

The Effect of Pregnancy and Lactation on Prolactinoma

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Introduction & objective

- Prolactinoma is the most common pituitary adenoma which accounts for 45% of all pituitary tumors.
- Hyperprolactinemia in these patients is associated with anovulation and infertility.
- Treatment of hyperprolactinemia with dopamine agonists, such as bromocriptine and cabergoline, is an important mode of treatment which can restore ovulation in about 90% of cases.
- In normal pregnancy
 - Pituitary gland increases in their size up to 136% throughout this period.
 - Serum prolactin level is also rises at the end of pregnancy.
- In patients with prolactinoma
 - About 10 to 35 % of patients showed remission of hyperprolactinemia.
 - Recently, about 68% of subjects showed normalization of serum prolactin level and no tumor growth up to 60 months after pregnancy.
- **Bromocriptine**
 - Used to be the first choice of treatment in prolactinoma
 - More than 6000 pregnancies were reported
 - 11 % of spontaneous abortions
 - 3.5 % of neonatal malformation
- **Cabergoline**
 - Treatment of choice for prolactinoma
 - Longer half-life & higher effectiveness
 - Fetal exposure to cabergoline at conception is not affected to miscarriage or fetal malformation.
 - Breastfeeding did not increase the recurrence of hyperprolactinemia.
- In this study, we aimed to analyze
 - the safety of exposure to dopamine agonists in the early period of pregnancy
 - the effect of lactation in the aspects of adenoma size and serum prolactin levels in Korean women with prolactinoma.

Materials and Methods

- Study population
 - Female patients over 18 years old
 - Previously diagnosed prolactinoma and treated with bromocriptine or cabergoline
 - Medical record review from January, 2005 to March, 2013
 - Pregnancy type, age at conception, previous and current medical history and treatment duration, postpartum medication, tumor size and extension by MRI, and serum prolactin level
 - Sella dynamic MRI and serum prolactin level
 - Initial visit
 - Three-month follow-up after the initiation of dopamine agonists
 - Within 1 year before pregnancy
 - Within 3 months after childbirth
 - Within 6 months after lactation

Results

Table 1. Baseline characteristics of study population

	Profile
Patients (n)	50
Patients' age (years, n = 50)	34.2 ± 3.8
Pregnancy counts	65
Age at conception (years)	31.7 ± 3.4
Lactation [n (%)]	39 (70.9)
Duration of lactation (months)	4.8 ± 4.4
Drug dosage	
Bromocriptine (mg/day, n = 33)	7.43 ± 4.4
Cabergoline (mg/week, n = 22)	1.49 ± 0.7
Initial adenoma size (cm)	0.99 ± 0.5
Initial prolactin level (ng/mL)	177.5 ± 522.4
Microadenoma [n (%)]	34 (61.8)
Macroadenoma [n (%)]	21 (38.2)

Results

Table 2. Pregnancy outcome of all patients

	N (%)
Total pregnancies	65
Spontaneous pregnancy	64 (98.5)
IVF	1 (1.5)
Live birth	55 (84.6)
Abortions	10 (15.4)
Term deliveries	55 (84.6)
Preterm deliveries	0 (0.0)
Normal birth weight	55 (84.6)
Low birth weight	0 (0.0)
Stillbirths	0 (0.0)
Premature deliveries	0 (0.0)
Multiple pregnancies	1 (1.5)
Ectopic pregnancies	0 (0.0)
Congenital malformation	0 (0.0)

Figure 1. Changes of adenoma size and prolactin level

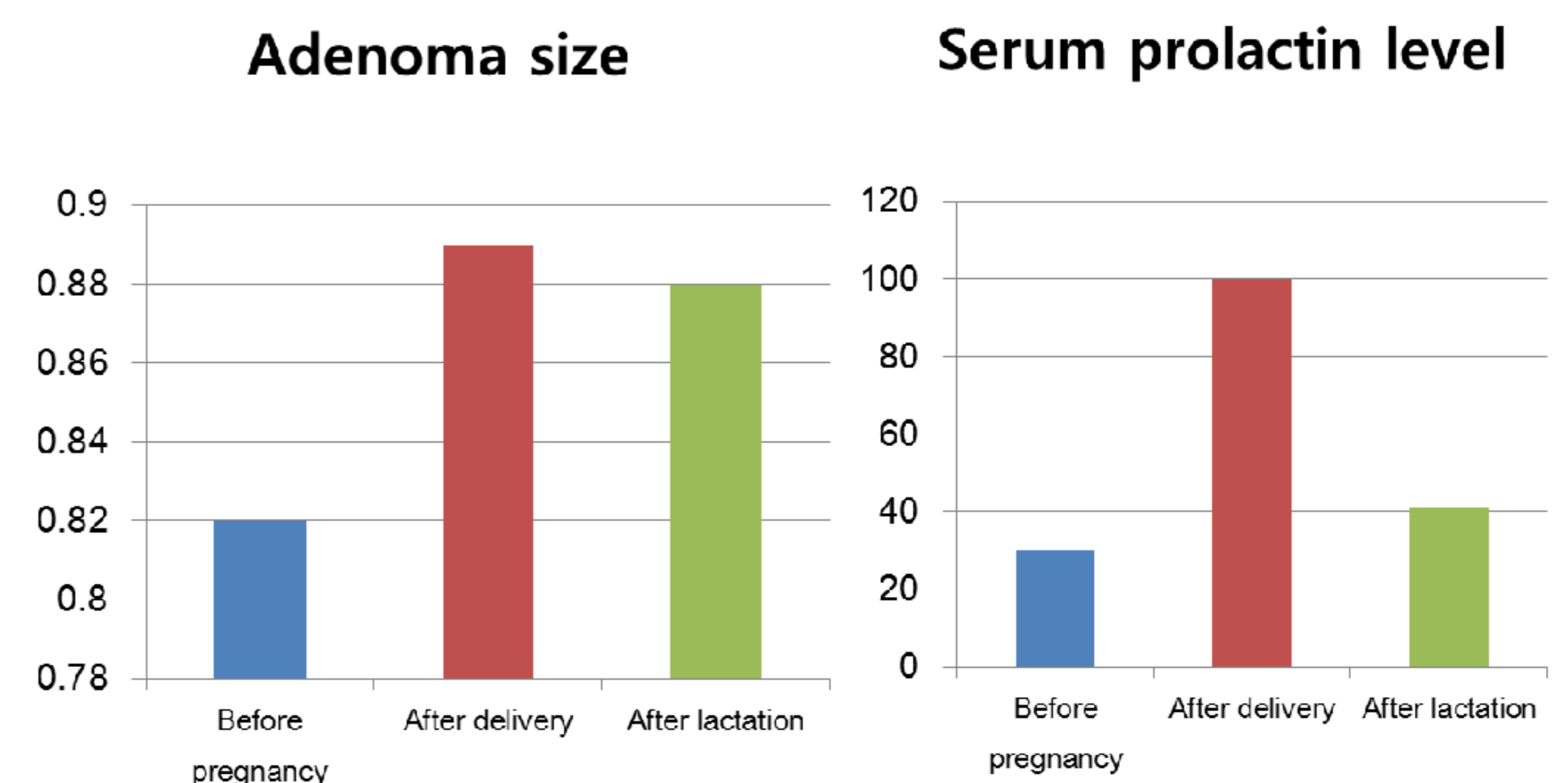


Table 3. Comparisons of several parameters in patients whose adenoma size decreased and/or no change or increased.

	Pts. With increased adenoma size (n = 2)	Pts. with decreased or no change of adenoma size (n = 14)	P-value
Age	36.0 ± 0.0	34.8 ± 4.0	0.333
Age at conception	31.5 ± 0.7	32.1 ± 3.9	1.000
No. of pregnancy	1.0 ± 0.0	1.4 ± 0.6	0.500
No. of delivery	1.0 ± 0.0	1.1 ± 0.4	0.817
Duration of lactation (month)	7.5 ± 5.0	4.3 ± 4.5	0.333
Drug duration before pregnancy	7.5 ± 0.7	22.5 ± 19.0	0.600
Drug cessation time after pregnancy confirmation (pregnancy week)	4.0	6.0 ± 1.5	0.308
Microadenoma (%)	1 (50.0 %)	7 (50.0 %)	
Initial adenoma size(cm)	1.23 ± 0.4	1.17 ± 0.5	0.700
Adenoma size before pregnancy (cm)	0.90 ± 0.1	1.04 ± 0.5	0.933
Adenoma size after delivery (cm)	1.23 ± 0.4	1.09 ± 0.4	0.600
Adenoma size after lactation (cm)	1.19 ± 0.4	0.84 ± 0.5	0.200
Initial serum prolactin level (ng/mL)	178.4 ± 19.9	364.7 ± 1001.4	0.200
Serum prolactin level before pregnancy (ng/mL)	25.8 ± 33.7	41.3 ± 50.9	0.817
Serum prolactin level after delivery (ng/mL)	128.3 ± 112.1	129.9 ± 70.1	0.933
Serum prolactin level after lactation (ng/mL)	40.8 ± 50.0	41.9 ± 43.8	0.700

Conclusion

- This study revealed the effect of early exposure of dopamine agonists did not affect to miscarriage or neonatal malformations.
- In addition, breastfeeding is not associated with the recurrence of hyperprolactinemia and enlargement of pituitary tumor.
- More patients with multi-center, prospective, long-term study will be needed to confirm the safety of dopamine agonists in prolactinoma patients on pregnancy and lactation.

