

# 알코올 의존의 치료에서 Naltrexone의 사용

## Use of Naltrexone in the Treatment of Alcohol Dependence

남 궁 기<sup>1</sup>  
Kee Namkoong, M.D.<sup>1</sup>

가 14% (Robins 1984).

### ABSTRACT

Two double-blind placebo controlled clinical trials have demonstrated that naltrexone, a pure opioid antagonist, appears to be an effective adjunct to treatment of alcohol dependence. Naltrexone alters endogenous opioids receptor activity, and its alteration blocks a positive reinforcing effect of alcohol in dopaminergic system. As a result, naltrexone reduces craving for alcohol and alcoholic high. Clinically, naltrexone, which is more compliant than disulfiram in alcoholics, results in fewer drinking days, less drinking amount and lower rate of relapse for alcoholic patients. Especially, those patients who initiated drinking, patients who received naltrexone and concurrent coping skill/relapse prevention therapy are the least likely to relapse. In addition, a recommendation for morning dosing and the development of a pill taking routine are likely to increase the patients compliance with naltrexone and ultimately the outcome of their treatment for alcoholic dependence.

In conclusion, the combined effects of naltrexone, psychosocial therapy and our patient support system need to be explored so that an optimal approach to the treatment of alcoholism, which is suitable for our own situation, should be developed.

**KEY WORDS :** Naltrexone · Alcohol dependence · Treatment.

가  
가  
( 1989 ; Namkoong 1990).  
(specific)  
tion)  
(detoxifica-  
가  
(Alcoholic Anonymous)  
가  
(psychosocial treatment)가

### 서 론

가  
Epidemiological Catchment Area  
(ECA)  
(alcohol use disorders)

가  
(Volpicelli 1995). Nathan(1986)  
(abstinence)

<sup>1</sup> Department of Psychiatry, Yonsei University College of Medicine, Seoul, Korea  
: Kee Namkoong, Yale University School of Medicine Department of Psychiatry 1 Long Wharf - Box 18 New Haven, CT 06511, U.S.A.  
TEL : 203 - 789 - 6988 · FAX : 203 - 789 - 6990  
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가  
1948 FDA  
disulfiram . disulfiram  
가

di-  
 sulfiram Fuller (1983 ; 1986) disulfiram  
 ram  
 , disulfiram  
 (medication compliance) 20%  
 ,  
 ,  
 , disulfiram  
 buspirone, homotaurine  
 GABAacamprosate,  
 D<sub>2</sub> receptor agonist bromocriptine,  
 (selective serotonin reuptake inhibitor ;  
 SSRI) fluoxetine, sertraline lithium ,  
 ,  
 (Schuckit 1996).  
 1990 naltrexone  
 ,  
 (O' Malley 1992 ; Volpicelli 1992).  
 (ideal pharmacological ad-  
 junct) (craving)  
 , 가  
 (reinforcing  
 effects) , 가  
 ,  
 (Volpicelli  
 1992). naltrexone  
 가  
 naltrexone FDA  
 ,  
 가 가 (Schuckit 1996).  
 ,  
 naltrexone

**naltrexone의 약리학적 특성**

1. naltrexone 개발의 역사적 배경  
 1900 (morphine) (heroin)

N - allylnorcodeine (an-  
 tagonism) ,  
 , 1940  
 (morphine intoxication)  
 nalorphine ,  
 . 1960 nalorphine  
 ,  
 naloxone . naloxone noroxymo-  
 rphine allyl , nalorphine 가  
 가  
 naloxone (over - dose)  
 가 ,  
 (euphoric effect)  
 .  
 1963 naltrexone  
 (Gonzales Brogden 1988)( 1).  
 2. naltrexone의 약동학(pharmacodynamics)  
 naltrexone oxymorphone cyclopropyl  
 naloxone nalorphine  
 (opioid receptor) 가 ,  
 (miosis), (dysphoria)  
 (agonist effect)  
 (Ginzberg MacDonald 1987). naltrexone  
 (competitive inhibition)  
 , naloxone  
 2.5 , nalorphine 12  
 . naltrexone 100mg  
 (reinforcement)  
 90% , 72  
 . naltrexone  
 naloxone 2 , nalorphine 17  
 (Martin 1993).  
 naltrexone  
 25 100mg - endorphin, cortisol  
 leutinizing hormone(LH)  
 . naltrexone prolactine testosterone  
 , adrenocortico -  
 trophic hormone(ACTH) 가  
 , follicular stimulating hormone(FSH)

naltrexone - endorphin

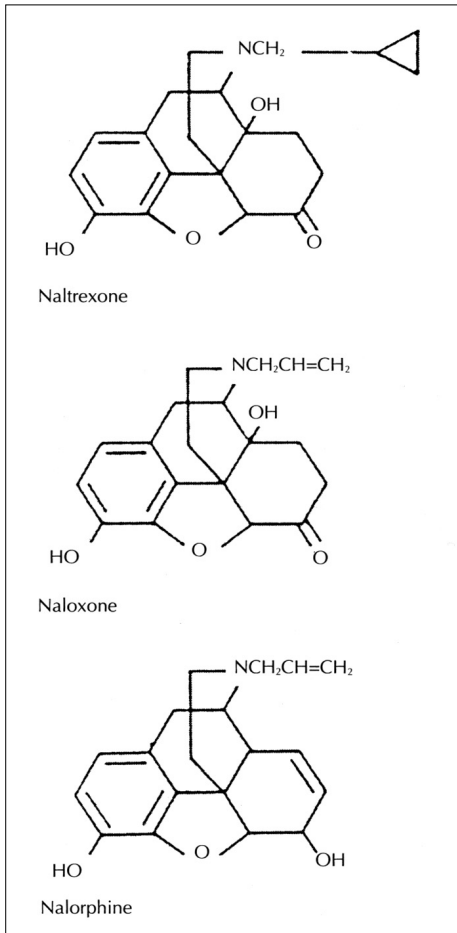


Fig. 1. Structural formula of naltrexone, naloxone(noroxymorphone) and nalorphine(a morphine derivative).(from Gonzales and Brogden 1988)

hypothalamus - pituitary - adrenal axis (Volavka 1979). naltrexone (competitive antagonist) 가 μ, , (tolerance) (dependence) (Temple 1982). naltr - exone locus coeruleus (supersensitivity) (Bardo 1983).

3. naltrexone의 약역학(pharmacokinetics)

naltrexone 19 44 μg/L (Meyer 1984 ; Verebey 1976), (multiple

dosing) 가 . naltrexone naltrexone 6 - - naltrexol . - naltrexol naltrexone 가 1.5 10 (bio - availability) 5 60% (Meyer 1984 ; Verebey 1976 ; Wall 1981), (healthy volunteer) , naltrexone 50, 100, 200mg (plasma concentration - time curve) naltrexone - naltrexol (linear) 가 (Meyer 1984). naltrexone , 20% 가 . naltrexone 6 - - naltrexol (reduction) , 6 - - naltrexol 2 - hydroxy - 3 - methoxy - 6 - - naltrexol, 2 - hydroxy - 3 - methyl - 6 - - naltrexol glucuronide conjugation (Verebey 1976 ; Wall 1981). 60%가 (systemic circulation) . naltrexone (renal clearance rate) 30 127mL/min , (renal elimination) (glomerular filtration) . naltrexone (elimination half - life) (enterohepatic recirculation) 1.1 10.3 (Meyer 1984 ; Verebey 1976).

알코올 의존의 치료에서 naltrexone사용의 이론적 근거

(intoxication) (dependence) naltrexone . 1. 알코올과 내인성 오피오이드계(endogenous opioid system)의 관계 가 (interac - tion) 가 20 (a tincture of morphine)가 (Goodwin 1981).

receptor activity) (motivation)  
 가 , (saturation)  
 ,  
 (moderate to high dose)  
 가 (Ho  
 가 (Anglin 1989). 1976 ; Sinclair 1974 ; Volpicelli 1991).  
 (agonist) (chronic)  
 , (compensation)  
 acetaldehyde가 tetrahy - 가 (Ho 1976 ; Volpicelli  
 dropapaveroline(THP) , 1991).  
 (opioid receptor agonist) tetrahydroiso - 가 (opioid compensation  
 quinoline alkaloids(TIQs) hypothesis) . 가  
 가  
 - endorphin met - enkephalin 가  
 , (activity) 가 (deficiency of endogenous opioid system) (com -  
 가 (social drinker) 가 (rebound phenomenon)  
 - endorphin (Swift 1995).  
 , 가 가  
 - endorphin 170% 가 (agonist)가  
 가 가 (motivation to drink) (primer)  
 (acute) 가 가  
 가 - endorphin (priming) 가  
 corticotropin (precursor) proopiomet - (sampling) 가 (loss of  
 anocortin(POMC) 가 anocortin(POMC) (control), 가 (heavy  
 (Gianoulakis 1996). drinking) 가  
 (endogenous opioid) (opioid compensation hypothesis)  
 (sensitivity) Reid (1991)  
 (fluidity) 가 , 가 ,  
 , 가 가  
 mu delta 가  
 , 50mM mu  
 가 50mM  
 mu  
 mu 가  
 (initial reinforcing effect)  
 (Ulm 1995). 가 가  
 (alcohol consumption) 가 (opioid response hypothesis)  
 가 (positive reinforcement effect)  
 (relative deficiency of opioid (dopamine system)가

nucleus accumbens  
 가 가  
 nucleus accumbens  
 (terminal) delta  
 (dopamine signal) (transduction)  
 , ventral tegmental area  
 mu GABA  
 nucleus accumbens  
 가  
 (arousal), (euphoria),  
 (positive reinforcement)  
 (alcohol self-administration habit)  
 (substrate) (Chiara  
 1996)( 2).

2. naltrexone과 알코올 섭취 행동(alcohol intake behavior)과의 관계

naltrexone  
 가  
 Altshuler  
 (1980) 1.0g/kg rhesus

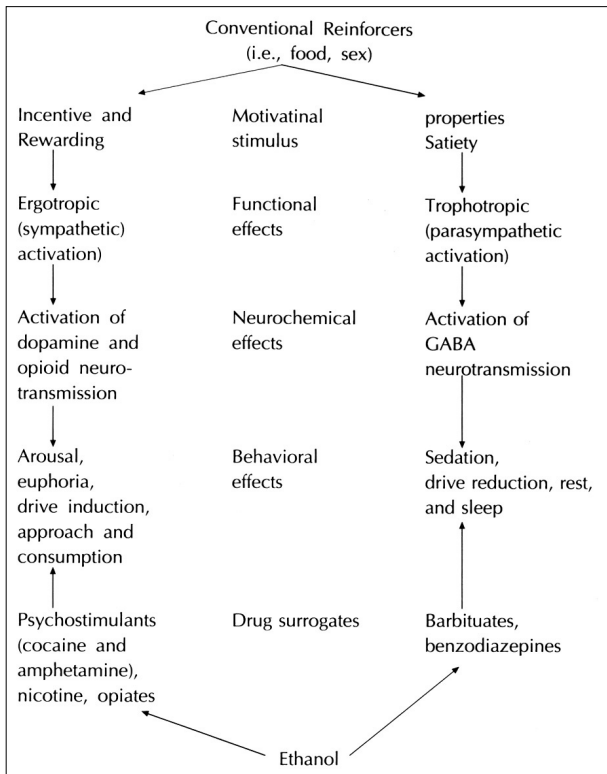


Fig. 2. Ethanol as a surrogates of conventional reinforcers : A schematic overview.(from Chiara et al. 1996)

monkey naltrexone naltrexone  
 5 가 (self-administration)가  
 , 가 가 50%  
 , naltrexone  
 naltrexone  
 가 가 ,  
 naltrexone  
 Volpicelli (1986)  
 naltrexone rat  
 (uncontrollable shock)  
 ,  
 5 6 (alcohol preference)가  
 25% 가 , naltrexone 가  
 가 가  
 가 가 가 , na-  
 ltrexone naltrexone  
 (positive reinforcing effect)  
 가 가 가  
 (opioid agonist)  
 -endorphin  
 (uncontrollable stresses) 가 가  
 (opioid antagonist)  
 (O'Brien 1996).  
 가 가 , 가  
 가  
 가 (maintain)  
 , naltrexone (blocking)  
 (positive reinforcing  
 effect)  
 Swift (1994) (social drinker)  
 naltrexone  
 ltrexone (pretreatment) na-  
 , , , (slow thought),  
 , naltrexone 가  
 naltrexone

가 .  
 H - P - A axis  
 ACTH, cortisol, -endorphin 가  
 (Volavka 1979).  
 -endorphin corticotropin (precursor)  
 proopiomelanocortin(POMC) 가  
 (mimicking alcohol's effect)

**알코올 의존의 치료에서 naltrexone의 임상적 효과**

naltrexone  
 O'Malley (1992) (the Yale University Study)  
 Volpicelli (1992) (the University of Pennsylvania - Veterans Affairs Study)

1. the Yale University Study  
 O'Malley (1992) 97 (out-patients with alcohol dependence) naltrexone (placebo)  
 (coping skill/relapse prevention therapy ;  
 ) (supportive therapy) 2 x 2  
 (factorial design) (clinical trial)  
 Marlatt Gordon (sub-stance abuse)  
 가  
 (coping skill)  
 1 1  
 (cognitive and behavioral rehearsal)  
 (homework exercise)  
 가  
 (abstinence violation)  
 (advise)  
 (double blind) 29  
 naltrexone 50mg 1  
 가 , 23 naltrexone 50

mg 1 가 25 (placebo)  
 1 가, 23 1  
 가 12  
 riboflavin  
 naltrexone  
 (medication compliance) (92% ).  
 naltrexone - 62%가 12  
 (abstinence) , naltrexone -  
 28%, - 21%,  
 - 19% (abstinence)  
 ( 3). naltrexone  
 가 (initiation of drinking)  
 가  
 , 1 5 , , 1  
 4 (relapse)  
 , naltrexone -  
 43%가, naltrexone - 34%가 12  
 (median)  
 - 35 , -  
 25 ( 4). ,  
 , naltrexone  
 (relative risk of relapse) -  
 2/3 . 12  
 , 58  
 , naltrexone -  
 12  
 , nal-  
 trexone - 32.5 , - 25  
 , - 14 . nalt-  
 rexone -  
 1/4 ( 5).  
 (frequency of drinking) (quantity  
 of drinking) naltrexone ( )  
 4.3 ± 1.4%, 13.7 ± 6.5 / ) ( )  
 9.9 ± 1.3%, 38.0 ± 6.2 / )  
 . naltrexone  
 (craving)  
 (O'Malley 1996). Addiction Severity  
 Index(ASI) (alcohol -  
 related problems) (severity) naltrexone

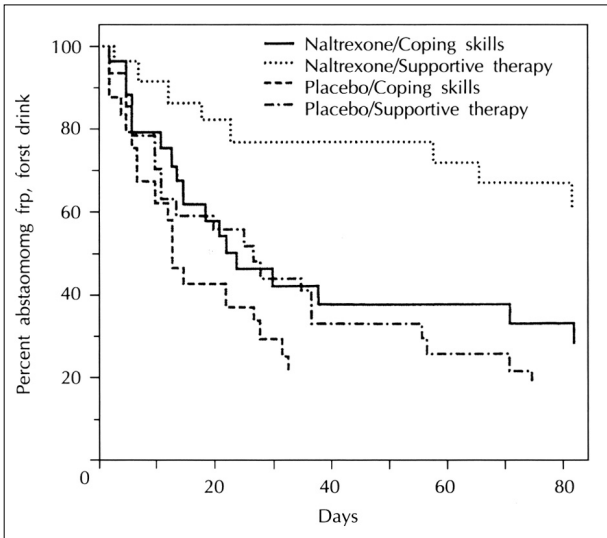


Fig. 3. Rate of continuous abstinence according to treatment groups(n=97). (from O'Mallley et al. 1992)

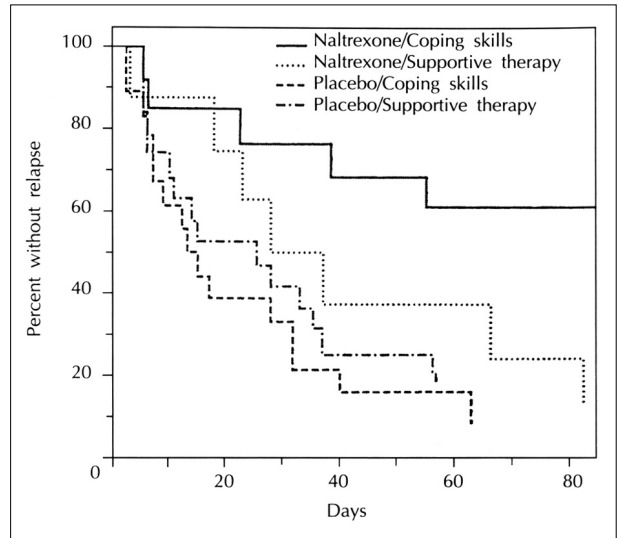


Fig. 5. Rate of never relapsing according to treatment groups for non-abstinent subjects (n=58) (from O'Malley et al. 1992)

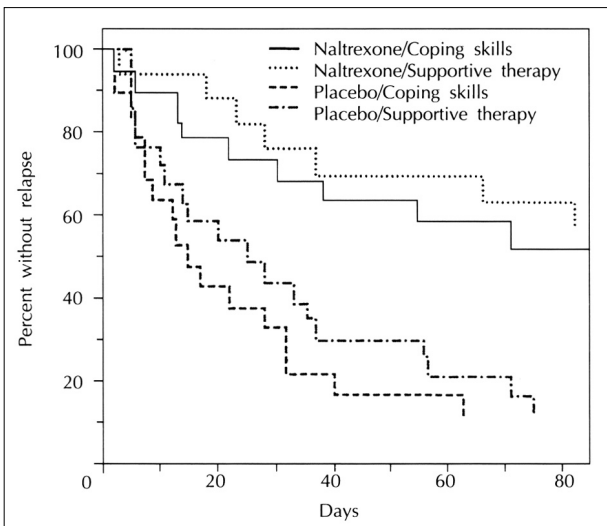


Fig. 4. Rate of never relapsing according to treatment groups (n=97). (from O'Malley et al. 1992)

O' Malley (1996) 97

80 (82%) 6

12 naltrexone

37 (46%) 12 1 80

12 naltrexone 12

(45% 78%)

(51% 71%) naltrexone

12 (heavy drinking) (25% 60%).

6 가 가 , 1

naltrexone (33% 63%),

naltrexone 4

가 , 5, 6

가 , naltrexone

6

10% 가 , -

19% 28%가 가 . 6

naltrexone

6 1 가

6 1

naltrexone SCID

6 24%가

, 39%가

naltrexone 13% 18%

12  
 6 (13% 39%) (10% 24%)  
 Namkoong(1997)  
 naltrexone (compliance) . 85  
 naltrexone 50mg (psychotherapy) 10 Medication Event Monitoring System(MEMS)  
 56 (80%) (compliance rate) 78 85%  
 63 70%가 80% , 50% 90%  
 (% of days abstinent) (average drinking amount per day)  
 (time of administration of dose) 가  
 , naltrexone 가  
 (morning dosing type) (evening dosing type) (atypical) 가  
 naltrexone disulfiram 가  
 naltrexone 가  
 (relapse) (quality of life) 가  
 (psy - chosocial treatment)가 naltrexone 가  
 naltrexone (alcohol - related consequence) . naltrexone 가

가  
 naltrexone  
 feedback  
 2. The University of Pennsylvania-Veterans Affairs Study Volpicelli (1992) (detoxification)  
 70 12 naltrexone (double - blind placebo controlled trial)  
 naltrexone 50mg 6 (partial day - hospitalization treatment) 2 (breathalyzer test), 1 (craving) 1 SCL - 90 1 , 4 가  
 naltrexone naltrexone (0.11 0.54 days/week, p<.025). (sampling) 가 naltrexone 46% 57%가 12 1 , naltrexone (study days) 3.6% 14.0% naltrexone 23%가 (relapse) , 54% ( 7). naltrexone 12 , 8 , 12 1 , naltrexone 50% 95%가  
 BPRS SCL - 90 가 naltrexone 17%



heavy drinking) 65%가 (he- naltrexone (high) (baseline level of somatic distress) naltrexone (high) (high) (Volpicelli 1995). naltrexone (sampling) (binge drinking) (priming) naltrexone (high) 가 (baseline level of craving)

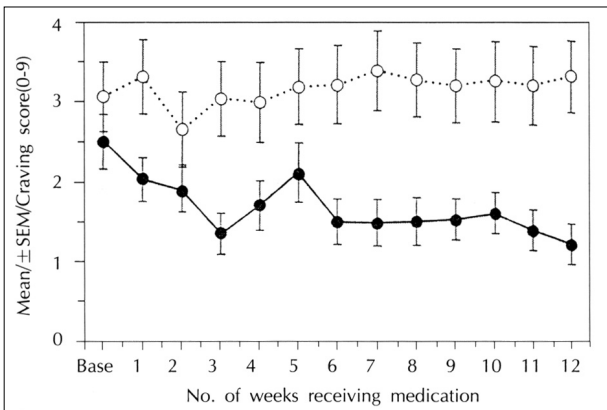


Fig. 6. Mean(SEM) craving scores for the naltrexone-(closed circles) and placebo-treated(open circles) groups across the 12 weeks of study.(from Volpicelli et al. 1992)

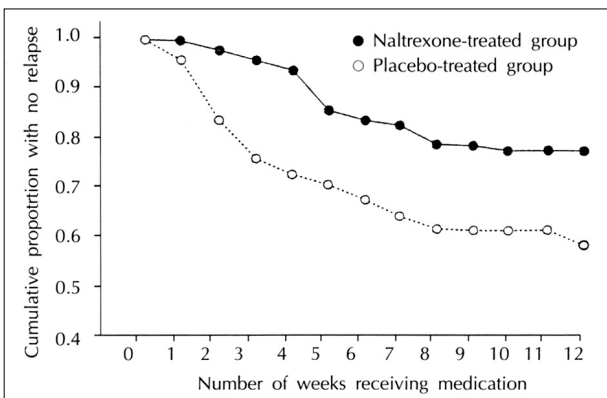


Fig. 7. Relapse rates for the naltrexone- and placebo-treated groups across the 12 weeks of study.(from Volpicelli et al. 1992)

알코올 의존 치료 시 naltrexone의 사용 지침(guideline)

1. 일반적인 naltrexone 사용 지침 naltrexone Yale (Guidelines for the use of naltrexone in the treatment of alcoholism)(Rounsaville 1995) 가 CAGE (screening) . CAGE 1) ? 2) ? 3) ? 4) 가 4 4 20 12 3 가 (motivation for treatment), 5 naltrexone ; 1) 30 , 2) 5 7 , 3) , 4) (renal failure) 가 3 , 5) bilirubin )가 , 6) naltrexone 50mg 1

(initial response) , naltrexone  
 가 . 4 , 8 , 12 , , naltrexone  
 가 . 12  
 가 . 12 , ,  
 , , , naltrexone  
 naltrexone 4 가 (response)  
 (int -  
 ensified counseling), (pharmacologically  
 assisted detoxification), , naltrexone 가 ,  
 , disulfiram , (supportive therapy)  
 (relapse prevention therapy)  
 . naltrexone 4 Ka -  
 가 (heavy dden (1989) .  
 drinking) (supportive interactional therapy)가 ,  
 , naltrexone (encourage) naltrexone 가  
 2  
 (maintenance psychosocial treatment),  
 (self - help group)

2. naltrexone의 사용과 정신사회 치료의 관계

naltrexone  
 naltrexone 가  
 . naltrexone  
 (synergy) .  
 (retention) .  
 (therapeutic alliance)  
 가  
 가 ,  
 (O'M -

alley Carroll 1996).

Jaffe (1992) naltrexone

3. 알코올의존 치료 시 naltrexone의 치료 용량 및 치료 기간

O'Malley (1992) Volpicelli (1992)  
 50mg naltrexone  
 naltrexone  
 naltrexone 50mg  
 25mg 24  
 50mg naltrexone .  
 Bohn (1994)  
 (brief counseling) 25mg 50mg  
 naltrexone ,  
 가 ,  
 가  
 naltrexone  
 . naltrexone  
 가 .

4. naltrexone의 부작용(side effect)

(nausea), (vomiting) 가  
 naltrexone ,

(decreased mental acuity), (loss of energy) (Gonzales Bregden 1988). naltrexone serum transaminase

ment) (intensity) (definition) 가 가 (Schuckit 1996).

(Atkinson 1985). naltrexone (nausea) (O'Malley 1992), naltrexone 800mg

naltrexone (self-report) (dependent variable)

ltrexone 가 , na- (Verebey 1976). naltrexone , naltrexone

가 가 naltrexone 가 naltrexone 가

가가 naltrexone 가 . naltrexone

naltrexone , naltrexone

Croop (1995) 570 naltrexone (safety) 10%가 (nausea) , 7%가 , 4%가 (dizziness) , 3%가 , 3%가 2%가 , 2%가

(high) , 가 naltrexone

결 론

가 가

(sociode-mographic resources) naltrexone

가 가 (subtype) 5 15%

(intensive) 가 naltrexone 가

가 (psychosocial treat-

중심 단어 : Naltrexone

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