It's No Toke! Why We Need More Info for Breastfeeding Moms

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Disclosures

• Mommy’s Milk receives grant funding or support from
  • Rady Children’s Hospital Academic Enrichment Fund
  • Altman Clinical and Translational Research Institute at UCSD
  • Gerber Foundation

• The views expressed in this presentation are those of the authors and not necessarily those of any funding body or others whose support is acknowledged
Agenda

• An overview of marijuana
  • Cannabinoids
  • Methods of Using

• Published research on marijuana and breastfeeding
  • Studies prior to 2013
  • Current studies

• Mommy’s Milk research study design and preliminary results
  • An overview on Mommy’s Milk
  • Preliminary marijuana results

An overview of marijuana
What is Marijuana?

• The dried leaves, flowers, stems, and seeds from the Cannabis sativa or Cannabis indica plant.

• Sativa = energy

• Indica = drowsy

Cannabinoids: The Major Players

• Cannabinoids are chemical compounds found in the cannabis plant that produce the various effects of marijuana

• The main cannabinoids reported by breastfeeding women:
  • Tetrahydrocannabinol (THC)
  • Cannabidiol (CBD)
Tetrahydrocannabinol (THC)

- The primary *psychoactive* compound in marijuana
- Short-term effects include:
  - Elation
  - Relaxation
  - Drowsiness / Sedation
  - Memory impairment
  - Hunger
  - Dry Mouth
  - Red Eyes
  - Pain Relief
  - Slowed perception of time
  - Laughter
  - Anxiety / paranoia

Cannabidiol (CBD)

- The primary *non-psychoactive* compound found in marijuana
- Potential medical uses
- Short-term effects include the reduction of:
  - Pain
  - Nausea
  - Vomiting
  - Anxiety
  - Depression
  - Sleepiness
How do Cannabinoids Work?

- The Endocannabinoid System (EC) is a communication system which consists of cannabinoids and their receptors.
- Two types of cannabinoid receptors:
  1) CB1 - Found in the brain
  2) CB2 - Found in other parts of the body
- THC binds to CB1 receptors in the brain
- CBD binds to CB2 receptors in other areas of the body

How are Breastfeeding Women Using Marijuana?

- Inhalation
  - Smoking
    - Hand pipes
    - Water pipes
    - Rolling papers/Blunts
    - Hookah
  - Vaporization
    - Vape pens
    - Dabbing (concentrates)

Dabbing Marijuana Concentrate using a Rig
How are Breastfeeding Women Using Marijuana?

- Oral Consumption
  - Tinctures
    - Liquid cannabis extract and solvent
    - Alcohol is the most common solvent
    - Drops are administered under the tongue and are absorbed immediately into blood stream
    - Fast acting effects

- Infused Food and Drinks
  - Any food or drink that contains cannabis
  - Longer onset then inhalation or tinctures
  - Cause powerful full-body, psychoactive effects
  - Examples of products available include gummy bears, soda, candies, cookies, sugar, coffee, wheatgrass powder, honey, butter, olive oil, fruit syrup

How are Breastfeeding Women Using Marijuana?

- Topical Delivery
  - Full cannabis extract that has been decarboxylated to activate cannabinoids which can then be absorbed through the skin
  - Don’t provide cerebral stimulation or a “high”
  - Includes transdermal patches, creams, lotions, salves
How Has Marijuana Changed Over Time?

- The potency of marijuana has increased dramatically
- The THC content present in marijuana has increased from 4% in 1995 to 12% in 2014
- New concentrated extracts are readily available

What Does The Research Show About Marijuana And Breastfeeding?
Presence of delta-9-tetrahydrocannabinol in Human Milk

- Two human milk samples had Δ9-THC concentrations of 105 ng/mL and 340 ng/mL
- One set of paired milk and maternal plasma samples showed a milk Δ9-THC concentration of 60.3 ng/mL which was eight times higher than the maternal plasma concentration of 7.2 ng/mL
- No developmental follow-up on the child

Maternal Marijuana Use During Lactation and Infant Development at One Year

- Article published in *Neurotoxicology and Teratology* in 1990
- Investigated the relationship between infant exposure to marijuana via breast milk and infant motor and mental development at one year of age
- Marijuana exposure via breast milk during the 1st month post-partum was associated with a decrease in infant motor development at one year of age
- Strong correlation between maternal pre- and postpartum marijuana use that could not be effectively reduced by matching
Simultaneous Analysis of Frequently Used Licit and Illicit Psychoactive Drugs in Breast Milk by LC-MS

- Article published in *Journal of Pharmaceutical and Biomedical Analysis* in 2011
- Barcelona, Spain
- 1 milk sample
- THC was detected and the level reported was 86ng/mL
- No developmental follow-up on the child

American Academy of Pediatrics

Current policy statement on “Breastfeeding and the Use of Human Milk” states that breastfeeding is contraindicated in women using illicit drugs
A Recap

What we know

• THC transfers into human milk

What we don’t know

• How does THC exposure via breast milk influence:
  • Child’s growth in the first few months of life (when exclusive breastfeeding is recommended)
  • Child’s neurodevelopment because the brain is rapidly developing during the first 3 years of life

Mommy’s Milk Research Study Design
Mommy’s Milk, The Human Milk Research Biorepository

• Study Design
  • All breastfeeding women over the age of 18 years are eligible.
  • A 50 mL (~2 ounces) milk sample is collected, but as little as 1 mL is accepted.
  • Samples can be collected either at the UCSD HMB Research Center or via a mailed milk sample.
  • Women are interviewed by trained study staff the same day as they express their milk samples either in person or via telephone
  • Samples are stored in a -80°C freezer

Study Recruitment

• Recruitment Sources
  • Social Media (Facebook)
  • MotherToBaby Pregnancy Studies
  • UCSD General Pediatrics Clinic
  • UCSD NICU and Post-Partum Floors
  • Rady Children’s Hospital - San Diego
  • Sharp Mary Birch Hospital for Women and Neonates
  • Breastfeeding Support Groups (digital and in-person)
Data Collection

• Interview Data
  • Demographics, maternal and child health, and breastfeeding habits
  • Current and past exposures to recreational drugs, alcohol, tobacco, caffeine, prescription medications, and over-the-counter medications
  • Infant adverse reactions (i.e., infant “toxicities”)

• Mailed/Online Questionnaires Data
  • Stress, anxiety, and depression questionnaires
  • Eating habits via a short Block Food Frequency questionnaire
  • Child developmental questionnaires (ASQ, ITSEA, CDI, MCHAT)

How Big Is Mommy’s Milk?

• To date, 925 samples banked in the biorepository from women across the United States

• Recruit 35-40 women per month

• Keep up-to-date with our sample and data collection using our data dashboards!  

Data Dashboard
Mommy’s Milk Preliminary Marijuana Results

Cannabinoid Analysis

• 54 human milk samples with known maternal marijuana exposure were analyzed in July at the UCSD Skaggs School of Pharmacy
  • 46 unique women; 4 women provided 2 samples at different time points

• Looking at THC, 11-OH-THC, CBD, and CBN simultaneously using saponification to extract the cannabinoids and LC-MS to quantify
### Selected Demographic and Maternal Characteristics of Breastfeeding Women with Marijuana Exposure Enrolled in the HMB, 2014-2016

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N= 50 mothers, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age (yrs)</td>
<td></td>
</tr>
<tr>
<td>≤25</td>
<td>7 (14)</td>
</tr>
<tr>
<td>25-30</td>
<td>17 (34)</td>
</tr>
<tr>
<td>30-35</td>
<td>18 (36)</td>
</tr>
<tr>
<td>≥35</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Maternal Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>9 (18)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>41 (82)</td>
</tr>
<tr>
<td>Maternal Race</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>44 (88)</td>
</tr>
<tr>
<td>Black</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Native American</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Maternal Education (yrs)</td>
<td></td>
</tr>
<tr>
<td>Partial High School</td>
<td>1 (2)</td>
</tr>
<tr>
<td>High School Graduate/GED</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Some College/ Specialization</td>
<td>27 (54)</td>
</tr>
<tr>
<td>College Graduate</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Post-Graduate</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Maternal Body Mass Index (BMI)*</td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>0 (0)</td>
</tr>
<tr>
<td>18.5-24.99</td>
<td>17 (34)</td>
</tr>
<tr>
<td>25-29.99</td>
<td>17 (34)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>9 (18)</td>
</tr>
</tbody>
</table>

### Selected Child Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N= 50 mothers, No. (%)</th>
<th>N=4 mothers who gave a repeat sample, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant Age (months)d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>3 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>3-6</td>
<td>20 (40)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>6-12</td>
<td>11 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>&gt;12</td>
<td>16 (32)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Infant Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22 (44)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28 (56)</td>
<td></td>
</tr>
</tbody>
</table>
Methods and Frequency of Marijuana Use in Breastfeeding Women

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N= 50 mothers, No. (%)</th>
<th>N=4 mothers who gave a repeat sample, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Route of Marijuana Exposure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation Only</td>
<td>32 (64)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Other Only</td>
<td>7 (14)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Both</td>
<td>11 (22)</td>
<td>2 (50)</td>
</tr>
<tr>
<td><strong>Frequency of Marijuana Use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 use/day</td>
<td>6 (12)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>1 use/day</td>
<td>23 (46)</td>
<td>3 (75)</td>
</tr>
<tr>
<td>&gt;1 use/day</td>
<td>21 (42)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Inhalation Only was defined as a dose unit of joints, puffs, or grams. Other Only was defined as a dose unit of drops, milligrams or servings. Both was defined as a dose unit from both the Inhalation Only and the Other Only groups.

The most common route of administration was by Inhalation Only (64%). Most women in the sample (88%) reported daily marijuana with one or more uses each day.

THC, 11-OH-THC, and CBD Levels Detected in Breast Milk

<table>
<thead>
<tr>
<th></th>
<th>Min.</th>
<th>1st Qu.</th>
<th>Median</th>
<th>3rd Qu.</th>
<th>Max.</th>
<th>AQL*</th>
<th>BQL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ9-THC (ng/mL)</td>
<td>1.01</td>
<td>2.29</td>
<td>9.47</td>
<td>46.78</td>
<td>323.00</td>
<td>34</td>
<td>20</td>
</tr>
<tr>
<td>11-OH-THC (ng/mL)</td>
<td>1.33</td>
<td>1.35</td>
<td>2.38</td>
<td>5.45</td>
<td>12.80</td>
<td>5</td>
<td>49</td>
</tr>
<tr>
<td>CBD (ng/mL)</td>
<td>1.32</td>
<td>2.92</td>
<td>4.99</td>
<td>5.97</td>
<td>8.56</td>
<td>5</td>
<td>49</td>
</tr>
</tbody>
</table>

*AQL (above quantification limits) was defined as ≥1ng/mL and BQL (below quantification limits) was defined as <1 ng/mL.

*The concentration of CBN was BQL in all 54 samples.

Δ9-THC was detectable in 34 of 54 samples (63%); among these, the median concentration of Δ9-THC was 9.47 ng/mL of breast milk (range: 1.01, 323.00).
The Timing Matters!

<table>
<thead>
<tr>
<th>Uses per Day</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>95% CI</th>
<th>t value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>2.21</td>
<td>0.55</td>
<td>(1.08, 3.33)</td>
<td>4.02</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hours</td>
<td>-0.02</td>
<td>0.01</td>
<td>(-0.037, -0.0002)</td>
<td>-2.25</td>
<td>0.032</td>
</tr>
<tr>
<td>Uses/Day&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.51</td>
<td>0.23</td>
<td>(0.03, 0.99)</td>
<td>2.17</td>
<td>0.039</td>
</tr>
<tr>
<td>Route&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Intercept)</td>
<td>3.37</td>
<td>0.37</td>
<td>(2.62, 4.12)</td>
<td>9.21</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hours</td>
<td>-0.02</td>
<td>0.01</td>
<td>(-0.04, -0.01)</td>
<td>-2.85</td>
<td>0.008</td>
</tr>
<tr>
<td>Route: Other Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Route: Both</td>
<td>-1.11</td>
<td>0.74</td>
<td>(-2.64, 0.41)</td>
<td>-1.50</td>
<td>0.146</td>
</tr>
<tr>
<td>Puffs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Intercept)</td>
<td>3.29</td>
<td>0.68</td>
<td>(1.87, 4.70)</td>
<td>4.81</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hours</td>
<td>-0.02</td>
<td>0.01</td>
<td>(-0.04, -0.00)</td>
<td>-2.31</td>
<td>0.031</td>
</tr>
<tr>
<td>Puffs</td>
<td>-0.04</td>
<td>0.15</td>
<td>(-0.34, 0.26)</td>
<td>-0.28</td>
<td>0.785</td>
</tr>
<tr>
<td>Heavy Use&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Intercept)</td>
<td>2.72</td>
<td>0.44</td>
<td>(1.80, 3.64)</td>
<td>6.14</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hours</td>
<td>-0.02</td>
<td>0.01</td>
<td>(-0.04, 0.00)</td>
<td>-1.97</td>
<td>0.062</td>
</tr>
<tr>
<td>Heavy Use</td>
<td>1.13</td>
<td>0.68</td>
<td>(-0.28, 2.53)</td>
<td>1.66</td>
<td>0.110</td>
</tr>
</tbody>
</table>

There is a reduction in milk Δ9-THC concentration of 2.6% per hour after exposure, which can be used to estimate a half-life of approximately 27 hours for Δ9-THC in human milk.
Study Limitations

• Samples were collected under different conditions, and not all breast milk collections were directly observed.

• We relied on maternal report of marijuana exposure. However, all participants completed a 14-day recall guided by trained study staff who prompted for specific daily use with the aid of a calendar.

Future Directions

• In the next 2 years, Mommy’s Milk will be:
  1) Completing medical record abstraction for child growth measurements and child toxicities
  2) Conducting ongoing neurodevelopmental testing
     • Mullen: Age 12 months – 47 months
     • WPPSI: Age 4-5 years
     • WISC: Age 6-10 years

• Future studies are required to better characterize the degree of distribution of cannabinoids into human milk through more intensive and paired (milk/plasma) sampling.

• In addition, longitudinal sampling of plasma of breastfeeding infants from single-dose to steady-state is needed to determine accumulation ratio of Δ9-THC for infants with mothers who are daily users.
Summary and Conclusions

- THC and CBD are the major players when we talk about marijuana
- Marijuana can be consumed via inhalation, ingestion or topically
- THC does transfer into breast milk!
- The concentration present in milk is dependent on the hours since last used and the number of times used per day
- The half-life is about 27 hours.
- We need more data in order to better advise breastfeeding women on how infant/child exposure to marijuana via breast milk impacts health and neurodevelopment.

Acknowledgements

- Dr. Christina Chambers
- Center for Better Beginnings
- UCSD Altman Clinical & Translational Research Institute (ACTRI)
- Rady Children’s Hospital, San Diego
- Mommy’s Milk Steering Committee
- Participating Moms!
Questions?
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Learn more about Mommy’s Milk:
MommysMilkResearch.org