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ORIGINAL RESEARCH

Comparative Meta-Analysis of Pharmacotherapy and Behavior Therapy for Persistent Insomnia

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Abstract

Objective: Although four meta-analytic reviews support the efficacy of pharmacotherapy and behavior therapy for the treatment of insomnia, no meta-analysis has evaluated whether these treatment modalities yield comparable outcomes during acute treatment. The authors conducted a quantitative review of the literature on the outcome of the two treatments to compare the short-term efficacy of pharmacotherapy and behavioral therapy in primary insomnia.

Method: Authors identified studies from 2000 through 2021 using MEDLINE, psycINFO, and bibliographies. Assessment was done in department of pharmacology, Jhalawar Medical College, Jhalawar, Rajasthan. Investigations were limited to studies using prospective measures and within-subject designs to assess the efficacy of benzodiazepines or benzodiazepine receptor agonists or behavioral treatments for primary insomnia. Benzodiazepine receptor agonists included zolpidem, zopiclone, and zaleplon. Behavioral treatments included stimulus control and sleep restriction therapies. Twenty studies summarizing outcomes for 470 subjects met inclusion criteria.

Results: Weighted effect sizes for subjective measures of sleep latency, number of awakenings, wake time after sleep onset, total sleep time, and sleep quality before and after treatment were moderate to large. There were no differences in magnitude between pharmacological and behavioral treatments in any measures except latency to sleep onset. Behavior therapy resulted in a greater reduction in sleep latency than pharmacotherapy.

Conclusions: Overall, behavior therapy and pharmacotherapy produce similar short-term treatment outcomes in primary insomnia.

Keywords: Meta analysis, insomnia, behavior therapy and pharmacotherapy

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Introduction

ICD-10 defines persistent insomnia as problems starting or maintaining sleep at least three nights per week along with daytime distress or impairment. This condition is linked to a number of negative personal and societal outcomes, such as increased medical and psychiatric morbidity (1–7), potentially fatal accidents, a lower quality of life, poorer job performance, and absenteeism. Ten to fifteen percent of individuals report ongoing sleep issues; the percentages are much higher for women and older people (8).

According to estimates, the yearly cost of insomnia in terms of missed productivity and accidents ranges from $77 to $92 billion. Despite these costs, the vast majority of people who suffer from insomnia do not receive treatment. Only around one-third of patients in primary care acknowledge their sleeplessness, despite the fact that more than 50% of them do (9).

The effectiveness of medication over the short term (2-4 weeks) as compared to a placebo is supported by pharmacotherapy meta-analyses. The most often prescribed drugs were benzodiazepine receptor agonists like temazepam, zolpidem, and zaleplon. Clinical improvements were reportedly fairly reasonable, with a preference for impacts on overall sleep duration (10). Lack of information on long-term efficacy may be the main drawback of medication. It has been hypothesised that long-term use leads to tolerance, dependency, and rebound insomnia after withdrawal. However, limited data from two uncontrolled open-label studies with zolpidem and zaleplon suggests that these drugs might be efficient for three to six months without dose escalation (11). There is no evidence to support ongoing improvement after medication withdrawal.

Two meta-analyses support behavioural sleep treatments (12). The goal of behavioural therapies is to change the circumstances that are thought to maintain persistent insomnia (13). Four to eight weekly sessions are usually needed for an effective treatment, and the patient must be highly motivated. The two elements that are thought to be the most effective are sleep restriction and stimulation control (14). Cognitive therapy and suggestions for good sleep hygiene could also be provided. Behavior therapy has few negative effects and offers long lasting recovery. Gains from treatment have been observed from six months to two years. A lack of qualified specialists, high costs, inconsistent insurance coverage, and the belief that drugs are more effective are the three main drawbacks to behavioural treatment. Both studies discovered similar treatment results, quicker recovery with sedative hypnotics, and more persistent recovery with behavioural therapies. The relative effectiveness of various treatments needs to be systematically documented. Unfortunately, due to a number of factors that make the literature on the outcomes of the two treatments different, it is not possible to directly compare the effect sizes from the behavioural and pharmacological meta-analyses. These elements include: 1) conflicting study designs; 2) various outcome measures; and 3) varying definitions of insomnia.(15)

The goal of the current study was to assess pharmacological and behavioural therapies using standards that would allow for the most accurate comparisons of the available research on the effects of pharmacotherapy and behaviour therapy.

Material and methods

Study type

Meta Analysis. After a thorough review of potentially appropriate methodological approaches, the most appropriate method for the reasons given is an exhaustive review of the literature in a non-systematic way.

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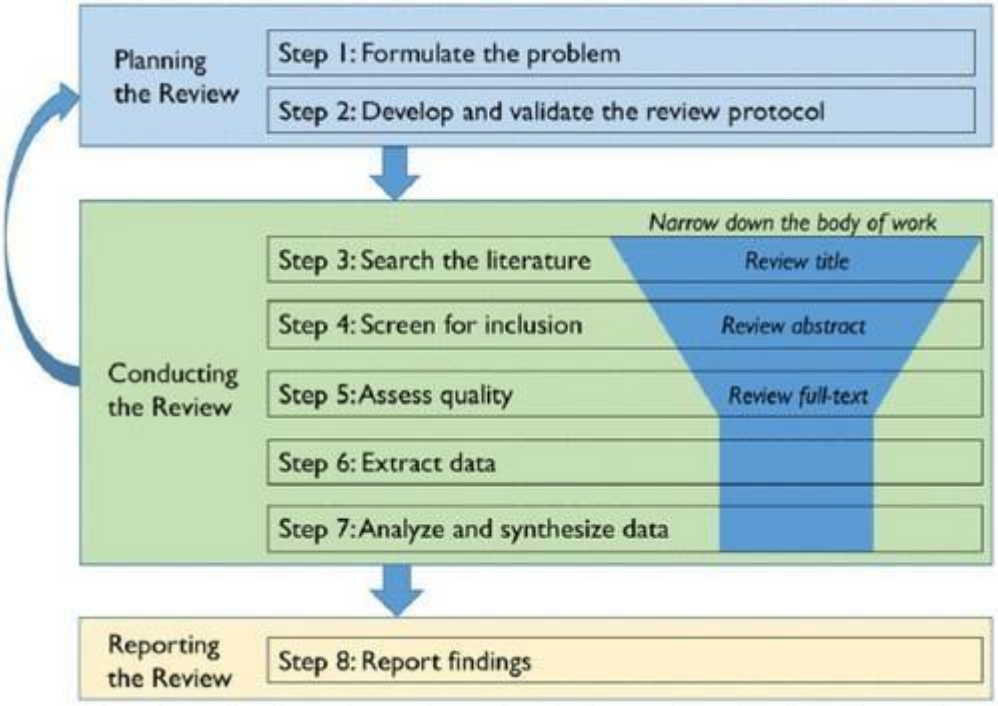
Steps in meta analysis



Study place

Department of pharmacology, Jhalawar Medical College, Jhalawar, Rajasthan.

1) IDENTIFICATION	Records identified through database searching(n=37). Published studies were identified by using the keywords "insomnia" and "treatment" in English-language searches of MEDLINE and psycINFO databases from 2000 to 2021 and from bibliographies provided by the authors of two meta-analyses of insomnia
	Records after duplicate removed (n=20)
3) ELIGIBILITY	1. Full text articles assessed for eligibility

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	(n=20) **Inclusion Criteria** 2. The investigation was a treatment study for primary insomnia. 3. Duration of insomnia was 1 month or longer. 4. Sleep diary measures were reported. 5. Pharmacological studies included benzodiazepines or benzodiazepine receptor agonists (zolpidem, zopiclone, zaleplon). 6. Behavior treatments included stimulus control or sleep restriction.
	7. Within -subject measurements were obtained before and after treatment. **Exclusion Criteria** 1. Sleep continuity variables were presented as ordinal data. 2. No means or standard deviations were presented. 3. Patients were not withdrawn from hypnotic medications before the trial.
4) INCLUSION	Studies included (n=20)

Data analysis

All studies were reviewed and coded by us to determine whether inclusion and exclusion criteria were satisfied. Studies were coded to extract major clinical variables, including demographics, type and duration of treatment, and the outcome variables. We resolved discrepancies between ratings of each study. All values entered into the final database were verified by a research assistant.

Results

Excluded Studies

37 primary insomnia treatment outcome studies with a duration of more than a month were found. Nearly 17 studies were disregarded because it was unable to compute the pretreatmentposttreatment effect sizes due to the parallel design or because means, standard deviations, or a F or t statistic were not provided. Twenty studies met the requirements for a meta-analysis.

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Characteristics of Selected Studies

TABLE 1. Characteristics of 21 Studies of Pharmacotherapy and Behavioral Treatment for Persistent Insomnia

Type of Study and Source Pharmacological treatment studies (220 subjects)	Year	Treatment Type	Number of Subjects	Mean Age (years)	Female Sex (%)	Duration of Treatment (weeks)	Diagnosis
Kripke et al. (16)	2000	Flurazepam, 15 mg/day (N=24)	72	37.9	61	3	Mixed insomnia
		and 30 mg/day (N=24);					
		midazolam, 15 mg/day (N=24)					
Lahmeyer et al. (17)	2002	Zolpidem, 10 mg/day (N=37)	74	45	33	1	Mixed insomnia
		and 15 mg/day (N=37)					
Mamelak et al. (18)	2002	Zopiclone, 7.5 mg/day	6	45	33	1	Mixed insomnia
Mamelak et al. (19)	2003	Quazepam, 30 mg/day (N=6);	12	45	33	1	Mixed insomnia
		triazolam, 5 mg/day (N=6)					
McClure et al. (20)	2004	Lorazepam, 2 mg/day (N=8);	16	46.1	88	1	Mixed insomnia
		flurazepam, 30 mg/day (N=8)					
Milby et al. (21)	2005	Triazolam, 25 mg/day	7	35	53	3	Initial insomnia
Morin et al. (22)	2007	Temazepam, 7.5 mg/day or more	17	65	64	8 b	Mixed insomnia
Roth et al. (23)	2008	Quazepam, 25 mg/day	16	18–65	0	< 1	Mixed insomnia

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Behavioral treatment							
studies (250 subjects)							
Alperson anad Biglan (24)	2009	Stimulus control therapy	14	< 55.0 (N=7) ≥ 55.0 (N=7) and	50	4	Initial insomnia
Bliwise et al. (25)	2011	Sleep restriction therapy	16	68.7	69	5	Mixed insomnia
Edinger et al. (26)	2012	Stimulus control therapy/sleep restriction therapy	7	61.9	57	6	Sleep maintenance Insomnia
Espie et al. (27)	2013	Stimulus control therapy	43	45.5	68	8	Initial insomnia
Guilleminault et al. (28)	2014	Stimulus control therapy	30	44	60	4	Mixed insomnia
Jacobs et al. (29)	2015	Stimulus control therapy/sleep	12	37.8	58	10	Initial insomnia
		restriction therapy					
Lacks et al. (30)	2016	Stimulus control therapy	7	43	60	4	Mixed insomnia
Lacks et al. (31)	2017	Stimulus control therapy	15	40.6	60	4	Initial insomnia

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Morin et al. (32)	2018	Stimulus control therapy/sleep restriction therapy	24	67.1	71	8	Sleep maintenance Insomnia
Morin et al. (33)	2018	Stimulus control therapy/sleep	18	64.4	64	8	Mixed insomnia
		restriction therapy					
Puder et al. (34)	2019	Stimulus control therapy	16	67	81	4	Initial insomnia
Riedel et al. (35)	2020	Sleep restriction therapy	25	≥ 60.0	— c	4	Mixed insomnia
Stanton (36)	2021	Stimulus control therapy	15	40	58	4	Initial insomnia

Studies that covered the years 1979 through 1999 compiled the results for 470 subjects. The clinical traits of the participants are shown in Table 1 according to the type of therapy. Thirteen studies evaluated only behavioural interventions (232 subjects),six studies (48-54) evaluated only pharmacological therapies (203 subjects), one study (34) compared pharmacotherapy with behavioural therapy (N=35), and one study (34) evaluated only behavioural interventions. The majority of research comprised both sexes and various groups (246 (55% of the 445 respondents in studies reporting gender were female) Participants received a diagnosis of mixed insomnia (difficulty initiating and maintaining sleep) for three months or more and were middle-aged (mean=47.2 years, SD=11).

There were seven different pharmacotherapies represented, and the typical course of treatment lasted about two weeks (SD=2). Three groups were administered flurazepam.

There were two groups each using zolpidem, triazolam, and quazepam. One group each of lorazepam, midazolam, and zopiclone was administered.

Twelve of the behavioural investigations employed either sleep restriction or stimulus control therapy; two research used sleep restriction alone; and four studies combined the two. Over a mean time of almost five weeks, there were five sessions on average (SD = 2) of behaviour therapy.

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Between medication and behavioural treatment, there were no variations in the subjects' pretreatment averages for sleep latency, number of awakenings, wake time after sleep onset, total sleep time, and subjective sleep quality (p>0.05). As anticipated, the duration of behavioural treatment outlasted medication by a significant amount (t=-4.38, df=26.49, p0.001). According to these findings, the two treatment populations were similar.

Comparison of Treatment Effects

Table 2. Efficacy of Pharmacotherapy Compared With Behavioral Therapy in 21 Studies of Persis

Subjective Sleep Outcome Measure (Based on Sleep Diary)	Pre treatment Value		Post treatment Value		Difference Between Pretreatment and Post treatment Values		Number of Studies	Number of Subjects	Weighted Effect Size	
	Mean	SD	Mean	SD	Mean	SD			Mean	SD
Sleep latency (minutes)										
Pharmacotherapy	48.85	29.73	34.36	26.26	–14.49	29.7	6	129	0.45	0.2
Behavioral therapy	54.24	28.52	30.93	16.03	–23.31	43	12	225	1.05 b	0.7
Number of awakenings										
Pharmacotherapy	3	1.99	1.83	1.37	–1.17	39	4	108	0.97	1
Behavioral therapy	2.44	1.84	1.67	1.59	–0.77	31.6	4	58	0.83	1.3
Wake time after sleep										

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Pharmacotherapy	55.09	37.8	29.49	19.5	–25.60	46.5	1	17	0.89	0.2
Behavioral therapy	68.6	40.27	30.22	23.98	–38.38	55.9	5	81	1.03	0.1
Total sleep time (minutes)										
Pharmacotherapy	332.08	55.32	372.59	48.97	40.51	12.2	6	130	0.84	0.7
Behavioral therapy	333.28	63.66	352.89	44.22	19.61	5.9	8	146	0.46	0.6
Sleep quality rating d										
Pharmacotherapy	3.1	0.64	3.73	0.93	0.63	20.3	4	109	1.2	1.3
Behavioral therapy	3.38	0.66	4.34	1.3	0.96	28.4	5	82	1.44	1.2

For each of the five main outcome variables, the mean values before and after treatment are shown in Table 2, along with the overall weighted effect sizes. Pharmacological treatment reduced sleep latency by 30% compared to behavioural therapies' 43% reduction. Each therapy reduced the number of nighttime awakenings by about 1. Pharmacotherapy reduced wake time after the start of sleep by 46%, and behaviour treatment lowered wake time by 56%.The amount of total sleep time improved somewhat with both therapies. Both pharmacotherapy and behaviour treatment lengthened total sleep by 12% and 6%, respectively. Pharmacotherapy and behaviour treatment both increased the quality of sleep by 20% and 28%, respectively. Pharmacotherapy and behaviour therapy both had mean effect sizes for all five outcome variables of 0.87 and 0.96, respectively, indicating comparable efficacy in terms of enhancing sleep continuity and quality at the conclusion of acute treatment. To compare the weighted impact sizes of medication and behavioural therapy, separate t tests for unequal variances were computed for each of the five individual sleep variables. The only impact sizes that significantly varied were those for sleep latency (Table 2). Behavioral therapy had greater variability in weighted effect sizes for sleep latency than pharmacological studies (F=8.05, df=20.62, p=0.01).

Discussion

By performing a metaanalysis of outcome studies, we compared the acute effects of medicati on and behavioural therapy for primary insomnia. Overall, the effects of both interventions were comparable. Both treatments had a mean effect size larger than 0.80, indicating a significa nt treatment effect. Across treatments, the majority of weighted individual impact sizes were substantial. Sleep latency and overall sleep time were the exceptions.

The behavioural treatment resulted in much greater treatment effects for sleep delay.

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The behavioural intervention's effect size for total sleep duration was moderate, but it was co mparable to the pharmacotherapy's effect size. Before any definitive conclusions can be made, three caveats must be taken into account. First, the 95% confidence interval estimate for the mean difference between the two effect sizes for sleep latency was 0.17 to 1.04. It is unclear whether behavioural therapy represents the better option for sleep initiation issues given this range, which suggests that the real difference between these effect sizes may be very low. Second, there was more variation in the effect sizes for behavioural treatment for sleep latency, indicating less consistency in the delivery of a treatment effect. Third, rather than the strength of hypnotics, it's probable that the modest finding for sleep latency with benzodiazepine receptor agonists is more connected to experimental design issues. The majority of research looked at drugs that took a while to reach their peak plasma concentration, such lorazepam, which takes 120 minutes.

As a result, sleep maintenance would be more likely to be influenced by the maximum sedati ve effect than sleep initiation.

Given these restrictions, it is still feasible that behaviour therapy is more beneficial for issues with sleep initiation. This may be because altering components involved in the homeostatic re gulation of sleep (by limiting sleep) may induce sleep more effectively than altering aminobutyric acid neurotransmission pharmacologically. The only mild shortterm effects of b ehavioural therapy on total sleep time may also be explained by the mechanism(s) of action f or behaviour therapy. Behavior therapies initially reduce the chance for sleep to boost the bo dy's natural desire to sleep. Only when sleep is stabilised does the potential for sleep improve consistently. Therefore, behavioural therapies are not very effective in shortterm increasing total sleep time. What happens over the long term may be the most crucial qu estion. One meta analysis revealed that the amount of time spent sleeping has increased even a fter receiving behaviour therapy as a short-term treatment.

Conclusions

Weighted effect sizes for subjective measures of sleep latency, number of awakenings, wake time after sleep onset, total sleep time, and sleep quality before and after treatment were moderate to large. There were no differences in magnitude between pharmacological and behavioral treatments in any measures except latency to sleep onset. Behavior therapy resulted in a greater reduction in sleep latency than pharmacotherapy. Overall, behavior therapy and pharmacotherapy produce similar short-term treatment outcomes in primary insomnia.

References

1. Ford DE, Kamerow DB: Epidemiologic study of sleep disturbances and psychiatric disorders: an opportunity for prevention? JAMA 1989; 262:1479-1484 Cross ref, Medline, Google Scholar
2. Breslau N, Roth T, Rosenthal L, Andreski P: Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. Biol Psychiatry 1996; 39:411418Crossref,Medline,Google Scholar
3. Kupperman M, Lubeck DP, Mazonson PD: Sleep problems and their correlates in a working population. J Gen Intern Med 1995; 10:25-32Crossref,Medline,Google Scholar
4. Katz DA, McHorney CA: Clinical correlates of insomnia in patients with chronic illness. Arch Intern Med ; 158:1099-1107Crossref,Medline,Google Scholar
5. Kennedy GJ, Kelman HR, Thomas C: Persistence and remission of depressive symptoms in late life. Am J Psychiatry ; 148:174-178Link,Google Scholar
6. Livingston G, Blizard B, Mann A: Does sleep disturbance predict depression in elderly people? a study in inner London. Br J Gen Pract ; 43:445-448Medline,Google Scholar

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

7. Dryman A, Eaton WW: Affective symptoms associated with the onset of major depression in the community: findings from the US National Institute of Mental Health Epidemiologic Catchment Area Program. Acta Psychiatr Scand; 84:1-5Crossref,Medline,Google Scholar
8. Zammit GK, Weiner J, Damato N, Sillup GP, McMillan CA: Quality of life in people with insomnia. Sleep; 22(suppl 2):S379-S385Google Scholar
9. Ohayon MM, Caulet M, Guilleminault C: How a general population perceives its sleep and how this relates to the complaint of insomnia. Sleep ; 20:715-723Medline,Google Scholar
10. Aldrich MS: Automobile accidents in patients with sleep disorders. Sleep ; 12:487494Crossref,Medline,Google Scholar
11. Balter MB, Uhlenhuth EH: New epidemiologic findings about insomnia and its treatment. J Clin Psychiatry ; 53:34-39Medline,Google Scholar
12. Johnson L, Spinweber C: Quality of sleep and performance in the Navy: a longitudinal study of good and poor sleepers, in Sleep/Wake Disorders: Natural History, Epidemiology, and Long-Term Evaluation. Edited by Guilleminault C, Lugaresi E. New York, Raven Press, , pp 13-28Google Scholar
13. Ancoli-Israel S, Roth T: Characteristics of insomnia in the United States: results of the 1991 National Sleep Foundation Survey, I. Sleep; 22(suppl 2):S347-S353Google Scholar
14. Gallup Organization: Sleep in America. Princeton, NJ, Gallup Organization, GoogleScholar
15. Karacan I, Thornby JI, Anch M, Holzer CE, Warheit GJ, Schwab JJ, Williams RL: Prevalence of sleep disturbance in a primarily urban Florida county. Soc Sci Med ; 10:239244Crossref,Medline,Google Scholar
16. Bixler EO, Kales A, Soldatos CR, Kales JD, Healey S: Prevalence of sleep disorders in the Los Angeles metropolitan area. Am J Psychiatry ; 136:1257-1262Link,Google Scholar
17. Mellinger GD, Balter MB, Uhlenhuth EH: Insomnia and its treatment: prevalence and correlates. Arch Gen Psychiatry ; 42:225-232Crossref,Medline,Google Scholar
18. Brabbins CJ, Dewey ME, Copeland JR, Davidson IA: Insomnia in the elderly: prevalence, gender differences and relationships with morbidity and mortality. Int J Geriatr Psychiatry ; 8:473-480Crossref,Google Scholar
19. Ohayon M: Epidemiological study on insomnia in the general population. Sleep; 19:S7S15Google Scholar
20. Bliwise DL, King AC, Harris RB, Haskell WL: Prevalence of self-reported poor sleep in a healthy population aged 50-65. Soc Sci Med ; 34:49-55Crossref,Medline,Google Scholar
21. Foley DJ, Monjan AA, Izmirlian G, Hays JC, Blazer DG: Incidence and remission of insomnia among elderly adults in a biracial cohort. Sleep; 22(suppl 2):S373-S378GoogleScholar
22. Stoller M: Economic effects of insomnia. Clin Ther ; 16:873-897Medline,Google Scholar
23. Shochat T, Umphress J, Israel AG, Ancoli-Israel S: Insomnia in primary care. Sleep; 22(suppl 2):S359-S365Google Scholar
24. Nowell PD, Mazumdar S, Buysse DJ, Dew MA, Reynolds CF III, Kupfer DJ: Benzodiazepines and zolpidem for chronic insomnia: a meta-analysis of treatment efficacy. JAMA ; 278:2170-2177Crossref,Medline,Google Scholar
25. Holbrook AM, Crowther R, Lotter A, Cheng C, King D: Meta-analysis of benzodiazepine use in the treatment of insomnia. Can Med Assoc J ; 162:225-233Medline,Google Scholar

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

26. Morin CM, Culbert JP, Schwartz SM: Nonpharmacological interventions for insomnia: a meta-analysis of treatment efficacy. Am J Psychiatry ; 151:1172-1180Link,Google Scholar
27. Murtagh DR, Greenwood KM: Identifying effective psychological treatments for insomnia: a meta-analysis. J Consult Clin Psychol ; 63:79-89Crossref,Medline,Google Scholar
28. Dement WC: The proper use of sleeping pills in the primary care setting. J Clin Psychiatry ; 53:50-56Medline,Google Scholar
29. Soldatos CR, Dikeos DG, Whitehead A: Tolerance and rebound insomnia with rapidly eliminated hypnotics: a meta-analysis of sleep laboratory studies. Int Clin Psychopharmacol 9; 14:287-303Crossref,Medline,Google Scholar
30. Kupfer DJ, Reynolds CF III: Management of insomnia. N Engl J Med ; 336:341346Crossref,Medline,Google Scholar
31. Schlich D, L'Heritier C, Coquelin J, Attali P: Long-term treatment of insomnia with zolpidem: a multicentre general practitioner study of 107 patients. J Int Med Res ; 19:1927Medline,Google Scholar
32. Scharf MG, Mendels J, Thorpy M, Weiss B: Safety of long-term zolpidem treatment in patients with insomnia. Curr Ther Res ; 55:1100-1111Crossref,Google Scholar
33. Spielman A, Caruso L, Glovinsky P: A behavioral perspective on insomnia treatment. Psychiatr Clin North Am ; 10:541-553Crossref,Medline,Google Scholar
34. Morin CM, Colecchi C, Stone J, Sood R, Brink D: Behavioral and pharmacological therapies for late-life insomnia: a randomized controlled trial. JAMA ; 281:991999Crossref,Medline,Google Scholar
35. acobs GD, Benson H, Friedman R: Home-based central nervous system assessment of a multifactor behavioral intervention for chronic sleep-onset insomnia. Behavior Therapy ; 24:159-174Crossref,Google Scholar
36. McClusky HY, Milby JB, Switzer PK, Williams V, Wooten V: Efficacy of behavioral versus triazolam treatment in persistent sleep-onset insomnia. Am J Psychiatry ; 148:121126Link,Google Scholar