

## Nefazodone 투여 후 지각이상을 보인 환자 4례

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## Nefazodone and Associated Perceptual Disturbance : A Report of Four Cases

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## ABSTRACT

Nefazodone, a newer antidepressant is a phenylpiperazine derivative that inhibits the reuptake of both norepinephrine and serotonin, and antagonizes 5-HT<sub>2A</sub> and  $\alpha_1$  adrenergic receptors. Compared with SSRIs, nefazodone caused the fewer activating symptoms, adverse gastrointestinal effects (nausea, diarrhea, anorexia) and adverse effects of sexual function, but is associated with the more dizziness, dry mouth, constipation, visual disturbances and confusion.

We report on 4 cases of visual disturbances and hallucinations in patients taking nefazodone.

It is not certain what mechanisms mediated these side effects, but three mechanisms are possible.

- 1) Nefazodone, as a 5-HT<sub>2</sub> antagonist, might induce visual disturbances.
- 2) mCPP, metabolite of nefazodone might contribute to the hallucination through action on 5-HT receptor.
- 3) Dopaminergic enhancing activity of nefazodone might cause hallucination.

This case report raises the possibility that dose-related perceptual disturbances may exist with nefazodone. The fact emphasizes the need to pay close attention to all possible drug interactions, particularly in patients treated with multiple psychoactive agents, older patients, and patients with decreased hepatic function.

**KEY WORDS** : Nefazodone · Adverse effect · Visual disturbance · Hallucination.

## 서 론

nefazodone phenylpiperazine, 5-HT<sub>2A</sub>, 5-HT<sub>1A</sub> (Catalano 1999 ; Davis 1997). (6 8 ) nefazodone, imipramine, fluoxetine, paroxetine,

sertraline (Fontaine 1994 ; Mendels 1995 ; Cohn 1996 ; Rickels 1994 ; Baldwin 1996 ; Feiger 1996 ; Gillin 1997).

nefazodone imipramine (selective serotonin re-uptake inhibitor, SSRI), (Baldwin 1996 ; Feiger 1996 ; Robinson 1996).

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Nefazodone cytochrome P450 3A4 isoenzyme, terfenadine, astemizole cisapride (Bristol - Myers Squi -

bb 1996).  
 Nefazodone , 2 200mg, 3  
 400mg, 4 500mg . 4  
 가 .  
 nefazodone 500mg 2 3 , ,  
 (Greene Barbhaiya 1997 ; Barbhaiya 1995).  
 Nefazodone hydroxynefazodone, triazolod-  
 ione, methylchlorophenylpiperazine( mCPP) .  
 hydroxynefazodone 5-HT<sub>2A</sub>  
 nefazodone . Triazo- 5 10  
 lodione nefazodone 5-HT<sub>2A</sub> 7 , 2 3 . Nefazodone  
 . mCPP nefazodone 200mg ,  
 , 5-HT<sub>2A</sub> 증례 2 : 31세 남자  
 (Barbhaiya 1996a ; Kahl 1995). 6  
 Nefazodone ,  
 . Fluoxetine 60mg, am -  
 Kraus(1996) nefazodone 가 itriptyline 125mg ,  
 (“ghosting trails of lig- nefazodone . Fluoxetine  
 ht ” ; palinopsia) amitriptyline , nefazodone 200mg  
 3 가 , 3 400mg, 6 500mg  
 , Schwartz(1997) visual trailing . Nefazodone 500mg  
 1 . Greenberg(1999) nef- 가  
 azodone (“ shimmering ” )  
 2 , nefazodone  
 5-HT<sub>2</sub> mCPP . 가 가  
 , 가 가  
 trazodone . 가 가 가  
 palinopsia trifluoperazine “ trai- 가  
 ling ” phenomenon (Hughes Lessel 1990 ;  
 Anderson O'Malley 1972). , nefazodone  
 nefazodone

### 증례 보고

4 증례 3 : 43세 여자  
 10 가  
 .  
 fluoxetine 20mg  
 (agitation) (irritability)  
 , paroxetine . Paroxetine  
 , paroxetine  
 nefazodone 100mg 200  
 mg . 200mg  
 가 가  
 . Nefazodone  
 Nefazodone 100mg .

증례 4 : 76세 남자

환자 76세 남자, 40년 전부터 시작된 만성 정신병력. 2002년 10월 200mg, 4주, 400mg 2. Nefazodone 100mg 2. paroxetine 10mg, nefazodone 200mg 가. paroxetine 20mg, nefazodone 200mg 가. (geometric hallucination), nefazodone 200mg 가. VDRL (4),

고 찰

Nefazodone 가, 5-HT<sub>2</sub> D-lysergic acid diethylamide( LSD) LSD synesthesia가 (true hallucination) (Crowley 1995). LSD geometric pseud-

ohallucinations, illusions of movement in the peripheral field, trailing phenomena, flashes of color, imagistic pseudohallucinations, halos around objects, intensified colors for brief periods of time, nefazodone (Abraham 1983). LSD 5-HT<sub>2</sub> (Abraham Aldridge 1993 ; Ag-hajanian 1994 ; Sadzot 1989). Penington Fox(1994) LSD가 5-HT<sub>1A</sub> 5-HT 5-HT LSD Risperidone 5-HT<sub>2</sub> LSD, risperidone LSD, 5-HT<sub>2</sub> LSD (Abraham Mamen 1996). Preskorn(1995) nefazodone 5-HT<sub>2A</sub> / nefazodone m-CPP가 5-HT mCPP(0.5mg/kg) 가 (1.5 2.5mg/kg) mCPP (derealization) (Mueller 1983). mCPP nefazodone 가, 5-HT<sub>1A</sub> 5-HT<sub>2C</sub>, 5-HT<sub>2A</sub> 5-HT<sub>3</sub> (Eison 1990 ; Hamik Peroutka 1989). Dextromethorphan extensive poor metabo- nefazodone hydroxynefazodone (steadystate) mCPP AUC Cmax poor metabolizer extensive metabolizer 4 mCPP가 CYP 2D6 (Bar-bhaiya 1996b). 3 paroxetine nefazodone, 4 nefazodone paroxetine CYP 2D6 paroxetine mCPP 가 가 paroxetine SSRI 가 CYP 2D6

, paroxetine CYP2D6  
 (Richelson 1997).  
 Paroxetine nefazodone mCPP  
 , Marino (1996)  
 fluoxetine nefazodone mCPP  
 4 가  
 John (1997) nefazodone paroxetine 가  
 (serotonin syndrome)  
 , nefa-  
 zodone paroxetine 가  
 SSRI  
 nefazodone 7 washout period 가  
 , nefazodone mCPP  
 가  
 , nefazodone paroxetine 가  
 가 nefazodone dopamine 가  
 . Nefazodone mesolimbic  
 dopamine system . Nefazodone nu-  
 cleus accumbens 28% 가 ,  
 nucleus accumbens 가  
 , HVA 가  
 (Olausson 1998). mCPP  
 , spontaneously hypertensive(SH)  
 rat hippocampus 가 , SH rat  
 nucleus accumbens striatum 가  
 (Eriksson 1999). , nefaz-  
 odone mCPP가 가  
 가  
 4 1 2 ne-  
 fazodone 500mg/day , 3 paro-  
 xetine nefazodone 200mg/day ,  
 4 paroxetine 20mg/day nefazodone 200  
 mg/day  
 . Kraus(1996)가 500mg/day  
 , Schwartz(1997)  
 200mg/day , Greenberg(1999)  
 550mg/day, 600mg/day  
 , nefazodone 가  
 ,  
 nefazodone 가 가 ,

가 , paroxetine  
 CYP450 2D6

Nefazodone

중심 단어 : Nefazodone

### 참고문헌

- Abraham HD(1983)** : Visual Phenomenology of the LSD flashback. *Arch Gen Psychiatry* 40 : 884-889  
**Abraham HD, Aldridge AM(1993)** : Adverse consequences of lysergic acid diethylamide. *Addiction* 88 : 1327-1334  
**Abraham HD, Mamen A(1996)** : LSD-like panic from risperidone in post-LSD visual disorder. *J Clin Psychopharmacol* 16 : 238-241  
**Aghajanian GK(1994)** : Serotonin and the action of LSD in the brain. *Psychiatr Ann* 24 : 137-141  
**Anderson WH, O'Malley JE(1972)** : Trifluoperazine for the "trailing" phenomenon. *JAMA* 220 : 1244-1245  
**Baldwin DS, Hawley CJ, Abed RT, Maragakis BP, Cox J, Buckingham SA, Pover GH, Ascher A(1996)** : A multicenter double-blind comparison of nefazodone and paroxetine in the treatment of outpatients with moderate-to-severe depression. *J Clin Psychiatry* 57 Suppl 2 : 46-52  
**Barbhaiya RH, Shukla UA, Greene DS(1995)** : Single-dose pharmacokinetics of nefazodone in healthy young and elderly subjects and in subjects with renal or hepatic impairment. *Eur J Clin Pharmacol* 49 : 221-228  
**Barbhaiya RH, Shukla UA, Chaikin P(1996a)** : Nefazodone pharmacokinetics : Assessment of nonlinearity, intra-subject variability and time to attain steady-state plasma concentrations after dose escalation. *Eur J Clin Pharmacol* 50 : 101-107  
**Barbhaiya RH, Buch AB, Greene DS(1996b)** : Single and multiple dose pharmacokinetics of nefazodone in subjects classified as extensive and poor metabolizers of dextromethorphan. *Br J Clin Pharmacol* 42 : 573-581  
**Bristol-Myers Squibb(1996)** : Nefazodone prescribing information. Princeton, New Jersey, USA  
**Catalano G, Catalano MC, Tumarkin NB(1999)** : Nefazodone overdose : Case report. *Clin Neuropharmacol* 22 : 63-65  
**Cohn CK, Robinson DS, Roberts DL, Schwiderski UE(1996)** : Responders to antidepressant drug treatment : A study comparing nefazodone, imipramine, and placebo in patients with major depression. *J Clin Psychiatry* 57 Suppl 2 : 15-18  
**Crowley TJ(1995)** : Hallucinogen-related disorders. In : *Comprehensive Textbook of psychiatry*. 6th ed. Vol I, Ed by Kaplan HI and

Sadock BJ, Baltimore, Williams & Wilkins, pp833-834

- Davis R, Whittington R, Bryson HM(1997)** : Nefazodone. A review of its pharmacology and clinical efficacy in the management of major depression. *Drugs* 53 : 608-636
- Eison AS, Eison MS, Torrente JR(1990)** : Nefazodone : preclinical pharmacology of a new antidepressant. *Psychopharmacol Bull* 26 : 311-315
- Eriksson E, Engberg G, Bing O, Nissbrandt H(1999)** : Effects of mCPP on the extracellular concentrations of serotonin and dopamine in rat brain. *Neuropsychopharmacology* 20 : 287-296
- Feiger A, Kiev A, Shrivastava RK, Wisselink PG, Wilcox CS(1996)** : Nefazodone versus sertraline in outpatients with major depression : Focus on efficacy, tolerability, and effects on sexual function and satisfaction. *J Clin Psychiatry* 57 Suppl 2 : 53-62
- Fontaine R, Ontiveros A, Elie R, Kensler TT, Roberts DL, Kaplita S, Ecker JA, Faludi G(1994)** : A double-blind comparison of nefazodone, imipramine, and placebo in major depression. *J Clin Psychiatry* 55 : 234-241
- Gillin JC, Rapaport M, Erman MK, Winokur A, Albala BJ(1997)** : A comparison of nefazodone and fluoxetine on mood and on objective, subjective, and clinician-rated measures of sleep in depressed patients : A double-blind, 8-week clinical trial. *J Clin Psychiatry* 58 : 185-192
- Greenberg WM(1999)** : Visual field "shimmering" associated with nefazodone [letter]. *J Clin Psychiatry* 60 : 124
- Greene DS, Barbhaiya RH(1997)** : Clinical pharmacokinetics of nefazodone. *Clin pharmacokinet* 33 : 260-275
- Hamik A, Peroutka SJ(1989)** : 1-(m-chlorophenyl) piperazine (mCPP) interactions with neurotransmitter receptors in the human brain. *Biol Psychiatry* 25 : 569-575
- Hughes MS, Lessell S(1990)** : Trazodone-induced palinopsia. *Arch Ophthalmol* 108 : 399-400
- John L, Perreault MM, Tao T, Blew PG(1997)** : Serotonin syndrome associated with nefazodone and paroxetine. *Ann Emerg Med* 29 : 287-289
- Kahl S, Shukla UA, Barbhaiya RH(1995)** : Nonlinear pharmacokinetics of nefazodone after escalating single and multiple oral doses. *J Clin Pharmacol* 35 : 830-839
- Kraus R(1996)** : Visual "trails" with nefazodone treatment [letter]. *Am J Psychiatry* 153 : 1365-1366
- Marino MR, Langenbacher KM, Uderman HD(1996)** : Interaction of nefazodone and fluoxetine. *Clin Pharmacol Ther* 59 : 180
- Mendels J, Reimherr F, Marcus RN, Roberts DL, Francis RJ, Anton SF(1995)** : A double-blind, placebo-controlled trial of two dose ranges of nefazodone in the treatment of depressed outpatients. *J Clin Psychiatry* 56 Suppl 6 : 30-36
- Mueller EA, Murphy DL, Sunderland T(1983)** : Neuroendocrine effects of M-chlorophenylpiperazine, a serotonin agonist, in humans. *J Clin Endocrinol Metab* 61 : 1179-1184
- Olaussen P, Ericson M, Peterson A, Kosowski A, Soderpalm B, Engel JA(1998)** : Nefazodone attenuates the behavioral and neurochemical effects of ethanol. *Alcohol* 15 : 77-86
- Penington NJ, Fox AP(1994)** : Effects of LSD on Ca<sup>++</sup> currents in central 5-HT-containing neurons : 5-HT<sub>1A</sub> receptors may play a role in hallucinogenesis. *J Pharmacol Exp Ther* 269 : 1160-1165
- Preskorn SH(1995)** : Comparison of the tolerability of bupropion, fluoxetine, imipramine, nefazodone, paroxetine, sertraline, and venlafaxine. *J Clin Psychiatry* 56 Suppl 6 : 12-21
- Richelson E(1997)** : Pharmacokinetic drug interactions of New antidepressants : A review of the effects on the metabolism of other drugs. *Mayo Clin Proc* 72 : 835-847
- Rickels K, Schweizer E, Clary C, Fox I, Weise C(1994)** : Nefazodone and imipramine in major depression : A placebo-controlled trial. *Br J Psychiatry* 164 : 802-805
- Robinson DS, Roberts DL, Smith JM, Stringfellow JC, Kaplita SB, Seminara JA, Marcus RN(1996)** : The safety profile of nefazodone. *J Clin Psychiatry* 57 Suppl. 2 : 31-38
- Sadzot B, Baraban JM, Glennon RA, Lyon RA, Leonhardt S, Jan CR, Titeler M(1989)** : Hallucinogenic drug interactions at human brain 5-HT<sub>2</sub> receptors : Implications for treating LSD-induced hallucinogenesis. *Psychopharmacology (Berl)* 98 : 495-499
- Schwartz K(1997)** : Nefazodone and visual side effects [letter]. *Am J Psychiatry* 154 : 1038