Prevalence of hyperprolactinemia and abnormal magnetic resonance imaging findings in a population with infertility

Hyperprolactinemia is rare among asymptomatic patients with infertility. Its prevalence and the mean PRL levels did not differ with [1] the infertility diagnosis, [2] the presence or absence of menstrual irregularities, or [3] the severity of menstrual dysregulation. Abnormal magnetic resonance imaging findings, though, are not uncommon among women with hyperprolactinemia despite the lack of symptoms and the mild PRL elevations. (Fertil Steril® 2010;94:1159–62. ©2010 by American Society for Reproductive Medicine.)

Key Words: Hyperprolactinemia, infertility, pituitary MRI, microadenoma

Hyperprolactinemia is a common endocrine disorder, the true prevalence of which is difficult to establish (1, 2). Although overt hyperprolactinemia is associated with a variety of symptoms (3, 4), with mild hyperprolactinemia symptoms can be limited or absent and affected patients are often unaware and do not seek medical attention. The standard infertility workup includes a measurement of serum PRL, and patients with persistently elevated levels usually undergo pituitary imaging (magnetic resonance imaging [MRI]) to exclude pituitary tumors (2, 5, 6).

The prevalence of hyperprolactinemia among asymptomatic patients with infertility is unknown. The goals of the present study were to estimate it and determine whether it correlates with the infertility diagnosis, the severity of menstrual irregularities (when present), or the outcome of fertility treatments. We also sought to determine the prevalence of abnormal MRI findings in patients with mild to moderate elevations of serum PRL.

Institutional Review Board approval was obtained, and the medical records of all female patients presenting for evaluation of infertility between January 2005 and July 2007 were reviewed. Breast-feeding women, patients receiving medications that could affect PRL levels, those with a history of [1] galactorrhea, [2] known pituitary adenoma, [3] tubal ligation or vasectomy, and [4] fertile patients requesting either a donor insemination or oocyte-embryo cryopreservation were excluded. All women had a serum PRL level measured, at least once, by the same laboratory, using the same assay, and those with a PRL level >20 ng/mL had a repeated measurement in the morning, in the fasting, nonstimulated state. Patients with a level >20 ng/mL on two occasions were evaluated further with a pituitary MRI with gadolinium administration. All women with confirmed hyperprolactinemia were given treatment with bromocriptine or cabergoline before the initiation of infertility treatments.

Data from 1705 infertile women were analyzed. The χ^2 test, Fisher exact test, Student *t*-test, analysis of variance, and Pearson correlation methods were used as indicated. *P* values of $\leq .05$ were considered statistically significant.

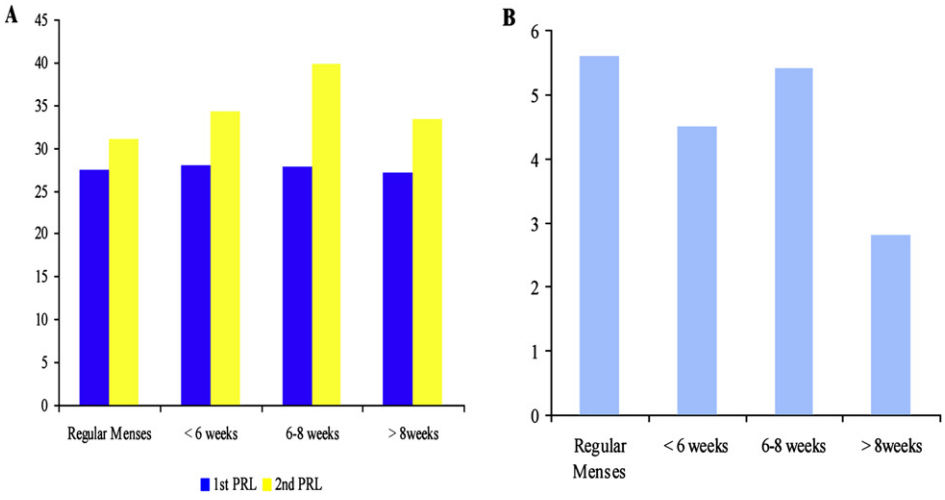
The population was predominantly white. In 12.1% of the patients one elevated serum PRL level was found. The result was confirmed in 88 women (5.2%) and in 42.5% of those with one elevated level. Levels >35 ng/mL (first measurement) were highly suggestive of true hyperprolactinemia (*P*=.04). Menstrual irregularities were reported by 22.1% of the patients. Hyperprolactinemia was diagnosed in 5.6% and 4% of patients with regular and irregular menstruation, respectively (*P*=not significant). The prevalence of hyperprolactinemia and the mean serum levels of PRL did not differ significantly with [1] the presence or absence of menstrual irregularities (first measurement: 27.6 ± 7.7 vs. 27.4 ± 8.1 ng/mL; second measurement: 35.7 ± 12.2 vs. 31.0 ± 13.3 ng/mL, respectively, *P*=not significant) or [2] the severity of the menstrual dysregulation (Fig. 1). The percentage of patients with confirmed hyperprolactinemia among patients with one elevated serum PRL level was similar among women with regular and irregular menstruation (42.8% and 41%, respectively). Furthermore, the prevalence of hyperprolactinemia and the mean serum levels of PRL did not differ significantly with the infertility diagnosis (5%, 10.6%, 5.8%, 4.9%, 4.8%, 1.9%, 11.1%, 6.4%, 1.0% and 33.9 ± 19.4, 29.3 ± 7.5, 26.9 ± 4.5, 32.5 ± 11.2, 37.1 ± 14.2,

Irene Souter, M.D.
Lina M. Baltagi, M.D.
Thomas L. Toth, M.D.
John C. Petrozza, M.D.
Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

Received August 8, 2008; revised December 3, 2009; accepted December 4, 2009; published online January 30, 2010.
J.C.P. is a consultant for Interlace Medical. I.S. has nothing to disclose. L.M.B. has nothing to disclose. T.L.T. has nothing to disclose.
Presented at the 64th Annual Meeting of the American Society for Reproductive Medicine, San Francisco, California, November 8–12, 2008.
Reprint requests: Irene Souter, M.D., Assistant Professor in Obstetrics/Gynecology and Reproductive Biology, Harvard Medical School, Massachusetts General Hospital Fertility Center, 55 Fruit Street—Yawkey 10A, Boston, MA 02114 (FAX: 617-726-8882; E-mail: isouter@partners.org).

FIGURE 1

(**A**) Mean serum PRL levels (ng/mL) and (**B**) prevalence of hyperprolactinemia (%) in patients with regular and irregular menses (stratified by menstrual intervals). *P* values were nonsignificant for all menstrual irregularity categories versus regular menstruation and for all categories among them.



Souter. Correspondence. Fertil Steril 2010.

29.0 ± 0.0, 44.9 ± 34.3, 32.5 ± 10.9, 24.3 ± 0.0 ng/mL for male, tubal, idiopathic, decreased reserve, ovulatory dysfunction, endometriosis, uterine, combined male-female, and multiple female factors, respectively). Among patients with an elevated TSH level (>5.0 μU/mL), three (4.76%) were found to have hyperprolactinemia. A very weak but significant correlation was noted between PRL and TSH levels ($r = 0.07$, P=.002). Levels of PRL did not correlate with either day 3 FSH or androgen levels (DHEAS and total T).

Of the 88 patients with confirmed hyperprolactinemia, 87 had a pituitary MRI. Table 1 summarizes the findings. A normal MRI was found in 60.9% of the patients. In 17 patients (19.5%) a pituitary microadenoma was found. The mean PRL levels of patients with abnormal MRI findings did not differ significantly from those with normal results of imaging of the pituitary (mean ± SD: 31.4 ± 10.9 ng/mL vs. 32.4 ± 14.7 ng/mL, respectively, P=.7). The vast majority of clinically important findings were in patients with mild elevations of PRL (88.2% and 100% of microadenomas diagnosed in patients with a PRL level of <40 ng/mL and <50 ng/mL, respectively). Interestingly, 59% of the microadenomas and 87.5% of other abnormal findings were noted in patients with minimal PRL elevations (<30 ng/mL). In our study population, the prevalence of abnormal MRI findings and/or pituitary microadenomas was 2% and 1%, respectively. The prevalence of abnormal MRI findings among infertile women complaining of irregular menses was lower (0.8% and 0.5% for abnormal MRI findings or pituitary microadenomas, respectively).

The spontaneous pregnancy rates, the pregnancy rates after ovulation induction–IUI or IVF, and the abortion rates did not differ significantly between patients with normal PRL levels and patients with hyperprolactinemia (all started a PRL-lowering medication after the initial diagnosis).

The prevalence of hyperprolactinemia among patients with the sole complaint of infertility (with or without menstrual irregularities) is unknown. Its prevalence in our unselected and rather asymptomatic population with infertility is lower that that reported in patients with classic symptoms of amenorrhea (9%) and/or galactorrhea (70% and 25%, respectively) (7), but at least 10 times higher than that of the general population (1). This finding suggests that PRL should be measured in all patients with infertility whether or not they present with any symptoms suggestive of hyperprolactinemia. Its prevalence did not differ significantly with [1] the presence or absence of menstrual irregularities, [2] the severity of the menstrual dysregulation, or [3] the infertility diagnosis. Our study population—unlike that of other investigators—had only mild to moderate elevations of PRL with a mean and median PRL level of 31.8 ± 13.2 ng/mL and 27.7 ng/mL, respectively. The prevalence of hyperprolactinemia (4.2%) among patients with polycystic ovary syndrome was no different than that seen in other infertility diagnostic groups and was similar to that previously reported in the literature (8, 9). We noted no association between hyperandrogenism and hyperprolactinemia (no correlation between PRL and DHEAS or T levels in patients with polycystic ovary syndrome). The prevalence of hyperprolactinemia among patients with hypothyroidism was small (4.8%), a rate similar to the 1% to 3% previously reported (10–13). A weak but significant correlation was noted between PRL and TSH levels, similar to that observed in men with idiopathic infertility (14). Furthermore, our findings suggest that once PRL levels normalize (often with the use of medication) the outcome of infertility treatments and that of pregnancy is comparable with that of patients with normal PRL levels undergoing ovulation induction–IUI and IVF (15, 16).

The MRI remains a valuable tool for visualization of the pituitary, providing greater diagnostic accuracy, better resolution and