

Improved Resiliency Against Depressed Mood in Early Postpartum After Dietary Supplement Administration

Y. Dowlati*^{ψ‡}, A. V. Ravindran*^{ψ‡}, Z. V. Segal*^ψ, D. E. Stewart^{ψ‡}, M. Steiner^{‡ϕ}, J. H. Meyer*^{ψ‡}

camh
Centre for Addiction and Mental Health

CAMH Research Imaging Centre and Campbell Family Mental Health Research Institute*; Department of Psychiatry^ψ and Institute of Medical Science[‡], University of Toronto; McMaster University^ϕ



Introduction

- ❖ The severity of postpartum blues is a strong predictor of PPD^{1,2}. Hence it is plausible that interventions that decrease postpartum blues, may prevent PPD.
- ❖ Postpartum blues occurs between days 4 to 6 postpartum in approximately 75% of women¹. Symptoms include, fatigue, insomnia, poor appetite, crying, anxiety and emotional lability³.
- ❖ PPD is the most common complication of childbearing with a prevalence rate of approximately 13%². Despite the large burden of PPD, there are no standard widespread prevention strategies.
- ❖ Underlying model: Estrogen levels drop >100 fold in the first three days postpartum⁴. Declines in estrogen are associated with elevations in MAO-A⁵, and our group previously discovered that in early postpartum, MAO-A levels are elevated by 40% in affect controlling regions such as the prefrontal cortex and anterior cingulate cortex⁶.
- ❖ MAO-A is an enzyme that creates oxidative stress, influences apoptosis and metabolizes serotonin, norepinephrine and dopamine.
- ❖ A dietary supplement kit, consisting of monoamine precursors, tryptophan and tyrosine, and blueberry antioxidants should have minimal effects on breastmilk, yet reduce severity of postpartum blues.

Hypotheses

1. Oral administration of tyrosine will not increase their total levels in breast milk.
2. Oral administration of tryptophan will not increase their total levels in breast milk.
3. Sadness after sad mood induction procedure (MIP), in day-5 postpartum women (during the typical peak of postpartum blues) will be attenuated in those receiving the dietary supplement (tryptophan, tyrosine and blueberry juice/extract) compared to those not receiving any supplements.

Methods

❖ Study 1:

- 24 healthy breastfeeding women were randomly assigned to 1 of 4 conditions: single oral doses of 2, 5, 10 g of tyrosine or a control condition of no supplements.
- 4 breast milk and 7 plasma samples were obtained from each subject.
- 12 different popular infant formulas (N=6) were analyzed for free tyrosine levels.

❖ Study 2:

- 30 healthy breastfeeding women were randomly assigned to 1 of 5 conditions: single oral doses of 1, 2 g of tryptophan, 20, 40 g of alpha-lactalbumin or a control condition of no supplements.
- 4 breast milk and 7 plasma samples were obtained from each subject.
- 12 different popular infant formulas (N=6) were analyzed for free tryptophan levels.
- Free tyrosine and tryptophan in plasma and breast milk were quantified by HPLC with fluorescent detection.
- For total tyrosine and tryptophan in breast milk, first protein hydrolysis was performed, followed by quantification by HPLC with fluorescent detection.

❖ Study 3:

- 41 healthy breastfeeding women were recruited into 2 groups:
 - Control group (N=20): not receiving any dietary supplement.
 - Supplemented group (N=21): receiving the dietary supplement consisting of 2 grams tryptophan, 10 grams tyrosine and blueberry juice + blueberry extract.
- Severity of postpartum blues was quantitated by the change in the visual analog scale (VAS) mood scores and profile of mood stated (POMS) depression scores from the sad MIP.
- Sad and neutral MIP was done based on Velten MIP. To facilitate this a piece of sad or neutral music from the work of Clark et al also accompanied the Velten MIP^{7,8}.

Results

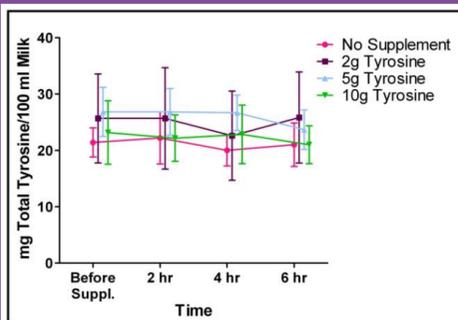
▪ Study 1:

- There was no rise in total tyrosine levels in breast milk, repeated measures of ANOVA (RMANOVA): (F(9,60)=1.87, p=0.074). There was a trend observed towards reduction (Figure 1)⁹.
- There was a significant elevation in maternal plasma free tyrosine concentrations with the magnitude of the supplement (RMANOVA: F(18,120)=6.37, p<0.005) (Figure 2).
- There was a significant elevation in free tyrosine concentrations in breast milk (RMANOVA: F(9,60)=5.26, p<0.005); however, free tyrosine is only less than 2% of the total tyrosine in breast milk.
- Free tyrosine in breast milk, after supplementation, was significantly lower than free tyrosine measured in extensively hydrolyzed and similar to partially hydrolyzed infant formulas (p<0.005) (Figure 3).

❖ Study 2:

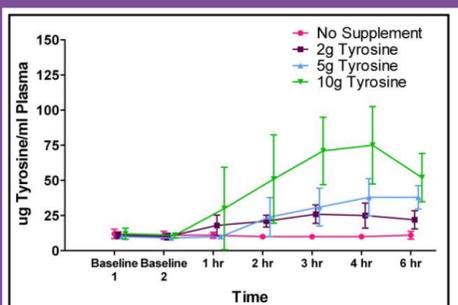
- There were no rise in total tryptophan levels in breast milk (RMANOVA: F(12,75)=1.309, p=0.232) (Figure 4)¹⁰.
- There was a significant elevation in maternal plasma free tryptophan levels (RMANOVA: F(24,150)=15.621, p<0.005) (Figure 5).

Figure 1- No Rise in Total Tyrosine in Breast Milk after Oral Tyrosine Doses



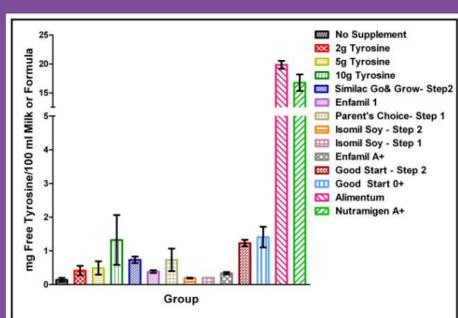
No Rise in Total Tyrosine in Breast Milk after Oral Tyrosine (n=6 per group) (F(9,60)=1.87, p=0.074)

Figure 2- Significant Elevation in Plasma Tyrosine with Oral Tyrosine Doses



Significant Elevation in Plasma Tyrosine Levels Over Time after Oral Tyrosine (n=6 per group) (F(18,120)=6.37, p<0.005)

Figure 3- Free Tyrosine in Breast Milk after Oral Tyrosine is Comparable to Free Tyrosine in Infant Formulas



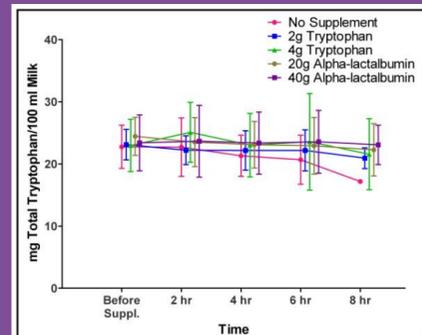
Results

- There was a significant elevation in free tryptophan levels in breast milk after oral tryptophan or alpha-lactalbumin (RMANOVA: F(12,75)=13.639, p<0.001); however, free tryptophan is only less than 1% of the total tryptophan in breast milk.
- Free tryptophan in breast milk, after supplementation, was significantly lower than free tryptophan in extensively hydrolyzed and partially hydrolyzed infant formulas (p<0.005) (Figure 6).

❖ Study 3:

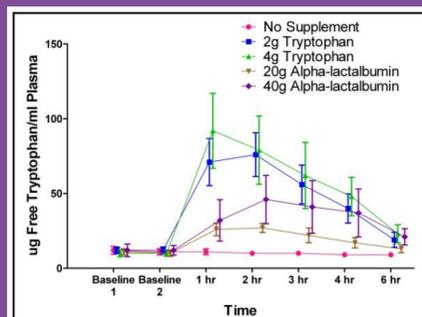
- Analysis of variance (ANOVA) showed a significant group effect on change in the visual analog scale (VAS) depressed mood scores after the sad mood induction (F(1,39)= 88.33, p<0.001) (Fig 7).
- The effect size observed was 2.9.
- Visual Analog Scale (VAS) depressed mood score change after the sad mood induction was 43.85±18.98 in controls and 0.05±9.57 in the supplemented group.
- Similarly, ANOVA showed a significant group effect on the change in profile of mood state (POMS) depression scores (F(1,39)=19.81, p<0.001).

Figure 4- No Rise in Total Tryptophan in Breast Milk after Oral Tryptophan or A-lac



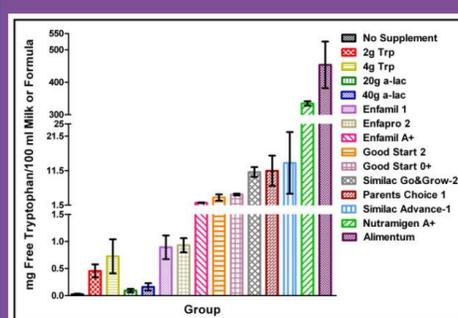
No Rise in Total Tryptophan in Breast Milk after Oral Tryptophan or A-lac (n=6 per group) (F(12,75)=1.309, p=0.232)

Figure 5- Significant Elevation in Plasma Free Tryptophan with Oral Tryptophan and A-lac



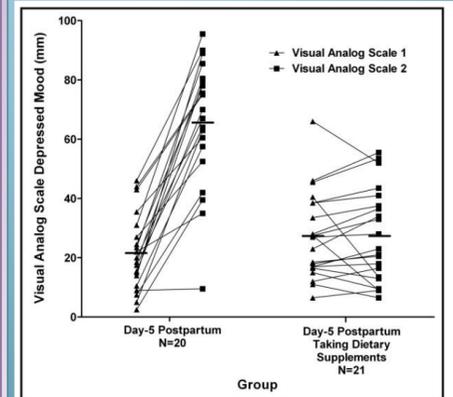
Significant Elevation in Plasma Tryptophan Levels Over Time after Oral Tryptophan or A-lac (n=6 per group) (F(24,150)=15.621, p<0.005)

Figure 6- Free Tryptophan in Breast Milk after Oral Tryptophan or A-lac is Comparable to Free Tryptophan in Infant Formulas



Open Trial Results Eliminate Postpartum Blues

Figure 7- Stronger Elevation in Depressed Mood Scores on Visual Analog Scale (VAS) in Day-5 Postpartum Women not Taking the Dietary Supplement.



Significant Elevation in Depressed Mood Scores as Measured by VAS in Day-5 Postpartum Women Not Taking Any Dietary Supplements Compared to Day-5 Postpartum Women Taking the Dietary Supplement (p<0.001)

Conclusion

- ❖ This is the first study to show that oral tryptophan and tyrosine do not increase total tryptophan and tyrosine levels in breast milk, while significantly increase free levels in maternal plasma. This is consistent with the composition of breast milk having 98% to 99% of amino acids in proteins and peptides.
- ❖ Although the free levels of amino acids increase in breast milk, they represent only 1% to 2% of total tryptophan and tyrosine in breast milk^{9,10} and are within the levels found in popular marketed infant formulas.
- ❖ This is the first study to show that the administration of the dietary supplement consisting of monoamine precursors, 2g of tryptophan and 10g of tyrosine, along with blueberry juice and blueberry extract, was able to reduce the intensity of postpartum blues on day-5 postpartum as measured by sad mood induction procedure in an open-label trial.
- ❖ One explanation to account for an active effect is that the supplement is compensating for the effects of monoamine metabolism and increased oxidative stress by elevated MAO-A levels.
- ❖ The results of the present study, albeit in an open trial, reflect by far the most robust effects of a dietary supplement on postpartum blues. Our effect size was 2.9. Previous trials have reported effect sizes of 0.07 to 0.28.
- ❖ Given the effect size of 2.9, and minimal effects of tryptophan and tyrosine on their total levels in breast milk, there is excellent reason to pursue this supplement in a randomized double blind placebo controlled trial to further assess its effects on postpartum blues.

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