

내외과계 환자의 정신과 약물치료에서 약물-약물 상호작용*

- 고려대학교 부속병원의 자문조정 경험을 통하여 -

이 민 수**† · 이 현 정**

Drug-drug Interactions between Psychotropic Agents and Other Drugs in Physically Ill Patients*

- Experience of Consultation-liason in Korea University Hospital -

Min Soo Lee, M.D., Ph.D.,**† Heon-Jeong Lee, M.D.**

ABSTRACT

Polypharmacotherapy, both psychotropic and nonpsychotropic, is widespread in various situations including psychiatric hospitals and general hospitals. As the clinical practice of using more than one drug at a time increase, the clinician is faced with ever-increasing number of potential drug interactions. Although many interactions have little clinical significances, some may interfere with treatment or even be life-threatening. The objective of this review is evaluation for drug-drug interactions often encountered in psychiatric consultation. Drug interactions can be grouped into two principal subdivisions : pharmacokinetic and pharmacodynamic. These subgroups serve to focus attention on possible sites of interaction as a drug moves from the site of administration and absorption to its site of action. Pharmacokinetic processes are those that include transport to and from the receptor site and consist of absorption, distribution on body tissue, plasma protein binding, metabolism, and excretion. Pharmacodynamic interactions occur at biologically active sites. In psychiatric consultation, these two subdivisions of drug interactions between psychotropic drugs and other drugs are likely to happen. We gathered informations of the drugs used in physically ill patients who are consulted to psychiatric department in Korea University Hospital. And we reviewed the related literatures about the drug-drug interactions between psychotropic drugs and other drugs.

KEY WORDS : Drug-drug interaction · Psychotropic agents · Cytochrome P450(CYP) · Physically ill patients.

서 론

가 . , (pharmacodynamic interact -
가 . , ion) (pharmacokinetic interaction)
30 80%가
(Rosholm 1994).

1998 6 20

(Ja - nicak 1997).

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† : , 136 - 705 5가 126 - 1
) (02) 920 - 5354,) (02) 923 - 3507

가

가

(agonism)

(antagonism)

가

MOA 가

MOA 가

가

가

TCA가

가가

가

(selective serotonin reuptake inhibitor : SSRI)

가

(1)

(Pharmacodyna-

mic interactions and neural wiring)

가

가

약물-약물 상호작용의 기전

1. 약물-약물 상호작용의 유형

3가

MOA

MOA

가

가

가

SSRI

pindolol

가

2 4

somatodentritic 5-HT_{1A}

가

(au-

1) 약력학적 상호작용(Pharmacodynamic interaction)

가

(mechanism

toreceptor)

rate

5-HT

5-HT_{1A}

firing

5-HT_{1A}

of action :

MOA)

가

MOA

pindolol

(Preskorn 1997).

가

MOA

(Preskorn 1997).

가

가

(tricyclic antidepressant : TCA), (an-

tiparkinsonian medication)

(2)

(Pharmac-

(anticholinergic delirium)

odynamic interaction involving multiple organ systems)

가

가

anethidine

amitriptyline

gu-

(-blocker), 1-

가

(1-adrenergic blocker)

guanethidine

가

1)

MOA

가(potency)

1-

(peripheral re-

2)

sistance)

, 3)

MOA

가

2) 약동학적 상호작용(Pharmacokinetic interaction)

(1) P - 450(Cytochrome P - 450 enzymes : CYP)
가 CYP (isoenzyme)

CYP1A2, CYP2D6, CYP3A3/4 (Wrighton Stevens 1992).

CYP

가

가 가

stylamine resin gel chole - phe -

nothiazine TCA (insoluble complex)

가 (plasma protein binding) 가

가 warfarin chloral hydrate chloral hydrate
warfarin (bleeding time) 가 가 (Ayd FJ 1994).

(biotransf - oration) . barbiturate (enzyme inducer)
inhibitor) (enzyme inh - 가

, fluoxetine, paroxetine
P450(cytochrome P - 450 : CYP)

MAOI monoamine oxidase
sympathomimetic amine

가

. sodium bicarbonate
phenobarbital barbiturate

(induction) , (inhibition)

가

2. 약물-약물 상호작용의 실제

가

(quantitative change)

(qualitative change)

가 가

Table 1. Effects of the SSRI in inhibiting the activity of various P450 (CYP) isoenzymes

Isoenzyme	Fluoxetine	Fluvoxame	Paroxetine	Sertraline
CYP1A2	-/+	+++	-/+	-/+
CYP2C9/10	?	?	?	+
CYP2C19	++	++	?	+
CYP2D6	+++	+	+++	+
CYP3A3/4	++	++	-/+	-/+

? : unknown - : no effect + : <50% change
++ : 50 - 150% change +++ : >150% change
SOURCE : Mitchell PB(1997)

MOA

Table 2. Common examples of substrate of cytochrome P450(CYP) isoenzymes

CYP1A2	CYP2C9/10	CYP2C19	CYP2D6		CYP3A3/4	
Phenacetin	S-Warfarin	Diazepam	Fluoxetine	Metoprolol	Imipramine	Cyclosporin
Caffeine	Phenytoin	Mephenitoin	Paroxetine	Timolol	Alprazolam	Lidocaine
Theophylline	Tolbutamide	Omeprazole	Sertraline	Propafenone	Triazolam	Acetaminophen
R-Warfarin	Diclofenac	Clomipramine	Venlafaxine	Codeine	Midazolam	Nefazodone
Clozapine	Mefenamic acid	Imipramine	Desipramine	Debrisoquine	Clozapine	Quinide
Amitriptyline	Piroxicam	Amitriptyline	Nortriptyline	Dextromethorphan	Terfenadine	Dapsone
Imipramine	Naproxen	Propranolol	Amitriptyline	Sparteine	Astemizole	Lavastatin
Clomipramine	Ibuprofen	Hexobarbital	Mianserin		Cisapride	Tamoxifen
Antipyrine	Antipyrine	Citalopram	Clozapine		Diltiazem	Vinblastine
Tacrine		Mephobarbital	Risperidone		Verapamil	
Propranolol			Haloperidol		Nifedipine	
Haloperidol			Thioridazine		Carbamazepine	
Verapamil			Propranolol		Erythromycin	

SOURCE : Mitchell PB(1997)

MOA가 , MOA가 , MOA가 () clozapine bupropion () MOA , TCA sodium channel , TCA 6% (major depressive disorder), (depressive disorder due to general medical condition) (depressive disorder)가 20 29.1% (delirium due to general medical condition) 12 17.4%, (alcohol abuse or dependence) 8 11.6%, 8 (11.6%) (somatoform disorder)가 (anxiety disorder), (dementia)

정신과 자문영역에서 약물사용 1998 2 1 4 30 3 69 51.78 ± 15.87 M : F = 39 : 30 15 , 8 , 7 , 6 , 5

1. 정신과에 자문의뢰된 환자의 특성 가 가 15 가 9 , 가 8 가 가 46 가 가 60

가 , cephalosporin 가 9 , quinolone 가 5 , aminoglycoside penicillin 가 4 , nizatidine(Axid[®]) 11 , famotidine(Gaster[®]) 10 , ranitidine(Curan[®]) 2 , roxatidine(Roxan[®]) 2 , cimetidine(Cimet[®]) 2 benzodiazepine 26 benzodiazepine clorazepate(Tranxene[®])가 12 , lorazepam(Ativan[®]) 6 , etizolam(Depas[®]) 4 , diazepam(Valium[®]) 2 , flurazepam(Dalmadorm[®]) 2 (NSAID) 17 , aspirin 5 , acetaminophen(Tyrenol[®]), mefenamic acid(Pontal), etodolac(Lodine[®]) 3 calcium channel blocker가 11 amlodipine(Norvasc[®]) 7 , felodipine(Munobal[®]) 2 , diltiazem(Herben), nicardipine(Perdipine[®]) 1 angiotensin - converting enzyme inhibitor(ACE inhibitor)가 5 cilazapril(Inhibace[®])가 3 , captopril(Capotene[®]) 2 12 가 Mylanta[®], Simeco[®], Mucagel[®] gel , 10 가 , 6 insulin sulfonylurea(Diamicron[®]) 가 3 , acarbose(Glucobay[®]) 가 1 . 10 , amitriptyline 5 , sertraline 2 , paroxetine 2 , moclobemide가 1 . 9 가 pr ednisone(5), dexamethasone(2) , 9 가 , fu rosemide(Lasix[®])가 7 , spiro lactone(Aldactone[®])가 2 . 6 가 omeprazole(OMP[®]) , ambroxol(Mucopect[®]) 9 , bromhexine(Bisolvon[®]) 2 , rebamipide(Mucosta[®])(8), sucralfate(Ulcermin[®])(2) . 가 theophylline 2 (3).

3. 정신과에 자문 의뢰된 환자에서 처방된 정신과 약물

가 39 . SSRI가 Sertraline 18 , paroxetine 10 , fluoxetine 1 . TCA amitriptyline 11 , dothiepin 3 , imipramine 1 , MAOI moclobemide 4 . 33 Lorazepam 26 , zopiclone 7 , diazepam 3 , alprazolam 2 , etizolam, clorazepate가 18 가 haloperidol 11 , perphenazine 7 .

Table 3. The drugs which were used in patients consulted to psychiatric department before consultation(Korea Univ. Hospital)

Rank	Class of drug	N(%)	Drugs	N(%)
1	Antimicrobials	32 (46.4%)	Cephalosporin	9(13.0%)
			Quinolone	5(7.2%)
			Aminoglycoside	4(5.8%)
			Penicillin	4(5.8%)
			Antituberculosis	2(2.9%)
			Others	8(11.6%)
2	H2 blockers	28 (40.6%)	Nizatidine(Axid [®])	11(15.9%)
			Famotidine(Gaster [®])	10(14.5%)
			Ranitidine(Curan [®])	2(2.9%)
			Roxatidine(Roxan [®])	2(2.9%)
			Cimetidine(Cimet [®])	2(2.9%)
3	Benzodiazepines	26 (37.7%)	Clorazepate(Tranxene [®])	12(17.4%)
			Lorazepam(Ativan [®])	6(8.7%)
			Etizolam(Depas [®])	4(5.8%)
			Diazepam(Valium [®])	2(2.9%)
			Flurazepam(Dalmadorm [®])	2(2.9%)
4	NSAID	17 (24.6%)	Aspirin	5(7.2%)
			Acetaminophen	3(4.3%)
			Pontal	3(4.3%)
			Lodine	3(4.3%)
5	Antihypertensive	16 (23.2%)	Amlodipine(Norvasc [®])	7(10.1%)
			Ca channel blocker Felodipine(Munobal [®])	2(2.9%)
			Diltiazem(Herben [®])	1(1.45%)
			Nicardipine(Perdipine [®])	1(1.45%)
			ACE inhibitor Cilazapril(Inhibace [®])	3(4.3%)
Captopril(Capotene [®])	2(2.9%)			
6	Antidepressant	10 (14.5%)	TCA Amitriptyline	5(7.2%)
			MAOI Moclobemide	1(1.45%)
			SSRI Paroxetine	2(2.9%)
			Sertraline	2(2.9%)

Table 4. The psychotropic medications which were prescribed in psychiatric consultation (Korea Univ. Hospital)

Rank	Class of drug	N(%)	Drugs	N(%)
1	Antidepressant	39 (56.5%)	Sertraline	18(26.1%)
			SSRI Paroxetine	10(14.5%)
			Fluoxetine	1(1.45%)
			TCA Amitriptyline	11(15.9%)
			Dothiepin	3(4.3%)
			Imipramine	1(1.45%)
			MAOI Moclobemide	4(5.8%)
2	Anxiolytics and hypnotics	33 (47.8%)	Lorazepam(Ativan®)	26(37.7%)
			Zopiclone(Imovane®)	7(10.1%)
			Diazepam(Valium®)	3(4.3%)
			Alprazolam(Xanax®)	2(2.9%)
			Etizolam(Depas®)	1(1.45%)
			Clorazepate(Tranxene®)	1(1.45%)
3	Antipsychotics	18 (26.1%)	Haloperidol(Haldol®)	11(15.9%)
			Perphenazine(Trilafon®)	7(10.1%)
4	Cerebrotonics	6 (8.7%)	Nicetile	3(4.3%)
			Hydergine	2(2.9%)
			Elen	1(1.45%)

acetylcarnitine(Nicetile®) 3, ergoloid mesylates(Hy-dergine®) 2, indeloxazine(Elen®) 1 (4).

정신과 약물과 타과 약물간의 약물-약물 상호작용

1. 항우울제(Antidepressants)

가

- 1) (tricyclic antidepressants : TCA)
- 2) (selective serotonin reuptake inhibitor : SSRI)
- 3) (moclobemide, nefazodone, venlafaxine)

가 (monoamine oxidase inhibitor : MAOI)가

MAOI (reversible inhibitor of monoamine oxidase A : RIMA) moclobemide

1) 삼환계 항우울제(Tricyclic Antidepressants : TCA)

TCA 가 (alcohol, barbiturate) 가

TCA aspirin, chloramphenicol, acetazolamide 가

(1) (anticoagulants)

Coumarin warfarin dicumarol vitamin K 가 warfarin dicumarol

가 Koch - Weser(1973) amitriptyline warfarin Pond (1975) TCA가 dicumarol 가 TCA

(2) (opioid analgesics)

Lee Spencer(1980) clomipramine TCA가 morphine pentazocine Taiwo (1985) morphine 가 amitriptyline, desipramine, sertraline

desipramine methadone morphine opioid 가 TCA opioid (Goldstein 1982 ; Liu Wang 1985).

(3) (anesthesia)

imipramine halothane pancuronium 가 (Edward tachyarrhythmia)

1979). imipramine pancuronium 가 가 digoxin (Dec 1984 ; Ra-
thane 가 halo - uch Jenike 1984).
(TCA) halot - digoxin
(7) Estrogen
hane pancuronium imipramine estradiol
(d - tubocurarine) , TCA (tremor), (hypotention), (drowsiness)
halothane enflurane , TCA (Khurana 1972).
estrogen
(4) (antihypertensives) imipramine 가가
(Abernethy 1984)
Leishman (1963) 3 imipramine gua -
nethidine (8) 2 - (Histamine2 - blocker : H2 -
TCA가 norepinephrine guanethidine)
Cimetidine TCA , TCA
hidine (benthanidine, debrisoquin) guanet - 가 imipramine ci -
TCA Briant metidine cimetidine , imipr -
(1973) clonidine TCA amine 가
(Miller Macklin 1983). imipramine
nsten (1984) clonidine 0.4mg/day cimetidine 가 imipramine
imipramine 50mg 2 , nortriptyline cimetidine
. Calcium channel blocker verapa - , imipramine cimetidine
mil diltiazem CYP3A4 imipramine 가 가
, TCA 가 (Henauer Hollister 1984). TCA H2
ann 1992), verapamil, diltiazem cimetidine ranitidine, famotidine,
TCA TCA nizatidine TCA
calcium channel blocker nifedipine
(Fadden 1992 ; Hullet
1988).
(5) (antimicrobials) Type (NIDDM) sulfonylurea
TCA 가 (True
Bebchuk Stewart(1991) rifampin, isoniazid, pyrazi - 1987). Type (IDDM) amitri -
namide, pyridoxine nortriptyline ptylene (Sherman Bor -
nortriptyline nemann 1988).
가 imipramine, nortriptyline TCA
. rifampin sulfonylurea sulf -
nortriptyline fluconaz - onylurea
ole , nortriptyline 가
(Gannon 1992). fluconazole, ketoconazole,
itraconazole CYP3A4 2) 세로토닌 재흡수 차단제(Selective Serotonin Reuptake
rifampin TCA Inhibitors : SSRI)
TCA SSRI CYP
가 . SSRI
(6) Digoxin CYP 가 . 1 SSRI
Digoxin trazodone digoxin CYP . 2

가 CYP CYP SSRI 가

(1) (anticoagulants) SSRI warfarin 가 가 SSRI가 warfarin 가 warfarin 가 warfarin (racemic mixture) S - enantiomer(S) R - enantiomer(R) 가 가 S , R S CYP2C9 R , R cytochrome CYP2C9 R CYP1A2/ 3A4 hydroxylation SSRI CYP1A2 R 가 가 , 가 S 가 가 (Harvey Preskorn 1996). , SSRI fluoxetine 가 가 (Aranth Lindberg 1992). SSRI warfarin prothrombin time

(2) (-adrenergic blocking agents) propranolol lorazepam fluoxetine 가 (complete heart block) 가 (Drake Gordon 1994). SSRI가 sotalol , propranolol, met - oprolol

(3) Calcium channel blocker Verapamil, nifedipine calcium channel blocker fl - uoxetine (edema), (th - robbing headache), (nausea), (flushing) (Sternbach 1991). fluoxetine calcium channel blocker 가 fluoxetine calcium channel blocker calcium channel blocker

(4) Digoxin SSRI digoxin (Ba - nnister 1989 ; Forster 1991).

(5) (opioid analgeics) Fluoxetine opioid fluoxetine morphine, codeine, fentanyl (catalepsy) opioid (antinociceptive action) (Larson Takemori 1977). Paroxetine dextromethorphan (serotonin syndrome) (Skop 1994). 가 가 SSRI (dextro - methophan, meperidine, pentazocine)

(6) Theophylline Fluvoxamine theophylline theo - phylline 가 (Diot 1991). fluv - oxamine CYP1A2 theo - phylline theophylline theophylline theophylline fluvox - amine , CYP1A2 SSRI sertraline, fluoxetine, paroxetine 가

3) 그밖의 새로운 항우울제

(1) Moclobemide Moclobemide 가 MAO - A 가 MAOI Moclobemide MAO 가 tyramine Moclobemide SSRI TCA가 (Ebert 1995)가 , clomip - ramine moclobemide (Gillman 1997)가 . Moclobemide CYP2D6

(2).
(2) Nefazodone
Nefazodone 5-HT₂ 가 .
. Nefazodone CYP3A4 . lo - (therapeutic index)가
razepam, cimetidine, warfarin . 5
, CYP3A4 alprazolam, triazo -
lam 가
nefazodone alprazolam (1) (antihypertensives)
alprazolam (Stoudemire Fo - 가
gel 1995 ; Nemeroff 1996). CYP3A4 . 가 propranolol .
terfenadine astemizole propranolol phenothiazine
(Ereshefsky 1991). chl -
binson 1996)(2). (Ro - opromazine thioridazine haloperidol
(Greendyke Gulya 1988).
Thioridazine chlorpromazine 가
(3) Venlafaxine 가 .
Venlafaxine 가 가
. ACE
. Venlafaxine 가
CYP2D6 thioridazine, quinidine .
, venlafaxine 가 가 . ve - (2) (antacids)
nlafaxine CYP2D6 . alu -
가 . cimet - minum and magnesium hydroxide chlorpromazine
idine venlafaxine , chlorpromazine 가
(Troy 1998). desmethyl - venlafaxine (Fann 1973), haldoperidol

Table 5. Drug interactions with Antipsychotics

Class of drug	Example	Clinical effect of interaction
Absorbent	Antacids, activated charcoal, cholestylamine, kaolin-pectin	Oral absorption decreased significantly when used simulataneously ; give at least 1h before or 2hr after the neuroleptic
Antihistamine	Terfenadine, astemizole	Potentiation of QT prolongation and torsades de pointes. Caution with mesoridazine, thioridazine, and pimozide
Antihypertensive	Methyldopa, enalapril	Additive hypotensive effect
-blocker	Guanethidine	Reversal of antihypertensive effect with chlorpromazine, haloperidol and thioridazine
Cimetidine	Propranolol, pindolol	Increased serum level of both neuroleptic and b-blocker
Disulfiram		Inhibited metabolism of clozapine and thiothixene, with resultant increase in plasma level and adverse effects
Rifampin		Decreased plasma level of perphenazine and an increase in its metabolite
Smoking		Decreased metabolism and increased plasma level of clozapine
Sympathomimetic	Epinephrine, norepinephrine	Decreased haloperidol plasma level due to induction of metabolism
		Decreased plasma level of neuroleptic due to induction of metabolism
		Paradoxical fall in blood pressure; benefits may outweigh risk in anaphylaxis

SOURCE : Benzchlibnyk-Butler & Jeffries(1996), Bernstein(1995)

가 (Goldstein 1982).
 gel
 가 gel 2 가
 (3) (antiarrhythmics)
 , Q - T T - 가
 (Risch 1981). Thioridazine
 가 - 가 . Chlorprom -
 azine , Q - T
 quinidine (quinidine, procainamide)
 phenothiazine
 가 (Ban St. Jean
 1964).
 (4) Cimetidine
 Chlorpromazine cimetidine chlo -
 ropromazine 가 (Howe 1983). Cloz -
 apine cimetidine , H2
 ranitidine
 cimetidine chlorpromazine
 가 , chlorpromazine 가
 chlorpromazine 가 ci -
 metidine clozapine
 가 (Szymanski 1991).
 (5) Alcohol
 Alcohol CYP2E
 가
 가
 (Lieber 1988). alcohol
 가 alcohol
 (Matilla 1990).
 Lutz(1976) , (akathisia)
 (acute dystonia)가
 . AI -
 al -
 cohol 가 가 가
 cohol 가 가 가

가 가
 (6) Disulfiram
 Hansen Larsen(1982) disulfiram perphenazine
 perphenazine 가
 sulpoxide 가 가 가 가
 3. Lithium
 Lithium 2 4
 . lithium
 . li -
 thium
 lithium
 lithium
 lithium
 가
 . Lithium
 6
 (1) Aminophylline, theophylline
 Aminophylline theophylline lithium 가
 . lithium toxicity
 . Perry (1984) theophylline lithium
 , theophylline 가 가
 lithium 가
 가 가 가 가 ,
 ,
 (2) (antimicrobials)
 tetracycline , spectinomycin, metronidazole
 lithium 가 가 lithium
 (Ayd 1978 ; Jefferson 1987).
 lithium
 , spectinomycin, tetracycline, metronidazole
 li -
 thium
 (3) (antihypertensives)
 Propranolol
 , lithium (tremor)
 lithium propranolol lithium
 가 가 , (Becker
 1989). Clonidine lithium clonidine
 가 가 가 (Goodnick 1984). ACE

Table 6. Drug interactions with lithium

Class of drug	Example	Clinical effect of interaction
Anesthetics	Ketamine	Increased lithium toxicity due to sodium depletion
Angiotension-converting enzyme inhibitor	Captopril, enalapril, lisinopril	Increased lithium toxicity due to sodium depletion
Antibiotics	Ampicillin, tetracycline, spectinomycin	Increased lithium toxicity due to decreased renal clearance of lithium
K ⁺ sparing diuretics	Amiloride, spironolactone, triamterene	Increased lithium toxicity due to decreased renal clearance of lithium
Diuretics	Thiazide, furosemide	Increased lithium toxicity due to increased Na, K excretion and lithium reabsorption
Calcium channel blocker	Verapamil, diltiazem	Increased neurotoxicity of both drugs, increased cardiotoxicity with verapamil
Caffeine		Increased renal excretion of lithium
Iodide salt	Calcium iodide	May act synergistically to produce hypothyroidism
L-tryptophan		Increased plasma lithium level
NSAID	Ibuprofen, ketorolac, indomethacin, mefenamic acid, naproxen (no interaction with ASA)	Increased lithium toxicity due to decreased renal clearance of lithium
Urinary Alkalizer	Potassium citrate, sodium bicarbonate	Enhanced renal lithium clearance and reduced plasma level
Theophylline	Aminophylline, oxtriphylline, theophylline	Enhanced renal lithium clearance and reduced plasma level

SOURCE : Benzchlibnyk-Butler & Jeffries (1996), Bernstein (1995)

enalapril lithium
 lithium (Douste - Blazy
 1986). ACE
 . DasGupta (1992)
 (cross over study) , enalapril lithium
 lithium lit -
 hium 가 .
 (4) (anti - inflammatory drugs)
 Lithium prostaglandin
 lithium , verapamil (blood -
 lithium 가 30 60% 가 가 (Ragheb brain barrier) verapamil delirium
 1990). NSAID가 (renal tubule) pros -
 taglandin lithium
 가 .
 NSAID lithium
 가 (Johnson 1993 ; Brater 1986). lit -
 hium 가
 lithium , sulindac(Cl -
 inoril®), aspirin lithium
 가 (Ragheb 1987).
 (5) (antithyroid agents)
 Lithium
 , (thyrot -
 oxicosis) (Barclay 1994 ; Chow 1993 ;
 Jefferson Sen 1994). Lithium me -
 thimazole, carbimazole, radioactive iodine
 (Mochinaga 1994 ; Takami 1994).
 lithium thyroxine triiodothyronine
 (6) Calcium channel blockers
 Lithium verapamil, diltiazem
 가 (Wright Jarrett 1991 ; Du -
 vosky 1987 ; Binder 1991). lithium ni -
 fedipine
 , verapamil (blood -
 brain barrier) verapamil delirium
 , lithium
 가 가 (Wright 1991 ;
 Jacobson 1987). verapamil
 5 - HT₂ receptor 가 lithium . lithium
 가 , Ca
 D₂ 가 . ca -
 Calcium channel blocker verapamil
 가 , (chorea -
 thetosis) (Gudelsky 1988 ; Helmuth
 1989).
 (7) Digoxin
 Lithium digoxin
 (Winters 1977). lithium di -
 goxin 가 potassium 가 ,

(8) lithium 가 Aldosterone
 spironolactone lithium
 lithium
 (loop diuretics) furosemide가 li-
 thium 가 가 (Hurtig Dyson
 1974). (loop of He-
 nle) Na⁺ lith-
 ium lithium 가 가
 (Jefferson
 Kalin 1979 ; Saffer Coppen 1983).
 lithium , lithium
 lithium , lithium
 potassium - sparing
 lithium , lithium
 lithium
 potassium - sparing
 가 lithium
 Thiazide lithium lithium
 (Coppen 1982). Thiazide
 lithium lithium 가
 (Hurtig Dyson 1974 ; Himmelhoch 1977 ; Solo-
 mon 1980). lithium
 lithium

4. 항경련제(Anticonvulsants)

1) Carbamazepine

Carbamazepine ,
 가 carbamazepine 가
 가 가
 가
 (7).

(1) Calcium channel blocker

Eimer Carter(1987) carbamazepine diltiazem

verapamil, diltiazem calcium channel blocker
 carbamazepine
 (Ahmad 1990 ; Beattie 1988 ; Gadde
 Calabrese 1990).
 diltia-
 zem verapamil calcium channel blocker
 carbamazepine 가
 nifedipine calcium channel blocker
 (Br-
 odie MacPhee 1986). carbamazepine diltiazem,
 verapamil , 가
 calcium channel blocker nifedipine
 가
 (2) 2 - (histamine2 - blocker)
 Carbamazepine cimetidine carb-
 amazepine 가 가 (Dalton 1986).
 cimetidine carbamazepine CYP
 가 cimetidine
 ranitidine, famotidine

(3) Corticosteroid

Carbamazepine dexamethazone prednisolone
 corticosteroid (Privitera 1982 ; Olivesi
 1986). carbamazepine corticosteroid
 ca-
 rbamazepine
 corticosteroid carbamazepine

(4) (antimicrobials)

Erythromycin carbamazepine
 carbamazepine
 (Hedrick 1983 ; Zitelli 1987). erythromycin
 macrolide 가 carbamazepine
 isoniazide
 carbamazepine carbamazepine
 가 (Valsalan Co-
 oper 1982).

(5) Theophylline

Theophylline carbamazep-
 ine theophylline 가
 (Rosenberry 1983). carbamaz-

Table 7. Drug interactions with carbamazepine

Class of drug	Example	Clinical effect of interaction
Antibiotics	Erythromycin, troleandomycin, clarithromycin Doxycycline (no interaction with other tetracyclines)	Increased plasma levels of carbamazepine due to reduced clearance (by 5 - 41%) Decreased serum level of doxycycline due to enhanced metabolism
Anticoagulant -blocker	Dicoumarol, warfarin Propranolol	Enhanced metabolism of anticoagulant Decreased serum level of propranolol due to enhanced metabolism
Ca ²⁺ -channel blocker	Verapamil, diltiazem (no interaction with nifedipine)	Increased plasma level of carbamazepine
Cimetidine		Transient increase in carbamazepine levels
Corticosteroid		Decreased plasma level of corticosteroid due to enhanced metabolism
Cyclosporin		Decreased plasma level of cyclosporin
Danazol		Plasma levels of carbamazepine increased by 50 - 100%
Etretinate		Therapeutic failure with etretinate due to decreased plasma level
Influenza vaccine		Decreased elimination and increased half-life of carbamazepine
Isoniazide		Increased plasma level of carbamazepine; clearance reduced by up to 45%
Muscle relaxant (non-depolarizing)	Gallamine, pancuronium	Decreased duration of action and efficacy of muscle relaxant
Propoxyphene		Increased plasma level of carbamazepine
Terfenadine		Increased free carbamazepine level due to reduced metabolism
Theophylline		Decreased theophylline level due to enzyme induction by carbamazepine ; decreased carbamazepine level by up to 50%
Thyroid Hormones		Decreased plasma level of thyroid hormone due to enzyme induction

SOURCE : Benzchlibnyk-Butler & Jeffries (1996), Bernstein (1995)

epine theophylline

theophylline

(2) Asprin

(6) Warfarin

Valproic acid가

asprin

Warfarin

carbamazepine

warfarin

valproic acid

(Goul -

가 (Hansen 1971 ; Kendall

den 1987). Valproic acid

Boivin 1981). Carbamazepine

salicylate

warfarin

valproic acid

prothrombin

(Fleitman 1980).

salicylate

valproic acid

warfarin

beta - oxidation

가

(Abbott

2) Valproic acid

1986).

Valproic acid

(3) 2 - (Histamine2 - blocker)

, 8

Cimetidine valproic acid

valproic acid

(Webster 1984).

(1)

valproic acid

aluminum

nitidine, famotidine

, 가

cimetidine

ra -

hydroxide - magnesium

val -

proic acid

가 가

(May

5. Benzodiazepines

1982).

valproic acid

가

가

가

Table 8. Drug interactions with valproate

Class of drug	Example	Clinical effect of interaction
Antibiotics	Erythromycin	Increased plasma levels of valproate due to decreased metabolism
Antacids	Aluminium-magnesium antacid	Increased plasma levels of valproate
Anticoagulant	Warfarin	Inhibition of secondary phase of platelet aggregation by valproate
Cimetidine		Decreased metabolism and increased half-life valproate
Salicylate	Acetylsalicylic acid bismuth subsalicylate	Displacement of valproate from protein binding and decreased clearance, leading to increased level of free drug, with possible toxicity

SOURCE : Benzchlibnyk-Butler & Jeffries(1996), Bernstein(1995)

1) 마취제와 신경근육차단제(Anesthetics and neuromuscular blocking agents)	(2) (antituberculosis drugs)
Diazepam gallamine , succinylcholine Idman Crawley 1970). 37 midazolam methonium pancron - ium , midazolam (Tassonyi 1984). flumazenil halothane (Murayama 1991). Diazepam diazepam succinylcholine	Isoniazide diazepam (Ochs 1983). isoniazide benzodiazepine (3) (antimycotics) Ketoconazole chlorodiazepoxide midazolam (Brown 1994 ; Olkkola 1994). ket - oconazole CYP3A4 be - nzodiazepine 가 가 가
2) 제산제 Chun (1977) clorazepate gel clorazepate desmethyldiazepam 가 24 가 benzodiazepine 가 single dose gel	6) 베타차단제(β-adrenergic blocking agents) Propranolol metoprolol diazepam demethylation 가 alprazolam hydro - xylation lorazepam, oxazepam, temazepam glucuroni - zation (Ochs 1984). 7) Digoxin Alprazolam 가 digoxin (Castillo - Ferrando 1980)가 , 가가 65 , digoxin (Gu - ven 1993). digoxin diazepam, alprazolam digoxin
3) 항염증제(Anti-inflammatory drugs)	
4) 항응고제(Anticoagulants)	
5) 항균제(Antimicrobials)	8) 히스타민2-차단제와 proton pump 억제제 Cimetidine , proton pump omeprazole CYP 2C (Andersson 1990). 가 가 가 (co - njugation) benzodiazepine , ranitidine, famotidine, nizatidine
(1) (antibiotics) Macrolide CYP3A triazolobenz - odiazepine 가 가 가 가	

가

9) Theophylline

Theophylline diazepam

가 (Henauer 1983).

theophylline benzodiazepine

(Paul 1980).

ophylline

the -

결 론

가

가

가

가

가

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