

CAN PHARMACOLOGIC HYPERPROLACTINEMIA AND BREAST-SUCTION INDUCE LACTATION IN WOMEN WITH NORMAL MENSTRUAL CYCLES?

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SUMMARY

Six women — age range 21/24 — with regular ovulatory cycles, voluntarily underwent with L-Sulpiride (100 mg/die) from the 5th to the 19th day of the cycle. On the 13th, 14th and 15th day of therapy breast suction by syringe breast-pump was performed on each woman every 6 hours and for 4' from either breast. Milk secretion was poor and showed no noticeable increase in the three days of breast suction. L-Sulpiride-induced hyperprolactinemia combined with nipple stimulation-induced increased PRL secretion failed to stimulate milk secretion at a level comparable with physiologic lactation in puerperium.

Hyperprolactinemia-inducing substances administered to women with regular menses cause cycle changes and appearance of galactorrhea proportionally to the amount of substance administered and the treatment duration (^{1, 2, 3}).

This induced hyperprolactinemia interferes with the progesterone secretion by the corpus luteum reducing the average circulating rate of this hormone, thus determining a shorter luteal phase (^{4, 5}).

Hyperprolactinemia can furthermore cause anovulatory cycles and amenorrhea (⁶).

In pregnancy and in the post-delivery period the effects of PRL on the breast are shown by the rapid and significant synthesis of caseine, alpha-lactoalbumine and lactose performed by the glandular acini (^{7, 8}).

Conversely, Sulpiride or metoclopramide treatments induce poor galactorrhea. This could be ascribable to the lack of nipple stimulation which induces the hypophysial release of PRL and Oxytocine in puerperium.

In pregnancy, moreover, oestrogens, progesterone and HPL exert an important eutrophic influence on the mammary gland.

Recent studies have stressed that Sulpiride can not only increase milk secretion but induce lactation in women in puerperium (^{9, 10, 11}).

This study is aimed at assessing whether the administration of Sulpiride to non-pregnant women with regular menses, combined with repeated breast stimulation by breast-pump can induce significant lactation.

MATERIAL AND METHODS

Six women, between 21 and 24 years of age, with no previous pregnancy and regular menses (B.T. controlled for two consecutive cycles) volunteered to take levogyral Sulpiride from the 5th to the 19th day of the cycle (2×50 mg/die per os at 8 a.m. and 8 p.m.).

We chose levogyral Sulpiride since this form has proved most effective in inducing hyperprolactinemia and galactorrhea.

Table 1. — Prolactin plasma level (ng/ml).

	Bas. val.	5. day	10. day	15. day	+30'	+60'
A. B.	12	34	56	80	210	138
E. B.	10	29	54	77	184	115
R. M.	14	32	59	75	199	129
S. T.	9	31	55	75	190	120
C. B.	11	27	51	77	187	112
T. R.	8	34	58	82	214	148
Average ±D.S.	10.6±2.1	31±2.7	55.5±2.8	77.6±2.8	197±12	127±14

On the 13th, 14th and 15th day of the treatment each patient underwent breast suction by syringe breast-pump every 6 hours for 4'. The amount of milk pumped out was related to 24 hours. Throughout the treatment cycle we took note of the B.T. and assayed plasma PRL (RIA method) on blood samples taken before the treatment (basal values) and on the 5th, 10th and 15th day of administration of the drug.

Moreover we took three blood samples on the 15th day when breast suction had just begun and at 30' and 60' from it.

RESULTS

In all our 6 patients the basal PRL level remained in the normal range. As expected, the administration of L-Sulpiride caused the PRL plasma level to rise progressively reaching 77.6 ± 2.8 ng/ml on average on the 15th day (tab. 1).

The fluctuation of PRL during breast suction (samples taken on the 15th day) was particularly significant: from 77.6 ± 2.8 ng/ml (level of sample taken before breast suction) to 197 ± 12 ng/ml (sample at 30') and 127 ± 14 ng/ml (sample at 60').

Table 2 shows figures concerning milk secretion over 24 hours on the 13th, 14th and 15th day.

Only two women (cases 1 and 5) showed milk secretion, though limited, before nipple stimulation by breast pump (on the 10th and 8th day of treatment, respectively).

Milk secretion by breast pump amounted to 16.1 cc on the 13th day, 17.1 cc on the 14th and 23.1 on the 15th.

The 3-day nipple stimulation failed to increase milk secretion significantly, despite massive release of PRL.

The recording of the B.T. showed shortening of the luteal phase (mean: 8 days) in cases 1, 2, 5 and 6 whereas in cases 3 and 4 the luteal phase lasted 12 days.

The B.T. was also recorded throughout the cycle following the treatment. In all 6 patients the thermal curve became normal, two-phased, with regular luteal phase.

Neither subjective nor objective side-effects were observed apart from moderate breast turgor and size increase.

DISCUSSION

Several studies have shown that the administration of Sulpiride in the immediate post-partum period or after the first menstruation induces lactation and increases daily milk secretion. This study has shown that the administration of L-Sul-

Table 2. — Milk secretion expressed in cc.

	13. day	14. day	15. day
A. B.	14	17	24
E. B.	10	15	21
R. M.	18	18	25
S. T.	15	15	23
C. B.	19	19	22
T. R.	21	20	24
Average ±D.S.	16.1±3.9	17.3±2	23.1±1.4

piride to non-pregnant women with physiologic cycles raises the plasma levels of PRL which increases significantly after nipple stimulation by breast pump, just as in puerperium.

Although milk secretion did occur, it was not significant nor did it increase noticeably after breast suction despite puerperal-like PRL values.

L-Sulpiride-induced hyperprolactinemia, combined with nipple-stimulation-induced PRL release alone, fails, to induce lactation or, at least, stimulate significant secretion.

These results confirms that the continuing and specific hormonal conditions of pregnancy play an essential role in preparing the mammary gland, just as a correct release of PRL, induced by nipple stimulation, is of fundamental importance.

BIBLIOGRAPHY

- 1) Linquette M., Gautier P., Gasnault J. P., Desmons F.: *C. R. Soc. Franç. Gyn.*, 3, 155, 1970.
- 2) Linquette M., Buvat J., Gasnault J. P., De-croix-Blacker G., Thomas K.: *Ann. Endocr. Paris*, 36, 49, 1975.
- 3) Delvoye P., Taubert H. D., Jurgensen O., L'Hermite M., Delogne J., Robyn C., Herlant M.: *C.R.A. Acad. Sc. Paris*, 17, 1463, 1974.
- 4) Pepperel R. J., McBain J. C., Winstone S., Smith A., Brown J. B.: *Br. J. Obst. Gyn.*, 84, 898, 1977.
- 5) Seppala M., Hirvonen E., Ranta G.: *Lancet*, 1, 229, 1976.
- 6) Jacobs H. S., Franks S., Murray M. A. F., Hull N. G. R., Steel S. J., Nabarro J. D. N.: *Clin. Endocrinol.*, 5, 439, 1976.
- 7) Houdebine L. M.: *Mechanisms of prolactin action*. In: *Central and peripheral regulation of prolactin function*. First Int. Congr. Hormones and Cancer, Taormina, Oct. 1979.
- 8) Archer D. F.: *Clin. Obst. Gyn.*, 23, 325, 1980.
- 9) Polleri A., Barreca T., Gallamini A., Gianrossi R., Masturro P., Murialdo G., Mizzo M. C., Rolandi E.: *Sulpiride and other secretion*. In: *Sulpiride and other benzamides. Exp. and Clin. Pharm.*, Royen Press, New York, 163, 1979.
- 10) Polatti F.: *Sulpiride isomers and milk secretion in puerperium*. In press: *Clin. Exp. Obst. Gyn.*, 1982.
- 11) Polatti F.: *Possibilità di induzione della montata e della secrezione lattea*. In press: *Gin. Clin.*, 1982.