDI-II—Beck Depression Inventory—Second Edition
CBT—cognitive behavioral therapy
DSM-IV-TR—Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision
DTS—Davidson Trauma Scale
PSS: NICU—Parental Stressor Scale: Neonatal Care Unit
PTSD—posttraumatic stress disorder
SASRQ—Stanford Acute Stress Reaction Questionnaire

Dr Shaw conceptualized and designed the study and drafted the initial manuscript; Dr St John contributed to the manual development, supervised the infant sessions, and reviewed and revised the manuscript; Ms Lilo contributed to the manual development, coordinated and supervised the data collection, and reviewed and revised the manuscript; Dr Jo participated in writing the proposal, carried out and drafted the data analysis, and reviewed and revised the manuscript; Dr Benitz facilitated the implementation of the study and reviewed and revised the manuscript; Dr Stevenson participated in the planning of the study, facilitated the implementation of the study, and reviewed and revised the manuscript; Dr Horwitz conceptualized and designed the study, collaborated on the data analysis, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

This trial has been registered at www.clinicaltrials.gov (identifier NCT01307293).

www.pediatrics.org/cgi/doi/10.1542/peds.2013-1331
doi:10.1542/peds.2013-1331

Accepted for publication Jul 19, 2013

Address correspondence to Richard J. Shaw, MD, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Rd, Palo Alto, CA 94305-5719. E-mail: rjshaw@stanford.edu

(Continued on last page)
It has long been documented that parents react negatively to the NICU experience. The complex reactions of these parents include feelings of guilt, sadness over the loss of the “perfect” child, depression, and posttraumatic stress disorder (PTSD). Vanderbilt et al found that 23% of NICU mothers met criteria for acute stress disorder (ASD) while Pierrehumbert et al documented the presence of symptoms of PTSD in 41% of NICU parents up to 14 months after their infant’s birth. Data also suggest that up to 83% of mothers who experience significant trauma also endorse distorted views of their infants. Parents of preterm infants are more likely to show rigid, intrusive, and, later, overprotective parenting styles. In addition, many preterm infants seem to be less resilient and more dependent on optimal parenting to achieve their full developmental potential compared with term infants.

Early interventions for parents with preterm infants have included supportive therapy and self-help techniques to address psychological distress. More recently, a small number of studies have evaluated intervention programs focused on reducing parent anxiety and trauma symptoms. However, studies in this population have not included the well-documented treatment components effective in treating PTSD or focused both on the trauma associated with a medically fragile infant and the loss of the expected parental role.

Interventions have also been developed to help parental engagement with their premature infants. These interventions recognize that parents’ perceptions of their infants and parent–infant interactions are influenced by parental characteristics, including trauma. Meyer et al, for example, advocate a family-based psychosocial intervention focusing on infant redefinition and re-education of the parents. Meta-analyses of interventions to improve maternal sensitivity conclude that interventions are effective, particularly in mother–child dyads with high clinical need such as prematurity and that short, focused interventions are more effective than longer ones. However, to our knowledge, no current interventions combine treatment directed both at parental trauma as well as parent education/infant redefinition.

In our own research, we identified ASD in 44% of mothers of NICU infants as well as a strong relationship with PTSD symptoms 4 months after delivery. We have also tested a brief 3-session cognitive behavior therapy (CBT)-based intervention developed with the goal of reducing trauma symptoms in NICU parents. Given the promise of this short intervention, we expanded the intervention to include: (1) evidence-based treatments to target maternal trauma symptoms; (2) strategies to facilitate the process of infant redefinition by addressing negative perceptions of the infant and alterations in the expected parental role; and (3) guidance around evidence-based parenting approaches for the premature infant. Our hypothesis was that women receiving the intervention would have statistically significantly different self-ratings of trauma, depression, and anxiety symptoms compared with women in a comparison group immediately postintervention.

METHODS

Subjects

Subjects were 105 English- and Spanish-speaking mothers aged ≥18 years of infants 25 to 34 weeks’ gestational age and weighing ≥600 g born at or transferred to 1 of our 4 participating NICUs within the first week of delivery. Our population of interest was that of mothers, unblinded, to receive either: (1) the manual-driven, CBT-based, trauma-focused plus mother redefinition/education intervention; or (2) an active comparison group. The study was approved by the Stanford University institutional review board. Recruitment and delivery of the intervention took place between July 2011 and December 2012. A random number generator created by the statistician was used to assign eligible participants, unblinded, to receive either: (1) the manual-driven, CBT-based, trauma-focused plus mother redefinition/education intervention; or (2) an active comparison group. The project coordinator assigned subjects to the groups and allocated subjects to the interventionists. The intervention lasted 3 to 4 weeks with one or two 45- to 55-minute sessions administered weekly. Participants in both conditions were assessed at baseline (1–2 weeks after the birth of the infant) and 1 week after the completion of the intervention or 4 to 5 weeks’ postbirth for the comparison group.

Study Design

The study was approved by the Stanford University institutional review board. Recruitment and delivery of the intervention took place between July 2011 and December 2012. A random number generator created by the statistician was used to assign eligible participants, unblinded, to receive either: (1) the manual-driven, CBT-based, trauma-focused plus mother redefinition/education intervention; or (2) an active comparison group. The project coordinator assigned subjects to the groups and allocated subjects to the interventionists. The intervention lasted 3 to 4 weeks with one or two 45- to 55-minute sessions administered weekly. Participants in both conditions were assessed at baseline (1–2 weeks after the birth of the infant) and 1 week after the completion of the intervention or 4 to 5 weeks’ postbirth for the comparison group.
Treatment Manual

The development and content of the 6-session treatment manual, which includes ratings of treatment fidelity and maternal satisfaction, has been previously described. Principles of trauma-focused CBT were incorporated with the expectation that reducing trauma-related symptoms would help mothers enhance their coping ability, feel more bonded to their infants, and improve their parenting ability. Sessions included: (1) psychoeducation to educate mothers about PTSD and common feelings and thoughts of NICU parents; (2) cognitive restructuring to help mothers recognize and challenge erroneous and maladaptive cognitions; (3) progressive muscle relaxation to reduce anxiety; and (4) development and processing of the mother’s trauma narrative. Two additional sessions, adapted with permission from the Creating Opportunities for Parent Empowerment program, were developed to enhance the mother–infant relationship by changing the mother’s negative perceptions of her infant and the parenting experience. This process, described as infant redefinition, is based on the assumption that if parents no longer view their child as abnormal and difficult, they will engage in more normative caregiving interactions.

Comparison Group

Participants in the information/usual care comparison group received one 45-minute information session on the policy, procedures, and environment of the NICU with education about parenting the premature infant. Mothers were referred to the existing parent mentor program for support and coping strategies to help ensure that the contact was similar to the intervention group and would approximate an attention-matched comparison condition. Mothers also received usual NICU care, including contacts with social workers, chaplaincy, and developmental psychologists.

Training and Supervision

Therapists were students from a clinical psychology graduate program and a NICU social worker. Therapists attended an 8-hour training during which they were educated about the specific goals of each session and role-played treatment sessions. Treatment fidelity to all components of the intervention, as measured by the therapists’ adherence to the written manual, was high both across sessions and across therapists. The intraclass correlation between raters varied between 0.78 and 0.80 (P < .001), which is considered a high level of reliability.

Measures

Sociodemographic Characteristics

Sociodemographic data, including age, race, ethnicity, primary language, country of birth, education, income, number of children, previous premature births, and marital status, were assessed at baseline.

Traumatic Events Questionnaire

The Traumatic Events Questionnaire is an 11-item questionnaire that is administered at baseline and used to assess specific trauma experiences capable of eliciting posttraumatic stress symptoms. The 2-week test–retest reliability for number of events is 0.91, and for specific events, it ranges from 0.72 to 1.0.

Davidson Trauma Scale

The Davidson Trauma Scale (DTS) is a 17-item scale, administered at baseline and
follow-up, that is used to assess Di-
agnostic and Statistical Manual of Mental
Disorders, Fourth Edition, Text Revision
(DSM-IV-TR), symptoms of PTSD. The
scale has solid test–retest reliability (R = 0.86) and internal consistency (r = 0.99).
At a score of 4, the DTS achieves an 83%
diagnostic accuracy with the Structured
Clinical Interview for DSM-IV.

Stanford Acute Stress Reaction Questionnaire
The SASRQ is a 30-item self-report
questionnaire used to assess DSM-IV-
TR symptoms of ASD. It was adminis-
tered at baseline. Psychometric prop-
erties of the SASRQ show good internal
consistency, test–retest reliability, and
predictive validity.

Parental Stressor Scale: Neonatal Care Unit
The Parental Stressor Scale: Neonatal Care Unit (PSS: NICU) is a 34-item scale
administered at baseline. It is used to evaluate
parents’ perceptions of the stressors
due to the infants’ NICU stay in 3 areas:
physical environment of the NICU, infant
behavior/appearance, and alterations in
parental role. The PSS: NICU is internally
consistent (>0.70 for all scales).

Beck Depression Inventory–Second Edition
The BDI-II is a 21-item questionnaire
that was administered at baseline and
follow-up. It is used to assess depressive
symptoms and has a reliability of 0.92.

Beck Anxiety Inventory
The BAI is a 21-item self-report mea-
sure, administered at baseline and
follow-up, to assess symptoms of anxiety.
The scale has good internal consistency
and 1-week test–retest reliability of 0.75.

Mini–International Neuropsychiatric
Interview
The Mini–International Neuropsychiatric
Interview is a structured interview
diagnosis, administered at baseline
and follow-up. It was used to establish
the DSM-IV-TR diagnoses of major de-
pressive episode, any anxiety disorder,
and PTSD. A multicenter study that com-
pared the diagnoses by general practi-
tioners obtained according to this
structured interview versus the diag-
noses obtained by psychiatrists accord-
ing to nonstructured interviews obtained
a κ coefficient between 0.41 and 0.68,
sensitivity between 0.41 and 0.86, and
specificity between 0.84 and 0.97.

Illness Health Severity Index
The illness health severity index is a
probability of death index (range: 0–1)
that was calculated by using a multi-
variable risk adjustment model. The
index was designed to capture import-
ant factors related to patient risk
based on the Vermont Oxford Network
model by using modifications tai-
lored to the California Perinatal Quality
Care Collaborative data. The model
includes terms for gestational age,
gestational age squared, race, gender,
location of birth, multiple birth, pre-
natal care, 5-minute Apgar score, small
size for gestational age (lowest 10th
percentile), major birth defect, and
California Children’s Services NICU
level. The NICU level is determined by
using modifications tailored to the da-
tabase according to a regional NICU
comparison chart.

Analyses
Means and SDs were used to summa-
rize continuous variables, and counts
and proportions were used to summarize
categorical measures. Two-sample t-tests
(for continuous variables) and χ² tests
(for categorical variables) were used to
compare baseline measures across the
intervention and comparison groups (2-
sided, α = .05). A standard linear mixed
effects modeling was used to formally
model the change from the preinterven-
tion to the postintervention assessment.

Specifically, we used a random intercept
model assuming a linear trend over
time. In line with the intention-to-treat
principle, we included all randomized
individuals in the analyses for whom
data were available from at least 1 of the
2 assessments (preintervention and/or
postintervention). Data points that were
not available were treated as missing at
random conditional on observed infor-
mation according to a maximum likeli-
hood estimation. All 105 individuals
randomized either to the intervention
(n = 62) or to the comparison condition
(n = 43) were included in the mixed
effects modeling. The retention rate was
high in both groups. At the time of the
postintervention assessment, there were
5 dropouts (8%) who were assigned to the
intervention and 2 dropouts (5%) who
were assigned to the comparison
group. We incorporated the MacArthur
framework into this longitudinal
modeling framework for our exploratory
moderator analysis. In our longitudinal
context, the change (slope) from pre-
intervention to postintervention is trea-
ted as the outcome in the moderator
analysis. The Mplus Program version 7
was used to conduct the maximum like-
lihood estimation for all of the longitu-
dinal mixed effects analyses.

RESULTS
Baseline Characteristics
Baseline demographic and clinical fea-
tures of mothers and infants are shown
in Table 1. There were no statistical dif-
fferences between the intervention and
comparison groups on most baseline
variables, including ratings of trauma
(SASRQ) and DTS), anxiety (BAI) and
depression (BDI-II), previous trauma his-
tory (Traumatic Events Questionnaire),
and current psychiatric diagnoses of
major depression, dysthymia, or anxiety.
With the exception of maternal age,
there were no differences in the socio-
demographic variables. Neither group
experienced any adverse events during
the course of the intervention. Mothers assigned to the intervention group rated their overall NICU experience (PSS: NICU global index) as being more stressful compared with the comparison mothers ($P = .02$) in addition to having higher ratings on the PSS: NICU subscales of infant behavior/appearance and alteration in parental role.

**Primary Outcomes**

Figure 2 shows longitudinal trajectories of primary (DTS) and secondary (BDI-II, BAI) outcomes. Scores on the DTS and BDI-II declined significantly more over time for mothers in the intervention group compared with those in the comparison group. By contrast, although both groups showed a significant decline in their scores on the BAI, the rate and magnitude of the change were not statistically significantly different between the groups.

Table 2 summarizes the results of the longitudinal analyses by using mixed effects modeling. Mothers under both conditions improved significantly on trauma symptoms (DTS). There was a significant moderate effect of the intervention on DTS scores (Cohen’s $d = 0.41$, $P = .023$). Mothers’ depression symptoms improved significantly under both conditions. As with trauma, BDI-II scores declined more under the intervention compared with the comparison condition (Cohen’s $d = 0.59$, $P < .001$). Patients under both conditions improved significantly in terms of anxiety (BAI). However, unlike for the DTS and BDI-II, the rate of decline was similar across the 2 conditions. To test the sensitivity of our results to the presence or absence of these baseline covariates, we compared the analysis with and without controlling for these baseline covariates. The differences between the 2 analyses were minimal and did not affect our conclusions with respect to the main outcome variables.

**Moderator Variables**

We examined potential moderators of the intervention effect on DTS scores, our primary outcome measure. Eleven baseline variables were considered to be potential moderators (infant illness severity index, length of stay, Traumatic Events Questionnaire, PSS: NICU global index, current major depressive episode, maternal education, maternal age, income, white/non-white race, Hispanic ethnicity, and US born), as described in Table 1. The analytical criteria used for detecting moderators conformed to the MacArthur approach. According to our mixed effects modeling, in which the key parameter of interest was the effect of the interaction between the intervention status and a potential moderator on the change in DTS, the global rating of NICU stress assessed by using the PSS: NICU was identified as a moderator of treatment effect on the DTS ($P = .036$). To further explore the differential effect of treatment depending on the ratings of baseline NICU stress, subjects were dichotomized into the top 30% and the bottom 70% based on their responses on the PSS: NICU. Figure 3 shows that mothers with higher ratings of baseline NICU stress benefited more from the intervention compared with mothers with lower ratings of baseline NICU stress.

Among the 11 baseline variables examined as potential moderators, mother’s education and household income were found to be nonspecific predictors of the outcome (ie, they predicted outcome regardless of which intervention they received).
received). Less educated mothers ($P \leq .001$) and mothers with lower household income ($P = .025$) showed a greater decline in DTS irrespective of whether they were in the intervention or comparison group.

**DISCUSSION**

The primary finding of the current study was that a brief, 6-session intervention based on principles of trauma-focused CBT paired with techniques developed to help enhance parenting confidence and alter negative parental perceptions of their premature infant was successful in reducing maternal symptoms of trauma and depression 4 to 5 weeks after their infant’s birth. Mothers who received the intervention had significantly lower scores on both the DTS ($P = .02$) and the BDI-II ($P < .001$) compared with mothers in the comparison group. The study is unique in that it integrates trauma-focused treatment with interventions previously found to be useful in enhancing parenting skills and infant outcomes in premature infants.$^{47}$ Results also showed a significant decline in maternal ratings of anxiety for both intervention and comparison groups. This finding is consistent with previous research showing a decrease in anxiety and depression in parents of premature infants over time, even without intervention.$^{48}$ However, it is important to note that the comparison group in our study was an active comparison group and not a passive control. Subjects in the comparison group received a combination of parent education and training in ways to negotiate the NICU environment. However, the failure of the comparison condition to produce comparable changes in trauma symptoms is consistent with findings showing that educational measures alone are insufficient to diminish trauma symptoms.

Results of the moderator analysis indicate that none of the sociodemographic variables had any effect on the
response to the intervention, suggesting that the intervention is effective and applicable for individuals of differing ethnic backgrounds and socioeconomic status. The severity of the infant’s mental condition and previous maternal psychiatric or trauma history similarly failed to influence the response to treatment. However, maternal rating of overall NICU stress was found to be a significant moderator of the treatment effect. The analysis found that the intervention was most effective for mothers who had the highest ratings of NICU stress, suggesting that mothers who rate the NICU experience as being particularly stressful were more likely to report benefits from participation. Thus, although the intervention was broadly successful in addressing trauma symptoms in a cross-section of participants, results show that women in the top one-third of the sample with respect to ratings of parental stress are most likely to show improvements in their trauma symptoms. This finding suggests that the intervention may be more applicable for highly stressed mothers, which is consistent with principles of stepped-care intervention programs for PTSD as proposed by Zatzick et al.49 Finally, with respect to the moderator analysis, less educated mothers and mothers with lower household income reported a greater decline in DTS scores irrespective of whether they were in the intervention or comparison group. This finding is consistent with work from our group showing that more highly educated women are at greater risk of PTSD in the NICU setting.50

The efficacy of our brief intervention has several potentially important clinical implications for NICU care. The findings that >90% of mothers completed all 6 sessions and were satisfied with the treatment suggest that this intervention can be successfully implemented in the NICU. The entire intervention is manualized; it can be easily taught to individuals without specialized training in psychological treatments; and treatment fidelity, as measured by the therapists’ adherence to the written manual, was high both across sessions and across therapists.28

Data from other settings have suggested a relationship between disturbances of attachment and traumatic stress reactions in mothers with a history of interpersonal violence. Schechter and Willheim51 found that greater severity of maternal baseline salivary cortisol levels and greater likelihood of distorted, inflexible, and negative mental representations of the child. Limited research on parents of preterm infants and parental traumatization suggest that up to 83% of mothers who experience significant trauma endorse distorted views of their infants.52,53 Negative or traumatic experiences of delivery have also been associated with eating and sleeping problems in preterm infants,8 and maternal psychological distress of the mother has been associated with subsequent emotional and behavioral problems of the child.52,53 Thus, successful intervention to reduce parental trauma in the NICU setting may have important implications for subsequent child development.

There are several limitations to the study. The sample size was relatively

#### TABLE 2 Estimated Change From Baseline to Postintervention Based on Mixed Effects Longitudinal Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Group Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>95% CI</td>
<td>–17.413 to –8.359</td>
<td>–10.732 to –0.285</td>
<td>–13.724 to –1.032</td>
</tr>
<tr>
<td>Effect sizea</td>
<td>–</td>
<td>–</td>
<td>–0.412</td>
</tr>
<tr>
<td>95% CI</td>
<td>–11.236 to –7.450</td>
<td>–7.128 to –2.854</td>
<td>–6.791 to –1.914</td>
</tr>
<tr>
<td>Effect sizea</td>
<td>–</td>
<td>–</td>
<td>–0.586</td>
</tr>
<tr>
<td>95% CI</td>
<td>–12.912 to –7.563</td>
<td>–11.545 to –5.580</td>
<td>–4.839 to 1.588</td>
</tr>
<tr>
<td>Effect sizea</td>
<td>–</td>
<td>–</td>
<td>–0.160</td>
</tr>
</tbody>
</table>

CI, confidence interval.

*Estimated slope difference/estimated SD of the slope, where SD = square root of the estimated variance pooled across the control and intervention conditions.

#### FIGURE 3

Baseline NICU stress moderating the effect of intervention on DTS decline. DTS trajectories are based on mixed effects growth model estimates. The thick lines represent means, and the thin lines represent 95% confidence bands. The moderator analysis was conducted by using the continuous NICU stress measure. The score was split into 2 categories in the graphic to help readers visualize the moderating effect of NICU stress.
small and although representative of the population in our hospital catchment area, African-American mothers were underrepresented. As a result, it is unknown whether the findings of the study would be generalizable to other ethnic groups. However, although our sample was skewed toward mothers of high socioeconomic status, the moderator analysis did not show any effect of maternal age, education, income, or ethnicity on the response to the intervention. Additional limitations include that, similar to many previous NICU interventions, fathers were not included in the sample; outcome data were based on self-report; and the data were short-term in nature. Finally, although the results are encouraging, they can only be generalized to the population of highly stressed NICU mothers who screened positive for inclusion in the study.

CONCLUSIONS
Our data found that a short, highly manualized intervention for mothers of preterm infants statistically significantly reduced symptoms of trauma and depression. The intervention is feasible in busy NICUs and had high ratings of maternal satisfaction. Given that improvements in mothers’ distress may lead to improved infant outcomes, this intervention has the potential for high public health impact.

ACKNOWLEDGMENTS
We acknowledge the contributions of Drs Kimberly Yonkers and Patricia Chamberlain from our Scientific Advisory Group and Dr Nancy Feinstein.

REFERENCES

(Continued from first page)
Prevention of Traumatic Stress in Mothers With Preterm Infants: A Randomized Controlled Trial
Richard J. Shaw, Nick St John, Emily A. Lilo, Booil Jo, William Benitz, David K. Stevenson and Sarah M. Horwitz
Pediatrics; originally published online September 2, 2013; DOI: 10.1542/peds.2013-1331

Updated Information & Services
including high resolution figures, can be found at:
/content/early/2013/08/28/peds.2013-1331

Citations
This article has been cited by 5 HighWire-hosted articles:
/content/early/2013/08/28/peds.2013-1331#related-urls

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2013 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.
Prevention of Traumatic Stress in Mothers With Preterm Infants: A Randomized Controlled Trial
Richard J. Shaw, Nick St John, Emily A. Lilo, Booil Jo, William Benitz, David K. Stevenson and Sarah M. Horwitz

*Pediatrics*; originally published online September 2, 2013;
DOI: 10.1542/peds.2013-1331

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/early/2013/08/28/peds.2013-1331