

주의력결핍 과잉행동장애와 공존질환의 약물치료

PSYCHOPHARMACOLOGY OF ADHD WITH COMORBID DISORDERS

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요 약 :

ADHD는 주로 자극제(stimulant)로 치료되며, 약 70~80%의 ADHD 환자가 공존질환을 동반한다. 공존질환은 ADHD의 진단과 치료에 영향을 미칠 수 있다. 공존질환이 있는 ADHD 환자는 약물 치료 시 주의가 필요하다. 공존질환의 종류에 따라 약물 선택과 용량 조절이 달라진다. 공존질환이 있는 ADHD 환자에게는 ADHD와 공존질환을 모두 치료할 수 있는 약물을 선택하는 것이 중요하다.

중심 단어 :

서 론

(Attention Deficit/Hyperactivity Disorder, ADHD)는 5~6세에 진단되며, 5)6) 가 3~ 가 , ADHD 5%)¹⁾, 9%²⁾ 7.6%³⁾ ADHD 가 30~50%⁴⁾ ADHD가 가 ADHD 30~60% ADHD

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ADHD 가 1. Psychostimulant Psychostimulant(stimulant) ADHD 가 가 13)14), Methylphenidate amphetamine 60 methylphenidate ADHD 75% 가 13)15), stimulant (Table 1). 1960 ADHD (placebo) stimulant 1996 Spencer ADHD (undertreat- 161 randomized controlled trial(RCT) ment) 가 4 1.300 4~30% 5% ADHD stimulant 5,899 13.6% 65~75% 17), stimulant methylphenidate(133), dextroamphetamine(22), pemoline(6) mixed amphetamine salts 3 18-20) 가 ADHD 가 12), methylphenidate dextroamphetamine ADHD , ADHD ADHD stimulant ADHD 38% stimulant st- imulant stimulant가 21), stimulant stimulant (switching) ADHD Stimulant 가 insomnia,

Table 1. Stimulants used in the treatment of ADHD

	Methylphenidate	Amphetamine	Pemoline
Short-acting agents	Ritalin, methylin	Dexedrine, dextrostat	
Intermediate-acting agents	Ritalin SR, metadate ER, methylin ER	Adderall, dexedrine spansule	
Long-acting agents	Concerta, metadate CD, ritalin LA	Adderall XR	Magnesium pemoline (cylert)

reduced appetite, stomach ache, headache, dizziness, rebound phenomenon

4% 579

ADHD 14

Multimodal Treatment Study of Children with ADHD(MTA)

85% stimulant

88 (35.9%)

122 (49.8%), 28 (11.4%)

, 7 (2.9%)

. stimulant

lant

Pemoline

가

1975

11)

13

stimulant

hepatic failure

15)24)

stimulant

stimulant

3

stimulant

가

25 - 27)

stimulant

drug holiday가

stimulant

가

drug holiday

28)

stimulant

가

(overfocused, restricted, withdrawal

phenomenon)

가

15)

stimulant

stimulant

가

stimulant

lants

short - acting stimu-

1

2

가

가

stimulant

Concerta, Metadate CD, Adderall XR

long - acting stimulants

ADHD

2. Antidepressants

30% ADHD

stimulant

stimulant

32)

stimulant

Tricyclic antidepressant(

TCA)가

. TCA

가

가

가

stimulant

28)

가

33)

ADHD

stimulant

stimulant

ADHD

stimulant

가

34)35)

TCA

1200

33

ADHD

TCA

가

28)

TCA

가

가

가

2

9

TCA

가

32) TCA

ADHD

34)

TCA

ADHD

가

28)32) TCA

29

imipramine

12 , desipramine 9 , nortriptyline 4 , amitriptyline

3 , clomipramine 1

32) 1970

imipramine 가
 noradrenergic system 45)
 secondary amine(desipramine, nortripty- ADHD
 line) bu-
²⁸⁾ imipramine 12 controlled study propion 가
 open study 10 ADHD . bupropion
 TCA 가
³²⁾ de- 가
 sipramine 5 RCT methylphenidate , ,
 sti-
 mulant 62 ADHD 가 가
 desipramine 68% ²⁸⁾
³⁶⁾ desipramine MAOI, SSRI, venlafaxine, buspirone, cholinergic
 sudden unexpected death drugs norepinephrine reuptake
 selective inhibitor atomoxetine stimulants ²⁸⁾
 TCA
 가 ³⁷⁻³⁹⁾ NIH conference
 sudden death가
 10 1~4%
²⁸⁾ de-
 sipramine sudden death가
 sudden death ³⁸⁾ ECG
 , TCA
 ECG monitoring
²⁸⁾
 35 nortriptyline pla-
 cebo - controlled discontinuation trials nortripty- 4
 line 6 80% 가 MPH
 FDA
 discontinuation phase . 62
 nortriptyline 가
⁴⁰⁾ open trial ADHD 가 1200
 oppositionality, anxiety nort- open trial clonidine - MPH
 riptyline ⁴¹⁾⁴²⁾ ⁵²⁾
 Nontricyclic antidepressant ADHD clonidine
 가 bupropion 가 controlled study 가
 . ADHD controlled study me- ⁵¹⁾ Texas children's medi-
 thylphenidate ADHD cation algorithm project ADHD
⁴³⁾⁴⁴⁾ ADHD

clonidine
 11). clonidine stimulants, TCAs, non-TCA
 antidepressants, bupropion
 ADHD
 stimulant
 aggression tic
 ADHD
 guanfacine open trial 53-55) controlled study
 ADHD clonidine
 ADHD
 clonidine
 tic
 Guanfacine
 가
 가
 Te-

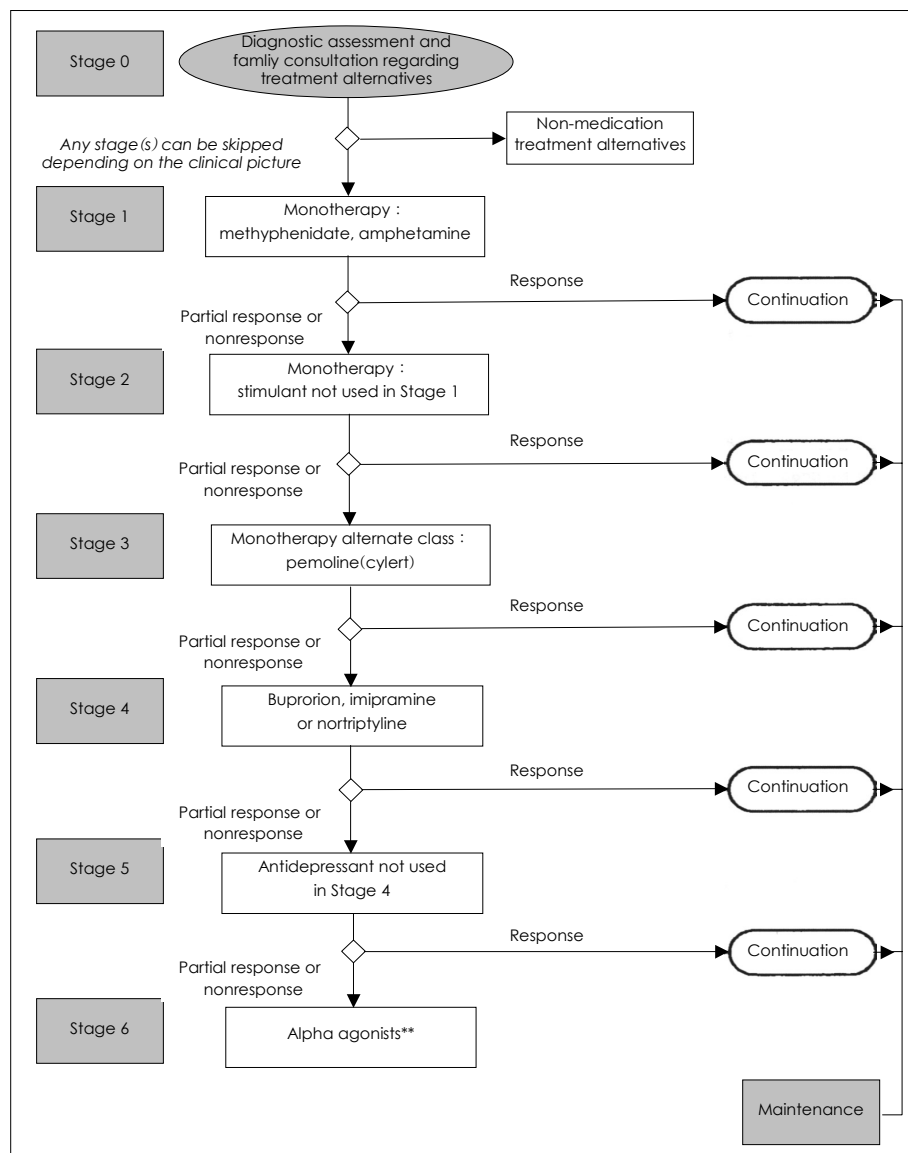


Fig. 1. Algorithm for the medication treatment of attention-deficit/hyperactivity disorder without comorbid psychiatric disorder. * : Plus liver function monitoring and substance abuse history, ** : Cardiovascular side effects.

Texas Children's Medication Algorithm project
 ADHD
 treatment algorithm

(Fig. 1).

ADHD with Comorbid Psychiatric Disorder

ADHD , 가
 ADHD , 가
 ADHD 30~50% conduct disorder(CD) , 25% oppositional defiant disorder (ODD)가 (anxiety disorder), 15~75% (Major depressive disorder ; MDD), 10~92% (Learning disability ; LD), 3% Tourette disorder가
 Tourette disorder 57)
 60% ADHD가
 58)59) ADHD가
 가 57)
 가 가
 1) phenotypic variation . 2)
 . 3)
 (vulnerability)
 . 4) genetic variant
 (subtype) . 5)
 . 6)
 가 60)61)
 가
 ,
 ADHD
 가
 가 ADHD stimulant
 가
 ADHD

1. ADHD with disruptive behavior disorder(CD/ODD)

ADHD CD ODD
 . ADHD+CD
 ,
 가
 ,
 stimulant 가 ADHD+CD 62)
 , stimulant 63)
 ,
 stimulant 가
 illegal drug
 가 가

2. ADHD with internalizing disorder(MDD/anxiety)

ADHD 3~75% MDD가
 57) MTA 6% 31)
 MDD
 가 ADHD MDD
 MDD ADHD MDD
 가 가
 가 ADHD
 57)
 ADHD+MDD
 , , ,
 stimulant 가
 64) Texas children's medication algorithm project 11) ADHD
 ,
 가
 MTA 1/3 31) ADHD
 가
 25~30% 가
 19)
 ADHD 가
 57)

가 stimulant
 stimulant
 ADHD+anxiety MTA
 ADHD+anxiety
 가 65)
 ADHD+anxiety stimulant
 ADHD 66)
 ADHD+BP
 가 mood stabilizer,
 antidepressant, stimulant, atypical antipsychotics
 bipolar disorder bipolar stimulant
 bipolar disorder
 70) ADHD+BP, bipolar disorder
 가 stimulant

3. ADHD with tic disorder(ADHD+tic)

ADHD Tourette syndrome(TS) 가
 ADHD
 stimulants가 TS
 ADHD+tic

5. ADHD with learning disability(LD)

ADHD LD
 10~90% 57) 가 가
 reading disability(RD) ADHD 62)

가 ADHD TS
 phenotypic variant 가
 67)
 Stimulant 가 ADHD+
 tic/TS stimulant

ADHD - RD RD 가 stimulant
 stimulant

6. ADHD with other disorder

Pharmacotherapy of ADHD with Comorbid Conditions

4. ADHD with bipolar disorder(BP)

ADHD
 DSM - IV
 ADHD+BP 68)
 ADHD 16%
 bipolar disorder 가
 69) 가 ADHD ADHD+BP
 ADHD+BP가
 ADHD+BP가

ADHD

1. ADHD+depression/anxiety

anxiety disorder ADHD
 stimulant
 71) MTA
 study anxiety disorder 가 stimulant 72)
 anxiety disorder 가 stimulant

contraindication . (Fig. 2) stimulant ADHD de-
ADHD tic disorder가 38 pression, anxiety 가
anxiety, depression methylp- depression anxiety stimulant
phenidate anxiety, antidepressant
depression stimulant . stimulant ADHD
tic 73) depression anxiety
Gammon Brown 74) ADHD mood disorder, antidepressant . stimulant
conduct disorder가 32 fluo- ADHD depression, anxiety
xetine MPH stimulant
ADHD+MDD ADHD+anxiety . depression antidepressant
가 ADHD stimulant
stimulant
stimulant 가 가
ADHD 가 9) ADHD anxiety, depression
depression, anxiety methylphenidate 43.8%, antidepre-
가 depression, anxiety ssant 34.4%, methylphenidate antidepre-
stimulant 가 21.9% ssant 가 21.9%
11) methylphenidate antidepressant ,
Texas Children's Medication Algorithm Project 41.9%, me-
11) treatment algorithm thylphenidate 41.9%

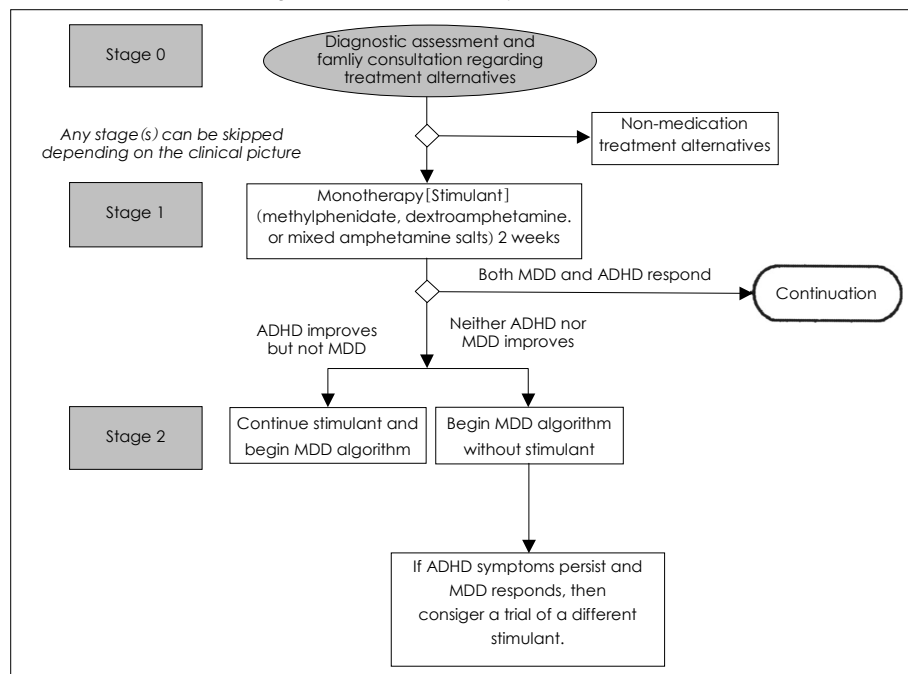


Fig. 2. Algorithm for the medication treatment of attention-deficit/hyperactivity disorder(ADHD) without comorbid depressive or anxiety disorder. MDD=major depressive disorder.

anxiety depression ⁷⁷⁾
methylphenidate Price Tourette syndrome stimulant
16.1% 6 monozygotic twin
stimulant stimulant
stimulant
antidepressant Te-
xas children s medication algorithm 가 ⁷⁸⁾ stimu-
, 가 stimulant lant tic . Law
가 methylphenidate antidepressant Schachar ⁷⁹⁾ 90 ADHD
secondary amine desipramine nor- Methylphenidate 1
trityline ADHD Methylphenidate
anxiety, depression
imipramine Tourette disorder
methylphenite dextroamphetamine,
SSRI
가 가
2. ADHD+tic disorder
ADHD tic disorder
ADHD tic 50% 가
tic/TS ADHD 20 1 dextroamphetamine ⁸⁰⁾
90% ⁷⁵⁾ 1970 stimulant 가
1980 ADHD 가
stimulant medication tic
chronic tic
disorder/TS 가 , chronic tic disorder/TS
가 stimulant treatment tic
⁷⁵⁾
stimulant가 tic disorder
stimulant
Gadow ADHD tic disorder 가 34 ADHD stimulant
ADHD methylphenidate double blind study ADHD
, ADHD stimulant
methylphenidate가 tic 가
⁷⁶⁾ ADHD chronic tic disorder
34 6 2
stimulant 가
motor tic vocal tic
Texas Children s Medication Algorithm Project
¹¹⁾ ADHD tic disorder가
(Fig. 3). sti-

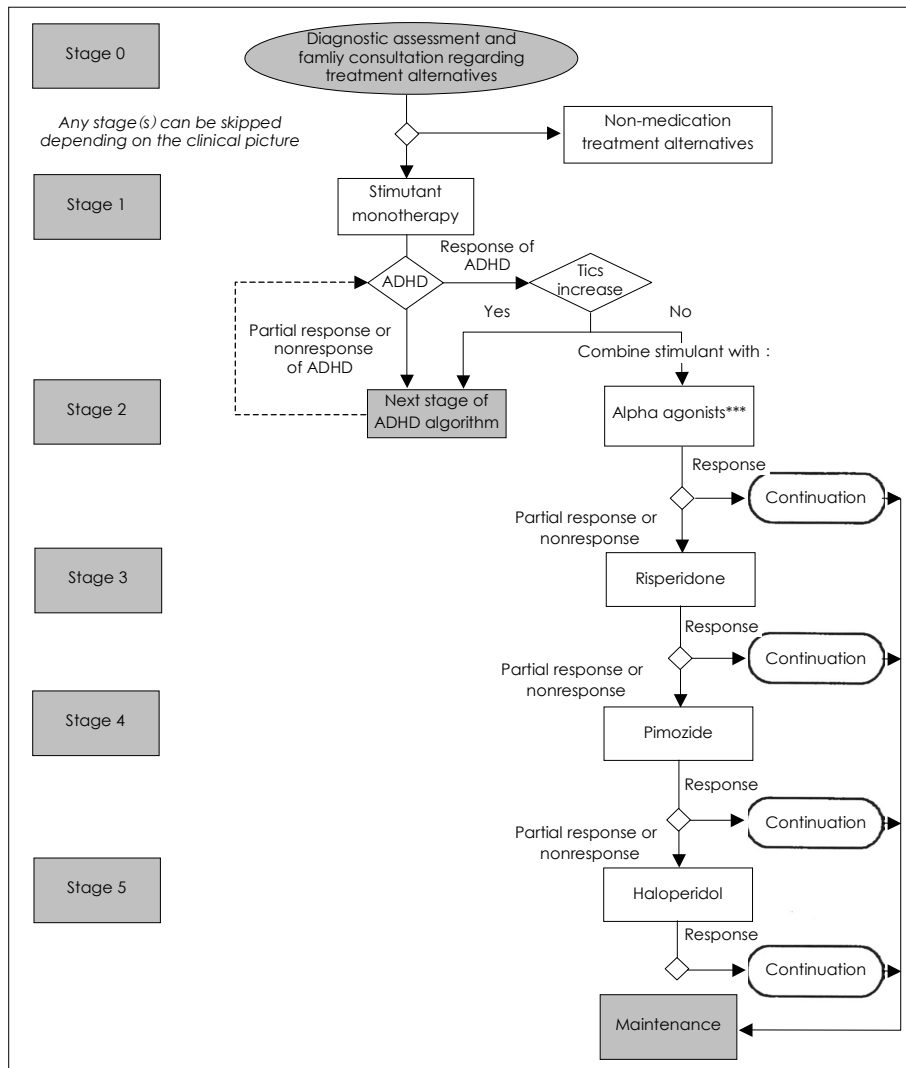


Fig. 3. Algorithm for the medication treatment of attention-deficit/hyperactivity disorder (ADHD) with comorbid tic disorder. *** : Caution ; cardiovascular side effects.

stimulant	ADHD			risperidone	haloperidol
tic	ADHD	ADHD			
algorithm		ADHD		가	ris-
	tic		peridone	risperidone	
	stimulant		tic	pimozide	halope-
		가	ridol	가	. Sallee
- agonist			pimozide, haloperidol, placebo		double blind
			cross over study		pimozide
			haloperidol		
	- agonist		QTc interval	가	pimozide
	antipsychotics	가	pimozide		가

sudden death 가 hotics, imipramine . 1,2
 ECG 1,2 가 stimulant
 sedation 가 61.3% 1,2 stimulant
 pimozide가 tic stimulant 38.7%
 haloperidol 가 . stimulant
 9) nonstimulant 가 stimulant
 66% 가 stimulant 25%, stimulant 가 stimulant
 가 9.4% 38.7% Texas children's medication algo-
 . nonstimulant clonidine, antipsyc- rithm group .

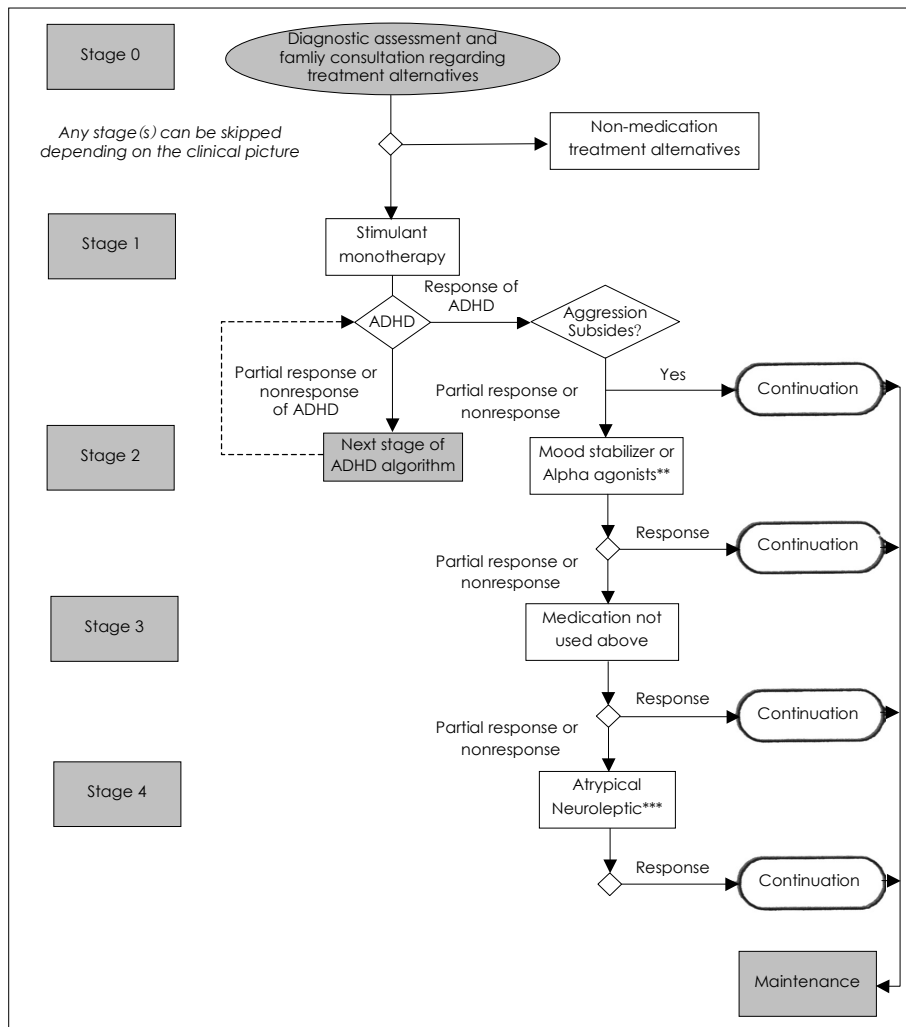


Fig. 4. Algorithm for the medication treatment of attention-deficit/hyperactivity disorder(ADHD) without comorbid intermittent explosive disorder. ** : Caution ; cardiovascular side effects, *** : caution ; risk of extrapyramidal symptoms or tardive dyskinesia.

3. ADHD with aggressive symptom(conduct disorder) 가 .

ADHD ADHD MTA

stimulant 가 ADHD .
¹¹⁾ conduct disorder ADHD 가 .
conduct disorder stimulant, antidepressant, - ago-

mood stabilizer lithium, divalproex sodium, carba- nist
mazepine aggressive symptom . stimulant MTA
controlled study 85%
⁸¹⁾⁸²⁾ - agonist clonidine .

ADHD impulsivity, explosiveness stimulant
aggression 2 , 3
¹¹⁾ stimulant stimulant

Texas Children's Medication Algorithm Project
¹¹⁾ ADHD antisocial beha- , nonstimulants
vior aggrssive outburst ADHD
(Fig. 4). ADHD

stimulant ADHD
aggressive symptom
mood stabilizer - . ADHD
agonist . conduct disorder, oppositional
atypical antipsy- defiant disorder, depression, anxiety, tic disorder
chotics . stimulant
⁹⁾ stimulant
methylphenidate 1
가 91% 가 stimulant .
methylphenidate 66%
antipsychotics,

mood stabilizer, antidepressant .
63% 1,2 methylphenidate medication algorithm
projects ,
Texas children's medication al-
gorithm project stimulant ADHD
aggressive symptom 가 .
internalizing symptom(depression, anxiety)
ADHD stimulant,
antidepressant,

결 론

ADHD , 가 aggression
conduct disorder ADHD

stimulant aggression
 bilizer, antipsychotics, mood sta- 가 1, 2
 tic disorder가 ADHD
 stimulant 가
 (treat-
 ment algorithm)
 (Fig. 5).
 medication algorithm ADHD

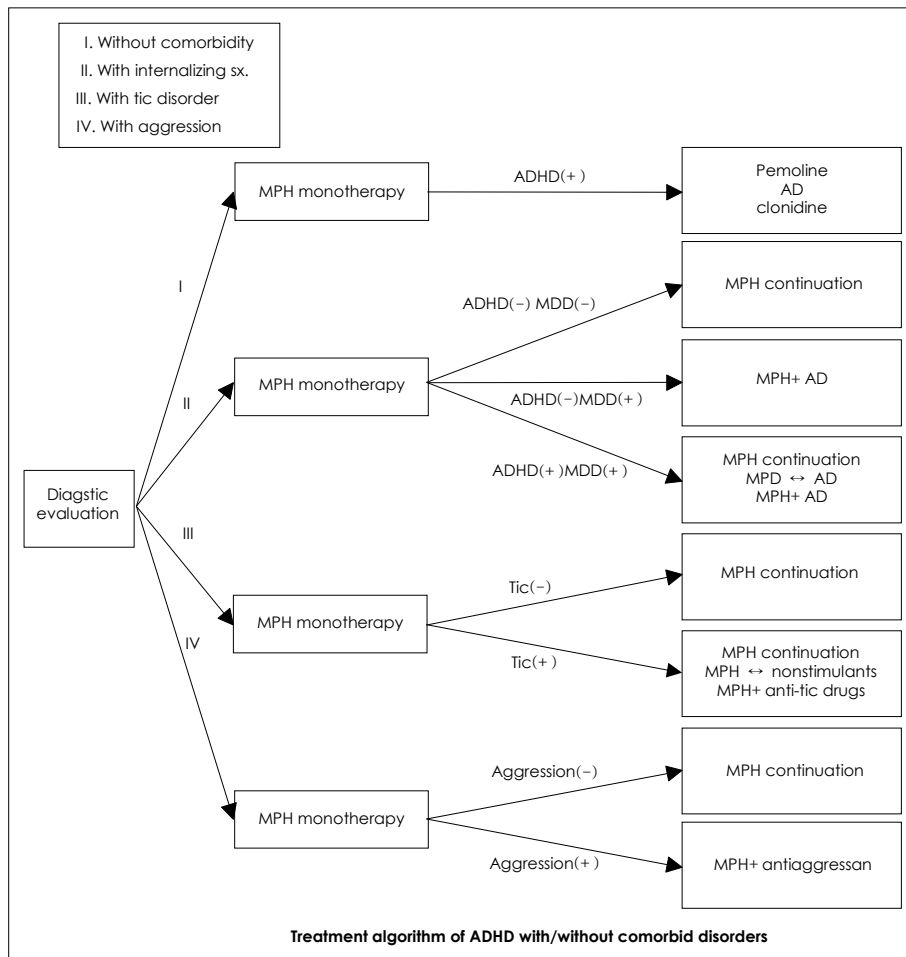


Fig. 5. Treatment algorithm of ADHD with/without comorbid disorders.

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ABSTRACT

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**PSYCHOPHARMACOLOGY OF ADHD WITH
COMORBID DISORDERS**

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Attention deficit/hyperactivity disorder is one of the most commonly treated conditions in the child psychiatric units and results in substantial impairment in peer, family and academic functioning.

For 70% to 80% of children with a diagnosis of ADHD, stimulant treatment results in successful improvement of the core ADHD symptoms. However, children with ADHD have high level of comorbidity and may respond differently from children with ADHD without comorbidity. Therefore they may need specific treatment plan.

We reviewed efficacy and safety of prescribed medication for treating children with ADHD, the relationship between ADHD and the comorbid conditions and treatment algorithm projects of ADHD with/without comorbid conditions performed Korean and American child psychiatrists.

Our main objective is to increase the uniformity of treatment and improve the clinical outcomes of children with comorbid ADHD.

KEY WORDS : ADHD · Comorbidity · Pharmacotherapy.