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Progesterone applications in current gynecology

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Introduction

Progesterone (P4) an endogenous steroid hormone, has been initially allowed in a pure form to be prescribed at 1932.[1] At first, it represented a positive regulator of estrogens action. To date, it is described and used as "participant". Based on recent data, its functional profile should be further evaluated.

Discussion

Progesterone (P) has been applied in cases of pregnant women with personal history of recurrent abortions. No side effects have been reported regarding exposure of mother or foetus to P. Clinical trials showed that P could prevent early pregnancy loss and premature labor. Symptomatic women have been treated with P (study 1: cyclogest or study 2: micronized P) and compared to women that received supportive care (study 1) or placebo (study 2) respectively.[2,3] P increased the rate of live births in both groups (80% in P group vs 67% in supportive care group and 66% in P group vs 63% in placebo group). This increase was not statistically significant (p=0.243 and p=0.45 respectively). Despite the absence of numerical significance, this augmentation mirrors the clinical improvement that P could induce in cases where the risk of abortion predominates. Differentiation in treatment (different chemical variants of P or unlike way of administration: per os, vaginally or rectal) did not affect P s effectiveness.[2,4] But it should be noticed the crucial different role of dydrogesterone; its administration resulted in 47% significant decrease in odds ratio for miscarriage and in 26% significant increase in live birth rates compared to women that were treated either by placebo or bed rest.[5] Dydrogesterone should be further prospectively evaluated in cases of symptomatic pregnant women menaced by the risk of preterm labor.

In non pregnant premenopausal women, P has been used in contraception as a part of Combined Oral Contraceptives (COCs) or as mini pill, P patches and P Intrauterine Devices.[6] It could be offered anytime in order to protect women from a unexpected pregnancy. Levonogestrel in a single or split dose has been proposed as the appropriate treatment when emergency contraception is mandatory; it is effective until 3days after unprotected intersource, while Ulipristal Acetate acting via P s receptors (PRs) could prevent unexpected pregnancy for a longer period of time (5days).[6] On the other hand, during menopause, P in the form of combination of "Stable Shaped Particles of Crystalline Organic Compounds" (cholesterol as carrier +natural progesterone microspheres in aqueous suspension) decreases symptoms and their intensity. This action could be attributed to significant decrease that P provokes in lipid peroxides and therefore to significant limitation of oxidative stress.[7,8]

P has been also applied in young girls in puberty suffering by hypogonadism;[9] the goal in these cases is to help these girls to achieve via a short and safe protocol the external appearance of their classmates. Estrogens treatment starts at the age of 12years old; patches have been shown as the safest route in order to avoid fluctuations of blood pressure and bone density malformation. P follows the unopposed estrogens treatment. Medroxyprogesterone acetate or micronized P could be prescribed for 12-14days each cycle.

On the other hand, regarding menstruation, it seems that P could be functionally combined. Painful menstruation, dysmenorrhea, could be treated via P; COCs inhibit ovulation, while P alone prevents the production of prostaglandins (PGF2α) and vasopressin eliminating the feeling of pain. When endometriosis underlies, gestrinone plus a low dose of mifepristone is really effective in decreasing significantly dysmenorrheal.[10] Pain before menstruation as a part of Premenstrual Syndrome (PMS) could be decreased via P usage. Combination of drospirenone and low dose of estrogen was really effective in ameliorating the clinical profile of PMS.[11] In addition, it was observed that dutasteride in a daily dose of 2.5mg decreased significantly irritability, anxiety and sadness observed in women suffering by PMS, by decreasing the levels of allopregnanolones (Ps products), without affecting P s levels during luteal phase of the menstrual cycle.[12] Allopregnalononones, being allosteric metabolites of the function of type A GABA neurotransmitter system in the brain, could alter its function producing anxiety, aggression, impulsive behaviour in high concentrations. Reschedule of menstruation for personal reasons could be achieved via norethisterone s prescription (10mgr/day; 3-4days before the expected date up to 2-3days after the desired event).

In cases of subfertile women, P is functionally included in Controlled Ovarian stimulation protocols. Recent data proved that shorter use of P before ovulation is combined to better quality of the produced blastocyst and higher implantation and pregnancy rates. P levels up to 1.4ng/ml corresponds to better ART outcomes.[13,14] The effectiveness of P is not altered if different variants are used and/or different methodologies are proposed (vaginally, rectally, per os). Regarding benign uterine diseases, such as myomas, P seems to play a pivotal role. Diminishing the blood loss that myomas cause improves significantly the hemotologique profile of the women. No effect has been observed regarding the size of myomas. But modulation of PRs via UPA could inverse this absence and further ameliorate women s life.[15–17] Regarding malignancy, it seems that P is also "implicated". It was shown that COCs users are protected against endometrial and ovarian Ca for a long period. Contraception usage could modestly increase the risk of breast Ca. But this risk is eliminating 5years after therapy ends. Endometrial hyperplasia does not any longer lead young premenopausal women to surgery because it was found that P eliminates the risk of Ca development. Via in vitro data it was

observed that P inhibiting PAX8 biochemical route suppresses the tubal transformation of ovarian epithelium and it might therefore interfere in the embarrassment of the lethal ovarian Ca.[18]

Conclusion

It seems that P plays a fundamental regulatory role in the construction of the female model during puberty, adult period and menopausal years. Its role should be further investigate in order to reveal significant not yet decoded parts of this steroid hormone.

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Conflict of interest

The author declares no conflict of interest.

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