

1) 가 .

2) 가 15% .

3) 가 .

4) 가 .

5) 가 .

6) cytochrome P450 isoenzyme CYP3A4 (bioavailability) 가 .

7) 가 .

8) 가 .

9) 가 .

1. 약물의 제거 및 반감기(Clearance and Half-Life)

18%, 33%, 가 36%, 가 48% 가 ³⁾ (volume of distribution) (clearance)

2. 흡수

(gastric acid) (gastric emptying)

⁴⁾

⁵⁾

(portal circulation)

3. 분포

(lean body mass)

4. 단백질 결합

1 - acid glycoprotein (AAG), lipoprotein 3가

⁹⁾

AAG

lipoprotein corticosteroid binding globulin sex hormonebinding globulin transport protein

⁷⁾¹⁰⁾

estrogen progesterone withdrawal 가 .²⁶⁾ volume of distribution 가 .
 isoenzyme 2C1 diazepam, estrogen progesterone CYP3A4
 propranolol, citalopram, TCA가 . gen progesterone CYP3A4
 diazepam (total and un- bound clearance) 가 .²⁷⁾ CYP1A2 carbamazepine (CYP1A2) 가
 mephenytoin, mephobarbital, piroxicam lithium 30~50% 가
 가 가 .²⁵⁾ CYP1A2 CYP3A4 lithium 가
 serotonin norepinephrine 가 .
 (upregulate) monoamine oxidase activity lithium 가
 .²⁸⁾ dopamine antipsychotics lithium 50%
 .²⁹⁾ TCA
 . CYP1A2 CYP3A4 가 .
 가 8 TCA 1.3~2.0
 CYP1A2 cloza- pine, fluvoxamine, caffeine 1.6 가 가 .³³⁾
 SSRI SNRI 가 .

7. 임신과 산욕기(Pregnancy and Postpartum)

(total body vo- lume), , 가
 trimester car- bamazepine valproic acid (neural tube defect) . Lithium
 Ebstein's anomaly가 가
 lithium 가 , trimester lithium, carbamazepine, valproic acid 가
 가 (volume of distribution) 가 .³⁰⁾ vo-

8. 생리주기(Menstrual Cycle)

estrogen progesterone (premenstrual syndrome) PMDD
 60% estrogen 가
 3~4 .³⁴⁾
 estradiol 가 se- rotonin 가 .³⁵⁾
 sertraline SSRI fluoxetine, citalopram, .²⁸⁾

9. 경구용 피임제

estrogen progesterone isoenzyme

Psychotropics Metabolism : Gender - Related Issues

가
 CYP3A4
 가 . St John's wort
 36)
 cimetidine
 CYP3A4 . carbamazepine, topiramate
 CYP3A4
 topiramate ethynyl estradiol 가
 36)
 Valproate sodium, gabapentin, lamotrigine, vigabatrin

가 36)
 분 문

가
 가
 가
 가

중심 단어 : (gender) (psychotropic metabolism).

참고문헌

1) Council on Ethical and Judicial Affairs of the American Medical Association. Gender disparities in clinical decision making. *JA-MA* 1991;26:562-559.
 2) Toran-Allerand CD. On the genesis of sexual differentiation of the general nervous system: Morphogenetic consequences of steroidal exposure and possible role of alpha-fetoprotein. *Prog Brain Res* 1984;61:63c-98.
 3) Greenblatt DJ, Sellars EM, Shader RI. Drug therapy: drug disposition in old age. *N Engl J Med* 1982;306(18):1081-1088.

4) Datz FL, Christian PE, Moore J. Gender differences in gastric emptying. *Necl Med* 1987;28:1204-1207.
 5) Kando JC, Yonkers KA, Cole JO. Gender as a risk factor for adverse events to medications. *Drugs* 1995;50:1-6.
 6) Kolars JC, Awni WM, Merion RM, Watking PB. First-pass metabolism of cyclosporin by the gut. *Lancet* 1991;338:1488-1490.
 7) Harris RZ, Benet LZ, Schwartz JB. Gender effects in pharmacokinetics and pharmacodynamics. *Drugs* 1995;50:222-239.
 8) Kashuba AD, Nafziger AN. Physiological changes during the menstrual cycle and their effects on the pharmacokinetics and pharmacodynamics of drugs. *Clin Pharmacokinet* 1998;34:203-218.
 9) Verbeeck RK, Carkinal JA, Wallace SM. Effect of age and sex on the plasma binding of acidic and basic drugs. *Eur J Clin Pharmacol* 1984;27:91-97.
 10) Wilson K. Sex-related differences in drug disposition in man. *Clin Pharmacokinet* 1984;9:189-202.
 11) Rowland M, Tozer TN. *Clinical Pharmacokinetics*. Philadelphia: Lea & Febiger;1989.
 12) Yukawa E, Mine H, Higuchi S, Aoyama T. Digoxin population pharmacokinetics from routine clinical data: role of patient characteristics for estimating dosing regimens. *J pharm Pharmacol* 1992;44:761-765.
 13) Richelson E. Pharmacokinetic interactions of antidepressants. *J Clin Psychiatry* 1998;59(suppl 10):22-26.
 14) Waxman DJ. Interactions of hepatic cytochrome P-450 with steroid hormones: Regioselectivity and stereospecificity of steroid metabolism hormonal regulation of rat P-450 enzyme expression. *Biochem Pharmacol* 1988;37:71-84.
 15) Nemeroff CB, DeVane CL, Pollock BG. Newer antidepressants and the cytochrome P450 system. *Am J Psychiatry* 1996;153(3):311-320.
 16) Barbhuiya RH, Buch AB, Greene DS. A study of the effect of age and gender on the pharmacokinetics of nefazodone after single and multiple dose. *J Clin Psychopharmacol* 1996;16(1):19-25.
 17) Tsunone SM, Harris RZ, Mroczkowski PJ, Benet LZ. Preliminary evaluation of progestins as inducers of cytochrome P450 3A4 activity in postmenopausal women. *J Clin Pharmacol* 1998;38:1137-1143.
 18) Pollock BG, Perel JM, Altieri L, Kirshner M, Fasiczka AL, Houck PR, et al. Debrisoquine hydroxylation phenotyping in geriatric psychopharmacology. *Psychopharmacol Bull* 1992;28(2):163-168.
 19) Lambert GH, Kotake AN, Schoeller D. The CO2 breath tests as monitors of the cytochrome P450 dependent mixed function oxygenase system. In: *Developmental Pharmacology*, MacLeod SM, Okey AB, Spielberg SP editions. New York: A.R.Liss;1996. p.119-145.
 20) Bruguerolle B, Toumi M, Faraj F, Vervloet D, Razzouk H. Influence of the menstrual cycle on theophylline pharmacokinetics in asthmatics. *Eur J Clin Pharmacol* 1990;39(1):59-61.
 21) Lane JD, Steege JF, Rupp SL, Kuhn CM. Menstrual cycle effects on caffeine in the human female. *Eur J Clin Pharmacol* 1992;43(5):543-546.
 22) Pollock BG, Wylie M, Stack JA, Sorisio DA, Thompson DS, Kirshner MA, et al. Inhibition of caffeine metabolism by estrogen replacement therapy in postmenopausal women. *J Clin Pharmacol* 1999;39(9):936-940.
 23) Hartter S, Wetzel H, Hammes E, Hiemke C. Inhibition of antidepressant demethylation and hydroxylation by fluvoxamine in depressed patients. *Psychopharmacology (Berl)* 1993;110(3):302-308.
 24) Laine K, Palovaara S, Tapanainen P, Manninen P. Plasma tacrine concentrations are significantly increased by concomitant hormone replacement therapy. *Clin Pharmacol Ther* 1999;66(6):602-608.

- 25) Llerena A, Cobaleda J, Martinez C, Benitez J. *Interethnic differences in drug metabolism: influence of genetic and environmental factors on debrisoquine hydroxylation phenotype. Eur J Drug Metab Pharmacokinet* 1996;21 (2):129-138.
- 26) Tamminga WJ, Wemer J, Oosterhuis B, Weiling J, Willfert B, de Leij LF, et al. *CYP2D6 and CYP2C19 activity in a large population of Dutch healthy volunteers: indications for oral contraceptive-related gender differences. Eur J Clin Pharmacol* 1999;55 (3):177-184.
- 27) Greenblatt DJ, Allen MD, Harmatz JS, Shader RI. *Diazepam disposition determinants. Clin Pharmacol Ther* 1980;27:301-312.
- 28) Hallbeich U, Smoller JW. *Intermittent luteal phase sertraline treatment of dysphoric premenstrual syndrome. J Clin Psychiatry* 1997;58 (9):399-402.
- 29) Turrone P, Seeman MV, Silvestri S. *Estrogen receptor activation and tardive dyskinesia. Can J Psychiatry* 1998;38:1137-1143.
- 30) Stowe ZN, Strader JR Jr, Nemeroff CB. *Psychopharmacology during pregnancy and lactation. In: Schatzberg AF, Nemeroff CB, editors. American Psychiatric Press Textbook of Psychopharmacology, Washington, D.C.: American Psychiatric Press; 1998. p.980.*
- 31) Aldridge A, Bailey J, Neims AH. *The disposition of caffeine during and after pregnancy. Semin Perinatal* 1981;5 (4):310-314.
- 32) Weinstein MR. *Lithium treatment of women during pregnancy and in the post-delivery period. In: Handbook of Lithium therapy, Johnson FN, editors. Baltimore: University Park*
- 33) Wisner KL, Perel JM, Wheeler SB. *Tricyclic dose requirements across pregnancy. Am J Psychiatry* 1993;150 (10):1541-1542, Press;1980.
- 34) Demers LM. *Premenstrual, postpartum and menopausal mood disorders. Baltimore: Urban and Schwarzenberg;1989.*
- 35) Hindberg I, Naesh O. *Serotonin concentrations in plasma and variations during the menstrual cycle. Clin Chem* 1992;38 (10):2087-2089.
- 36) Shader RI, Oesterheld JR. *Contraceptive effectiveness: cytochromes and induction. J Clin Psychopharmacol* 2000;33:229-231.