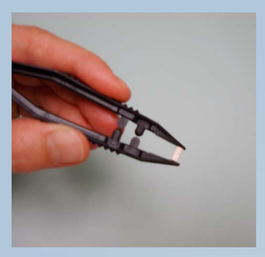

Safety of maternal testosterone therapy during breast feeding

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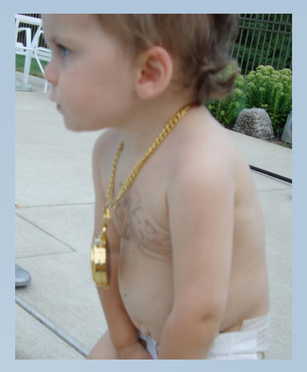


BACKGROUND

Testosterone, delivered by pellet implant, has been successfully used to treat anxiety, depression and fatigue in women. 'Breast feeding' has been listed as a contraindication to testosterone therapy, despite a paucity of data to support this recommendation.

Previously, in our practice, testosterone therapy has been withheld from nursing mothers until they discontinued breast feeding.

PURPOSE AND HYPOTHESIS

The purpose of this study was to evaluate maternal absorption of testosterone and its excretion into breast milk by three methods of delivery:

- •Sublingual drops, 1 mg twice daily
- •Vaginal cream, 0.5 mg applied daily in the morning
- •Pellet implant, 100 mg implanted in subcutaneous tissue

Research hypothesis: Based on the pharmacokinetics of drug excretion in breast milk, testosterone is not expected to be significantly excreted in breast milk (molecular size > 200, non basic pH. fat solubility, significant protein binding) or absorbed into infant blood**.** In addition, testosterone has a low/no intrinsic toxicity.

MATERIALS AND METHODS

A 34 year-old breast feeding mother presented with symptoms of depression, anxiety, irritability, memory loss, aches and pains (MRS validated survey). Testosterone tested low by capillary bloodspot and serum. The patient was treated with testosterone delivered by; sublingual lozenge, vaginal cream and lastly, subcutaneous pellet implant. Sublingual hormones are known to peak rapidly in serum and be measurable for up to 4 hours. Vaginal hormones have been shown to be readily absorbed and peak in serum between 4 and 6 hours.Testosterone delivered by pellet implant shows continuous serum levels above endogenous ranges with diurnal variation. Elevated serum testosterone levels, above normal ranges, are expected with exogenous testosterone, delivered by pellet implant. Doses of 100 mg and above have been shown to relieve symptoms without evidence of major side effects or complications .

The mother was monitored for symptomatic improvement (MRS validated survey) and signs of testosterone excess (none). The infant was monitored for clinical signs of testosterone excess (none).

Specimen Collection

Baseline **testosterone levels** were obtained from **maternal capillary blood** and **breast milk**. During sublingual and vaginal testosterone therapy, serial maternal capillary testosterone levels and testosterone levels in breast milk were measured at 2 hour intervals.

With maternal testosterone therapy delivered by pellet implant, testosterone levels were measured in maternal capillary blood and breast milk at once/twice daily intervals. **Infant capillary bloodspot** (heel-stick) testosterone was monitored day 2, day 7, week 4 and month 5.

Methodology: Breast milk, ZRT laboratory, Beaverton, OR

Breast milk samples (Collected into specimen tubes, labeled and frozen) were liquid extracted with hexane. After removal of the hexane layer, an additional liquid extraction was performed by adding acetonitrile to the hexane solution to remove nonpolar lipids. After removal of the acetonitrile layer, the solvent was dried under nitrogen, and the sample reconstituted in an aqueous buffer. The same procedure was followed for assay commercially with purchased whole milk spiked with known amounts of testosterone. Reconstituted samples were assayed on a commercially available serum testosterone enzyme immunoassay (DRG International) following the given SOP following the addition of extracted standards and breast milk samples.

Methodology: Capillary Bloodspot, ZRT laboratory, Beaverton, OR

A minimum of 6 drops of capillary blood from the fingertip (or heel of the infant) were collected onto filter paper and allowed to dry. 6mm blood spot samples were punched from dried samples. After steroid extraction, the samples, along with standards, were added to a 96-well enzyme immunoassay for testosterone (DRG). From this point the standard procedure for serum testing was followed and results given in ng/dL.

ABSTRACT

Testosterone, delivered by pellet implant, has been successfully used to treat depression and fatigue in women. 'Breast feeding' has been listed as a contraindication to testosterone therapy, despite a paucity of data to support this recommendation.

This study examined 3 methods of delivery of testosterone therapy in a breast-feeding mother who presented with low testosterone and symptoms of testosterone deficiency. Sublingual drops containing 1 mg of testosterone were dosed twice daily. Vaginal cream containing 0.5 mg of testosterone was applied daily in the morning. Lastly, a 100 mg testosterone pellet was implanted into the subcutaneous tissue with re-implantation at 3 months.

Serial testosterone levels were measured in breast milk, capillary blood in the mother (finger-stick) and capillary blood in the infant (heel-stick). Capillary bloodspot* testosterone ranges are variable and are approximately three times higher than serum ranges (baseline, females).

Testosterone was measurable in the mother's blood and absent from both breast milk and the infant's blood by all three methods of delivery; sublingual drops, vaginal cream and pellet implant.

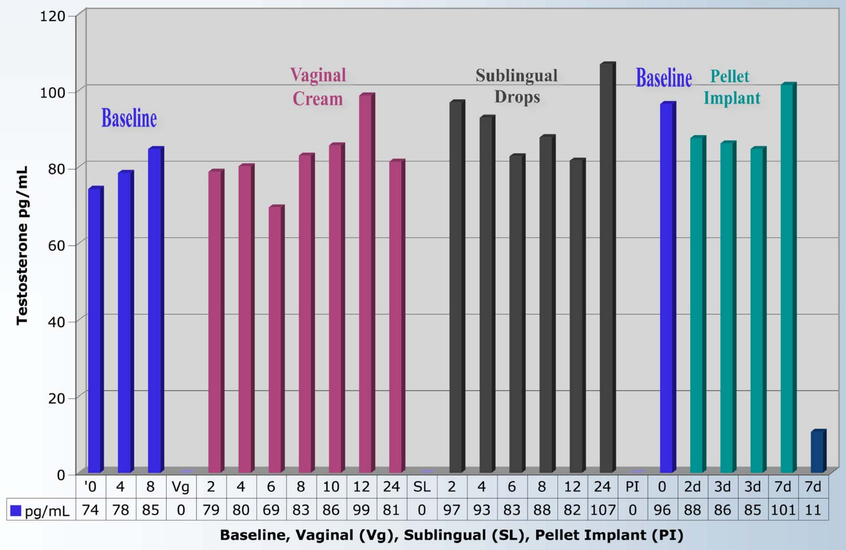
After 5 months of maternal testosterone therapy by pellet implant, there were no adverse affects noted in the infant. Testosterone levels in infant blood remained unaffected. The mother's symptoms of depression, irritability, anxiety, decreased libido, aches, pains, physical and mental exhaustion, resolved with testosterone therapy delivered by pellet implant.

Testosterone therapy by sublingual drops, vaginal cream and subcutaneous pellet implant in breast feeding mothers does not increase the level of testosterone in breast milk or infant's blood and does not have adverse clinical effects in the infant. Further studies are recommended. Unsubstantiated 'contraindications' should be questioned.

RESULTS

- •Testosterone was measurable in maternal blood by all three methods of delivery
- •No significant increase of testosterone in breast milk by vaginal delivery (p =.57), sublingual drops (p =.12) or pellet implant (p =.17)
- •Testosterone was absent from infant blood (<10 ng/dL) during testosterone therapy by pellet implant
- •There were no adverse clinical affects in the infant after 7 months of subcutaneous testosterone therapy by pellet implant
- •Testosterone therapy by **pellet implant** was the effective in relieving maternal symptoms of depression, anxiety, fatigue, decreased libido, aches, pains and memory problems without side effects

Testosterone levels (pg/mL) in breastmilk



pg/mL	'0	4	8	Vg	2	4	6	8	10	12	24	SL	2	4	6	8	12	24	PI	0	2d	3d	3d	7d	7d
	74	78	85	0	79	80	69	83	86	99	81	0	97	93	83	88	82	107	0	96	88	86	85	101	11

Baseline, Vaginal (Vg), Sublingual (SL), Pellet Implant (PI)

	Maternal Capillary Testosterone (ng/dL)	
Time (h)	Vaginal Cream	Sublingual Drops
0	<10	16
2	284	186
4	104	155
6	10	58
8	<10	10
10	<10	
12		<10

	Maternal Capillary Testosterone (ng/dL)
Time (days)	Pellet Implant
0	< 10
2	283
3, am	170
3, pm	93
7, am	148
7, pm	123

CONCLUSIONS

Maternal testosterone therapy is safe for the breast fed infant.

Testosterone delivered by sublingual drops, vaginal cream and pellet implant is absorbed (measurable in maternal blood) but not measurably excreted into breast milk.

Testosterone, delivered by **pellet implant** is effective in relieving symptoms of testosterone deficiency and was not measurably increased in breast milk or measurable in infant serum.

Testosterone, by pellet implant may be a safer and more physiologic alternative to psychotropic medications.

Further studies should be done and guidelines revised.

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