The Effects of Hormonal Contraception on the Voice: History of Its Evolution in the Literature

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Summary: Objectives. Women of reproductive age commonly use hormonal contraceptives, the vocal effects of which have been studied. Otolaryngologists should be aware of this relationship to make recommendations on hormonal contraception as it relates to each patient's voice requirements.

Methods/Design. A comprehensive literature review of PubMed was completed. The terms "contraception," "vocal folds," "vocal cords," and "voice" were searched in various combinations. Articles from 1971 to 2015 that addressed the effects of contraception on the vocal folds were included.

Results. In total, 24 articles were available for review. Historically, contraception was believed to affect the voice negatively. However, more recent studies using low-dose oral contraceptive pills (OCPs) show that they stabilize the voice. However, stabilization generally occurs only during sustained vowel production; connected speech appears unaffected. Therefore, singers may be the only population that experiences clinically increased vocal stability as a result of taking hormonal contraceptives. Only combined OCPs have been studied; other forms of hormonal contraception have not been evaluated for effects on the voice. Significant variability exists between studies in the physical attributes of patients and parameters tested.

Conclusions. Hormonal contraception likely has no clinically perceptible effects on the speaking voice. Singers may experience increased vocal stability with low-dose, combined OCP use. Other available forms of contraception have not been studied. Greater consistency in methodology is needed in future research, and other forms of hormonal contraception require study.

Key Words: Oral contraceptive–Voice–Contraception–Oral contraceptive pill.

INTRODUCTION: THE MENSTRUAL CYCLE AND THE VOICE

The fluctuation of hormones in the menstrual cycle has significant effects on the voice.[1–5] Vocal symptoms, known as dysphonia premenstrualis, accompany the better-known symptoms of premenstrual syndrome (PMS) during the luteal phase of the menstrual cycle.[6] The most common symptoms of dysphonia premenstrualis are difficulty singing high notes, decreased flexibility, huskiness, fuzziness, breathiness, decreased volume, difficulty bridging passaggios, and intonation problems. The most common symptom is difficulty reaching high notes.[6,7] Davis and Davis[7] concluded that, on average, singers experience 33 general symptoms of PMS and three symptoms of dysphonia premenstrualis. Chae et al[8] showed that approximately 57% participants met the DSM IV criteria for PMS and also had acoustic evidence of dysphonia premenstrualis, whereas the PMS-negative group did not. The risk of vocal stress and possible damage during the premenstrual period led many European opera houses to offer singers contracts that included "grace days" during their premenstrual period. This accommodation is no longer followed in Europe and was never practiced generally in the United States.[9]

The mechanisms that cause these symptoms lie not just in the actions of the hormones themselves but also in the cyclic fluctuation of hormone levels. The actions of the hormones on the vocal folds can be correlated with their effects on cervical mucus production. Cervical mucus in the preovulatory or follicular phase is thinner and slippery to aid insemination, whereas in the premenstrual or luteal phase, it is thicker and more viscous.[10] Receptors for estrogen and progesterone have been identified in vocal fold mucosa.[3] Increased estrogen causes increased vocal fold mucus secretions and reduced mucosal viscosity and may increase vocal fold mass or thickness. Estrogen levels are highest in the follicular phase or preovulatory phase. Increased progesterone causes decreased mucous secretions, dehydration of the mucosa and lamina propria, increased mucous viscosity, associated with decreased mass, or thinning of vocal fold mucosa. Progesterone levels are highest during the premenstrual phase or luteal phase.[11–13] Dehydration and thinning of the vocal folds in the premenstrual phase contribute to the symptoms of dysphonia premenstrualis.

THE PHYSIOLOGY OF THE MENSTRUAL CYCLE

The menstrual cycle begins with approximately 5 days of menstrual flow. Both estrogen and progesterone levels are low during the menstruation phase. The follicular phase follows, in which the level of estrogen increases daily until day 14 when ovulation occurs, triggered by a surge in luteinizing hormone (LH). The luteal phase follows in which the estrogen level quickly decreases to midlevel. It plateaus there until the end of the cycle, when it drops quickly before menstrual flow. Progesterone remains low after the fifth day of menstrual flow. After ovulation, the progesterone level rises steadily to reach a peak halfway through the luteal phase. Then, progesterone

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starts to decrease and reaches its lowest level before menstrual flow.[14]

THE PHYSIOLOGY OF ORAL CONTRACEPTION

Oral contraceptive pills (OCPs) reduce the overall fluctuation of hormones during the menstrual cycle that results in the depression of ovarian function. They function by feedback inhibition of hypothalamic secretion of gonadotropin-releasing hormone. The progesterone derivative also suppresses LH secretion from the anterior pituitary, which prevents ovulation. The estrogen derivative suppresses follicle-stimulating hormone (FSH) secretion from the anterior pituitary, which inhibits follicle growth before ovulation. The major suppression of ovulation is accomplished by the progesterone derivative of the OCP. However, most pills combine estrogen and progesterone derivatives. The estrogen component has a role in the suppression of ovulation, but the progestin component alone would perform this task. The estrogen component stabilizes the endometrium, minimizing breakthrough bleeding. It also potentiates the action of the progestin component, allowing the dose of progestin in the pill to be reduced. The combination pill is generally more popular among women, but the progestin-only method is prudent in women at increased risk for cardiovascular and thromboembolic events.[10,13,14]

OCPs are either monophasic or multiphasic. Monophasic pills have the same formulation for 21 days of the cycle, followed by seven placebo pills. Monophasic pills introduce the lowest levels of estrogen and progesterone needed to inhibit ovulation. Multiphasic (typically triphasic) OCPs attempt to mimic the fluctuation in hormones of the menstrual cycle. Their aim is to lessen the metabolic effects of the drugs and decrease the incidence of breakthrough bleeding and amenorrhea. Given the higher cost, greater complexity of triphasic pills in administration, and lack of evidence of a significant benefit of triphasic pills, monophasic pills are currently recommended as the first choice for initiation of oral contraception, by the Cochrane Database of Systematic Reviews.[15]

HISTORY OF ORAL CONTRACEPTION AND THE VOICE

The first OCP, Enovid (G.D. Searle Co., Chicago), was tested in 1957 in Japan and Puerto Rico in a formulation containing 75 μg of mestranol and 10 mg of norethynodrel. The dose was lowered to 5 mg norethynodrel before being sold in the United States in 1960.[16] Mestranol was found to increase thromboembolism risk. Norethynodrel is a nortestosterone derivative that has androgenic and metabolic effects that include voice virilization.[3] The second-generation oral contraceptive developed in the 1970s included a progestin derivative, levonorgestrel (LNG), that allowed inhibition of ovulation at a lower dose. Many of the new, standard, low-dose pills contain 100–250 μg of LNG combined with 20–50 μg of ethinyl estradiol. The second-generation OCPs began being marketed in the late 1960s and are, to this day, the most popular contraceptive option for women.[16–18] The 1980s brought the third-generation progestins, gestodene, and desogestrel. They are less androgenic and thus result in decreased impact on metabolism, weight gain, acne, and mood changes. Drospirenone, a spironolactone derivative without androgenic effect and with antimineralocorticoid effect, is the progestin component in fourth-generation contraceptives released in 2006. Controversy remains as to the safety of third- and fourth-generation progestins, as some data have shown an increase in thromboembolism risk. As a result, they are not used as frequently as LNG.[16,19]

Through the 1980s, the voice community believed strongly that oral contraceptives were damaging to some female voices, resulting in hoarseness, loss of vocal efficiency, lowering of range, and loss of high notes. It was said that these permanent effects could occur after only a few months of therapy.[20] Ovosiston (2 mg chlormadinone acetate, 0.1 mg mestranol) was shown in 1969 to be associated with a lower mean speaking frequency by 0.8 half tone as well as an increase in vocal intensity by 5 dB in lower third of pitch range.[21,22] Because of findings such as these, oral contraceptives were recommended only to alter the timing of menstruation to allow for crucial performances and occasionally to lower cyclical recurrent hemorrhage. The voice was to be monitored closely when oral contraceptives were in use.[9,20–25]

Studies have since found that first-generation contraceptives containing a high-dose nortestosterone derivative did cause virilization of the voice. However, second- and third-generation contraceptives are of a lower dose and do not have a deleterious effect on the voice.[1,2,4–6,9,11,12,25–36] First-generation progestins are no longer used in the United States and, thus, the long-held belief that OCPs are harmful to the voice has been refuted.[8]

THE EVIDENCE

Twenty-four articles were identified that address the effects of oral contraception on the vocal folds. The overall conclusion is that oral contraceptive pills do not affect the voice negatively. In fact, current OCP formulations tend to stabilize the singing voice through dampening of hormonal variation throughout the menstrual cycle.[1,2,25–36] However, the quantity and quality of the evidence are not ideal. There were many inconsistencies between the studies, as well as other shortcomings. Moreover, only combined oral contraceptives have been studied. There are many other forms of hormonal contraception used commonly by women on which there is no literature delineating their effects on the voice. There is also no evidence comparing monophasic to triphasic oral contraceptives.

Most of the literatures investigated sustained vowel production. One study evaluated a German lied while others evaluated various vowels or vowel combinations.[1,2,21–37] The formant frequencies of each vowel differ, which theoretically would affect the objective measures used to analyze the voice. No comparison has been made between the various vowels studied in the literature as they relate to hormonal contraception on the voice.