

Estrogen Estrogen-androgen

A Study of Estrogen only Therapy and Estrogen Plus Androgen Combination Therapy in Surgical Menopause Patients

Kwang Bum Bai

Department of Obstetrics and Gynecology, College of Medicine,
Seoul National University, Seoul, Korea

Objective: To evaluate the difference between estrogen only therapy and estrogen-androgen combination therapy in surgical menopause patients.

Materials and Method: Surgical menopause patients received 0.625 mg conjugated equine estrogens or 0.625 mg conjugated equine estrogens plus 1.25 mg methyltestosterone for 2 years. Bone mineral density, menopausal symptoms, lipoprotein profiles were measured.

Results: Both groups showed increased bone mineral density. In the combination group, total cholesterol, high density lipoprotein cholesterol and triglycerides decreased. In the estrogen only group, low density lipoprotein cholesterol decreased but high density lipoprotein cholesterol increased significantly. In both groups, menopausal symptoms were much improved. Side effects were easily tolerated in both groups.

Conclusions: Estrogen-androgen combination therapy had comparable benefits compared with estrogen only therapy.

Key Words: Estrogen-androgen therapy, Surgical menopause

가 가 가
estrogen 2-7
tes- androgen 가 8
tosterone 40%, androstenedione 20% 가 가
1
gen
androgen-estrogen
estrogen
Estrogen androgen

: ,) 156-707 395,
Tel: (02) 840-2170, Fax: (02) 831-2826, e-mail: kbbai@brm.co.kr

estrogen
 가
 가⁹⁻¹¹
 가
 cholesterol 가,
 cholesterol , cholesterol
 가가 estrogen
 cholesterol 가, cholesterol
 cholesterol .¹² est-
 rogen
 .¹³
 estrogen 가 andro-
 gen 가 estrogen
 , estrogen
 , cholesterol, triglyceride, chole-
 sterol 6
 cholesterol Friedewald
 formula¹⁵
 profile student t test
 two-way analysis
 for variance
 Cochran-Mantel-Haenszel test¹⁶
 60 . Estrogen
 conjugated equine estrogen 0.625 mg
 estrogen-androgen
 conjugated equine estrogen 0.625 mg
 methyl testosterone 1.25 mg
 가
 , , ,
 1, 12, 24
 .
 1 6
 1
 1 2 X-ray (DEXA) ±0.6% (p<0.05) 가
 , ,
 가 (Table 1).
 estrogen-androgen
 가 1 3.0 ±1.0% (p<0.01), 2
 3.5 ±1.3% (p<0.01) estrogen
 1 2.0 ±0.4% (p<0.05), 2 25
 ±0.6% (p<0.05) 가
 가
 (Figure 1).

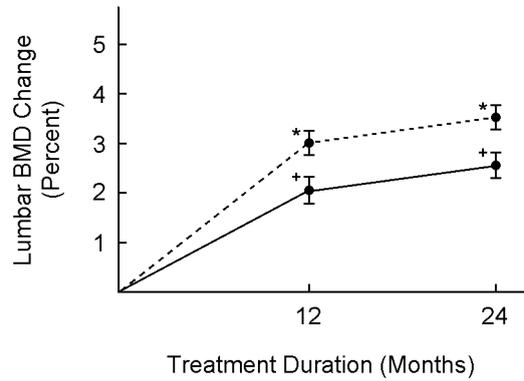


Figure 1. Mean percent changes from pre-treatment. Broken line = estrogen-androgen group; solid line = estrogen only group. * p<0.01, † p<0.05

Kupperman¹⁰
 0 () 7
 ()
 , ,
 cholesterol, triglyceride, chole-
 sterol 6
 cholesterol Friedewald
 formula¹⁵
 profile student t test
 two-way analysis
 for variance
 Cochran-Mantel-Haenszel test¹⁶
 가 (Table 1).
 estrogen-androgen
 가 1 3.0 ±1.0% (p<0.01), 2
 3.5 ±1.3% (p<0.01) estrogen
 1 2.0 ±0.4% (p<0.05), 2 25
 ±0.6% (p<0.05) 가
 가
 (Figure 1).

Table 1. Demographic data

	Conjugated equine estrogen 0.625 mg	Methyltestosterone 1.25 mg + conjugated equine estrogen 0.625 mg
Total no. of patients	95	80
No. of evaluable patients	60	60
Age (year)	52.1 ±3.8	50.5 ±3.5 (mean ±S.D.)
Time since oophorectomy (year)	3.5 ±1.7	4.1 ±1.5 (mean ±S.D.)

Table 2. Hot flush reduction score during treatment period

Reduction score	Tx. period (months)				
	1	2	12	24	
Estrogen only	0	-2.5*	-3.1*	-3.2*	* p<0.05
Estrogen + Androgen	0	-3.0*	-3.2*	-3.5*	* p<0.05

No significant differences between groups

Table 3. Vaginal dryness reduction score during treatment period

Reduction score	Tx. period (months)				
	1	2	12	24	
Estrogen only	0	-2.3*	-2.5*	-2.6*	* p<0.05
Estrogen + Androgen	0	-2.1*	-2.2*	-2.1*	* p<0.05

No significant differences between groups

Table 4. Insomnia reduction score during treatment period

Reduction score	Tx. period (months)				
	1	2	12	24	
Estrogen only	0	-1.8*	-2.0*	-2.3*	* p<0.05
Estrogen + Androgen	0	-1.6*	-2.0*	-2.1*	* p<0.05

No significant differences between groups

Table 5
 , Ward triangle,
 가
 1 , ,
 2
 (Table 2~4).
 cholesterol
 estrogen- androgen
 sterol estrogen
 6 , 12 24
 가
 Triglyceride estrogen 가
 Estrogen- androgen
 cholesterol
 cholesterol

Table 5. Lipid profiles between treatment groups

Index	Baseline (mg/dl)	Percent change from baseline		
		6 mo	12 mo	24 mo
HDL				
E	48.5 ±13.5	4.5 ±7.5*	3.3 ±8.5*	6.6 ±9.5*
E+A	45.3 ±12.2	-8.5 ±10.5 ⁺	-9.5 ±11.5 ⁺	-10.5 ±12.5 ⁺
P value	NS	<0.05	<0.05	<0.01
LDL				
E	141.1 ±35.4	-13.5 ±10.5 ⁺	11.5 ±9.5 ⁺	-10.5 ±11.5 ⁺
E+A	135.4 ±29.6	-5.5 ±9.5	-4.1 ±10.5	-1.5 ±8.5
P value	NS	<0.05	NS	NS
Total cholesterol				
E	217.5 ±36.5	-8.5 ±7.5 ⁺	-9.1 ±9.5 ⁺	-7.5 ±9.8 ⁺
E+A	209.4 ±31.4	-10.2 ±11.5 ⁺	-10.8 ±12.2 ⁺	-8.5 ±7.5 ⁺
P value	NS	NS	NS	NS
Triglycerides				
E	122.5 ±36.6	13.5 ±25.4	9.5 ±18.5	15.4 ±21.3
E+A	128.5 ±40.5	-15.6 ±22.5 ⁺	13.5 ±26.5	-20.3 ±28.5 ⁺
P value	NS	<0.01	NS	<0.01

HDL: high density lipoprotein; E=estrogen group; E+A=estrogen+androgen group; LDL: low density lipoprotein; NS=no significance. Data are presented as mean ±standard deviation. * p<0.05, ⁺ p<0.01

Table 6. Adverse effects during treatment

Adverse effect	Estrogen only (n=60)	Estrogen + androgen (n=60)	Odds ratio	P between groups
Headache	20 (33%)	9 (15%)	2.3	0.075
Hot flush	12 (20%)	6 (10%)	1.9	0.125
Edema	15 (25%)	14 (27%)	1.1	0.855
Breast pain	18 (30%)	21 (35%)	0.8	0.467

choles-
terol triglyceride 가
cholesterol rogen , (가)
가 estrogen-and-
cholesterol (가)
6 (Table 6).
cholesterol
triglyceride 6 ,
24 , 12
Estrogen 가

testosterone 가 가
 가 가 가
 estrogen-androgen .²¹
 Estrogen
 가가 가
 가 30% 70%
 , androgen androgen
 가 .¹³
 estrogen-androgen ,
 estrogen estrogen-androgen
 가가 ,
 가 estrogen
 , nandrolone stanozolol 0.625 mg estrogen 1.25 mg methyltesto-
 ,
 ,^{17,18} sterone estrogen 가
 estrogen androgen 가
 cholesterol 가 cho-^{17,19} estro-
 lesterol cholesterol gen androgen 가
 estrogen androgen 가
 estrone sulfate equilin sulfate가
 estrogen estrogen
¹⁹
 Estrogen-androgen Gonen ²²
 cholesterol 가
 cholesterol, triglyceride Myers ²³
 cholesterol estrogen 5 mg methyltesto-
 가 . sterone 1.25 mg
 progestin estrogen 가
 cholesterol ²⁰
 androgen progestin methyltestosterone (50~500 mg/
 estrogen estrogen day)
 estrogen-androgen triglyceride
 가 , triglyceride methltestosterone
 가
 cholesterol estrogen
 cholesterol triglyceride androgen

estrogen-
estrogen androgen
가

1. Adashi EY. The climacteric ovary as a functional gonadotropin-driven androgen-producing gland. *Fertil Steril* 1994; 62: 20-7.
2. Notelovitz M. Osteoporosis: Screening, prevention, and management. *Fertil Steril* 1993; 59: 707-27.
3. Adami S, Suppi R, Bertoldo F, et al. Transdermal estradiol in the treatment of postmenopausal bone loss. *Bone Miner* 1987; 7: 79-86.
4. Lufkin EG, Wahner HW, O'Fallon WM, et al. Treatment of postmenopausal osteoporosis with transdermal estrogen. *Ann Intern Med* 1994; 117: 1-9.
5. Quigley MET, Martin PL, Burnier AM, Brooks P. Estrogen therapy arrests bone loss in elderly women. *Am J Obstet Gynecol* 1987; 156: 1516-23.
6. Weiss NS, Ure CL, Ballard JH, Williams AR, Daling JR. Decreased risk of fractures of the hip and lower forearm with postmenopausal use of estrogen. *N Engl J Med* 1980; 303: 1995-8.
7. Harris ST, Genant HK, Baylink DJ, et al. The effects of estrone (Ogen) on spinal bone density of postmenopausal women. *Arch Intern Med* 1991; 151: 1980-4.
8. Davidson BJ, Ross RK, Paganini-Hill A, Hammond GD, Siiteri PK, Judd HL. Total and free estrogens and androgens in postmenopausal women with hip fractures. *J Clin Endocrinol Metab* 1982; 54: 115-20.
9. Greene JG, Cooke DJ. Life stress and symptoms at the climacterium. *Br J Psychiatry* 1980; 136: 486-91.
10. Kupperman HS, Wetchler BB, Blatt MHG. Contemporary therapy of the menopausal syndrome. *JAMA* 1959; 171: 1627-37.
11. Burger HG, Hailes J, Menelaus M, Nelson J, Hudson B, Balazs N. The management of persistent menopausal symptoms with oestradiol-testosterone implants: Clinical, lipid and hormonal results. *Maturitas* 1984; 6: 351-8.
12. Walsh BW, Schiff I, Rosner B, Greenberg L, Ravnikar V, Sacks FM. Effects of postmenopausal estrogen replacement on the concentrations and metabolism of plasma lipoproteins. *N Engl J Med* 1991; 325: 1196-204.
13. Sarrel PM. Ovarian hormones and the circulation. *Maturitas* 1990; 590: 287-98.
14. Sherwin BB, Gelfand MM. Transactions of the 40th annual meeting of the society of Obstetricians and Gynaecologists of Canada: Differential symptom response to parenteral estrogen and/or androgen administration in the surgical menopause. *Am J Obstet Gynecol* 1985; 151: 153-60.
15. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499-502.
16. Kuritz SJ, Landis JR, Koch GG. A general overview of Mantel-Haenszel methods: Applications and recent developments. *Annu Rev Public Health* 1988; 9: 123-60.
17. Chesnut CH III, Ivey JL, Gruber HE, et al. Stanozolol in postmenopausal osteoporosis: therapeutic efficacy and possible mechanisms of action. *Metabolism* 1983; 32: 571-80.
18. Erdtsieck RJ, Pols HAP, van Kuijk C, et al. Course of bone mass during and after hormone replacement therapy with and without addition of nandrolone decanoate. *J Bone Miner Res* 1994; 9: 227-83.
19. Hickock LR, Toomey C, Speroff L. A comparison of esterified estrogens with and without methyltestosterone: Effects on endometrial histology and serum lipoproteins in postmenopausal women. *Obstet Gynecol* 1993; 82: 919-24.
20. Miller VT, Muesing RA, LaRosa JC, Story DB, Philips EA, Stillman RJ. Effects of conjugated equ-

- ine estrogen with and without three different progestogens on lipoproteins, high-density lipoprotein subfractions, and apolipoprotein A-I. *Obstet Gynecol* 1991; 77: 235-40.
21. Johansson BW, Kaij L, Kullander S, Lenner H-C, Svanberg L, Astedt B. On some late effects of bilateral oophorectomy in the age range 15~30 years. *Acta Obstet Gynecol Scand* 1975; 54: 449-61.
22. Gonen R, Sharf M, Lavie P. The association between mid-sleep waking episodes and hot flushes in post-menopausal women. *J Psychosom Obstet Gynecol* 1986; 5: 113-7.
23. Myers LS, Dixen J, Morrissette D, Carmichael M, Davidson JM. Effects of estrogen, androgen, and progestin on sexual psychophysiology and behavior in postmenopausal women. *J Clin Endocrinol Metab* 1990; 70: 1124-31.
-