Treating primary insomnia

The efficacy of valerian and hops

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Objective

To evaluate the efficacy of valerian and hops in the treatment of primary insomnia.

Methods

The AMED and MEDLINE databases were searched for primary sources of literature published between 1950 and 2009, using keywords: herbal medicine, medicinal plants, herbal, *Valeriana officinalis*, valerian, *Humulus lupulus*, hops, sleep, insomnia.

Studies were included if they evaluated the efficacy of valerian or hops in improving primary insomnia in adults: sixteen studies met the inclusion criteria. Twelve of these found that the use of valerian, on its own, or in combination with hops, is associated with improvements in some sleep parameters (eg. sleep latency and quality of sleep). However, these results need to be interpreted cautiously as there were significant differences in design between the studies.

Conclusion

Further randomised, double blind, placebo controlled trials are needed before such herbal treatments can be confidently recommended for the treatment of primary insomnia.

Keywords: valerian; humulus; insomnia

Sleep disorders are common in the general population and may be associated with considerable economic costs as well as psychological and social disruption, and reduced wellbeing.[1–4] The conventional definition of a sleep disorder and the one this article will adopt, is any disturbance of a person's normal pattern of sleep that affects their ability to function.[5] Primary insomnia is the most common of the sleep disorders;[5] it may be acute or chronic[6] and is characterised by difficulty falling or staying, asleep; nocturnal awakenings; early morning awakenings; nonrefreshing sleep; or a combination of these symptoms.[7] It is more prevalent in females and in older people.[7] For the purpose of this review, a sleep disorder will include any subjective complaint of sleep due to primary insomnia, as defined above.

Many herbs have a long history of use as mild sedatives and hypnotics. *Valeriana officinalis* (valerian) for example, was recognised by the ancient Greeks more than 2000 years ago as an effective treatment for nervous unrest, stress and sleep disorders.[8] It is difficult to quantify the extent to which Australians use herbal medicines for sleep disorders due to a paucity of data. A recent study[9] that measured the use of 24 common medicinal herbs, in a sample of approximately 2500 Victorians, found that 4.3% (n=107) reported having used valerian in the preceding year, predominantly for sleep disorders. (This study did not measure the prevalence of the use of *Humulus lupulus* [hops].)

In general, both valerian and hops are considered safe when consumed within the recommended dosage range.[10] Adverse reactions to these herbs are rare.[10,11] One clinical trial reported that three participants experienced 'vivid dreams' while taking valerian.[12] Atopic individuals have been reported to have experienced allergic dermatitis when coming into contact with hops.[11] Theoretically, valerian and hops consumed in high doses, and taken long term, could potentiate the effects of pharmaceutical sedatives; however, this has not been tested under clinical conditions.[11]

This literature review will evaluate the evidence for efficacy of valerian and hops, two herbs traditionally used for sleep disorders, using

primary literature sources. These herbs will be referred to using their common names, rather than Latin binomial nomenclature. The results of this review will assist patients and practitioners to make informed decisions about the role of herbal treatments in improving sleep.

Methods

The AMED (Allied and Complementary Medicine Database) and MEDLINE databases from 1950–2009 (September) were searched for articles using the keywords: herbal medicine, medicinal plants, herbal, *Valeriana officinalis*, valerian, *Humulus lupulus*, hops, sleep, insomnia.
To focus the results, the MeSH term 'sleep initiation and maintenance disorders/treatment' was used. The limits of 'English language' and 'human' were applied. The literature lists created from these database investigations were searched for relevant articles.

Studies were included if they discussed the efficacy of valerian or hops in altering sleep in adults. Outcome measurements included a range of common sleep parameters, including:

- total sleep time (measured in a laboratory)
- sleep latency (ie. time to fall asleep)
- slow wave sleep (measured in a laboratory)
- nocturnal awakenings, and
- sleep quality.

Studies were excluded if they did not use these outcome measurements or if the study patients suffered from nonprimary forms of sleep disorders (eg. circadian rhythm disturbance, or insomnia due to a medical or psychiatric condition). Secondary sources of literature were also excluded. The literature search yielded 397 articles; however, only 16 studies[13–28] met the inclusion criteria, and these studies form the basis of this review. A summary of the key methodological features of the studies included in this review are presented in *Table 1*.

Results

Valerian

Twelve studies on the use of valerian met the inclusion criteria for this review (*Table 1*). There were:

- nine randomised, double blind, placebo controlled trials[13–16,18, 20–23]
- two randomised, double blind, no placebo controlled trials,[17,24] and
- one randomised, single blind, placebo controlled trial.[19]

Studies ranged from 1 day to 6 weeks in duration, and sample sizes ranged from 8–405 participants. In most studies valerian was administered for 1 day only.

Nine of these studies[13,16–22,24] found valerian to be effective in improving at least one of the sleep parameters measured. However, it is important to note that five of these studies had significant methodological flaws, which limits the reliability of their findings, and therefore the extent to which they can be applied to clinical practice (*Table 2*). For example, two studies failed to include a placebo control group;[17,24] one study recruited only female participants;[22] three studies had differences in important sample characteristics such as age and baseline sleep parameters,[13,22,24] and in one study the control preparation contained small amounts of valerian to mimic the taste and smell of the treatment preparation.[20]

The early landmark study conducted by Leathwood et al[19] almost 3 decades ago found that subjects given a 400 mg preparation of valerian experienced a statistically significant improvement in sleep latency and sleep quality. Subgroup analysis found that valerian had the greatest effect on poor or irregular sleepers, particularly females. A later study by the same author[18] demonstrated efficacy only for 450 mg of valerian and not a 900 mg dose.

The study by Balderer and Borbely[13] divided the sample receiving treatment into two groups: one assessed in the laboratory, the other group assessed at home. Valerian was found to be effective in two sleep parameters (sleep latency and night awakenings) but only in the treatment group assessed at home. This finding raises some interesting questions about the influence of the sleep environment on the efficacy of treatment interventions.

Ziegler et al[24] compared the effects of valerian extract 600 mg/day to oxazepam 10 mg/day for 6 weeks in 202 patients. The researchers found that the valerian treatment was at least as efficacious as oxazepam, with both treatment groups reporting improvements in sleep quality. Subjectively, 83% of patients receiving valerian rated it as 'very good', compared with 73% receiving oxazepam.

A recent large scale, double blind, randomised, placebo controlled trial[21] found that 5.5% (95% CI 0.2–10.8) more participants in the valerian group perceived their sleep as better or much better (p=0.04) compared to the control (placebo) group.

The three studies[14,15,23] (all randomised, double blind, placebo controlled trials) in which valerian was found to be ineffective in improving sleep outcome measurements, suffered from similar study design limitations (*Table 2*). For example, Diaper and Hindmarch[15] objectively analysed only single day treatments of valerian. In the study conducted by Taibi et al,[23] in which all the participants were female, there were no significant changes in sleep parameters, according to objective data. And the study by Coxeter et al[14] used a series of n-of-1 trials, with self assessed outcomes, where the control treatment contained 3% active valerian.

Valerian and hops combination

Four studies of a combination of valerian and hops met the inclusion criteria for this review (*Table 1*). There were:

- three randomised, double blind, placebo controlled trials,[25,27,28] and
- one randomised, single blind, no placebo controlled trial[26]

Three of these studies[25–27] found the valerian and hops combination to be effective in improving at least one of the sleep parameters measured (*Table 2*).

The study by Dimpfel and Suter[25] found that the combination of valerian and hops was associated with improvement in total sleep time, sleep quality and deep sleep, according to both objective and subjective measurements. In contrast, the study by Koetter et al[27] found that the valerian and hops combination was efficacious in reducing sleep latency, yet valerian alone was no better than placebo in improving this sleep parameter. This finding raises some interesting questions about whether this combination of herbs might be more effective than valerian alone in improving sleep latency. Improvements in three sleep parameters (sleep latency, nocturnal awakenings, sleep quality) were observed in the study by Fussel et al;[26] however, this study lacked a placebo control group. And finally, Morin et al[28] found in a multicentre trial

Table 1. Key methodological features of the 16 studies for the use of valerian and hops in primary insomnia included in this review

Study first author	Study year	Sample size (n)	Median age (years)	Study design	Treatment arms	Treatment duration (days)
Valerian						
Balderer[13]	1985	18	27.6	RCT, DB, C/O (7 day washout)	Valerian (450 mg in aq*) Valerian (900 mg in aq)	1
Coxeter[14]	2003	24	54	n-of-1 trials, each: RCT, DB, C/O (3 day washout)	Valerian (450 mg)	7
Diaper[15]	2004	16	55.9	RCT, DB, C/O (6 day washout)	Valerian (300 mg in eth*) Valerian (600 mg in eth)	1
Donath[16]	2000	16	49	RCT, DB, C/O (13 day washout)	Valerian (600 mg in eth)	14
Herrera-Arellano[17]	2001	20	45	RT, DB	*Valeriana edulis* (450 mg in eth) *Valeriana officinalis* (450 mg in eth)	1
Leathwood[18]	1985	8	45	RCT, DB, C/O	Valerian (450 mg in aq) Valerian (900 mg in aq)	1
Leathwood[19**]	1982	128	Not disclosed	RCT, SB, C/O	Valerian (400 mg in aq) Valerian, hops (400 mg, 200 mg in aq)	1
Lindahl[20**]	1989	27	54	RCT, DB, C/O (0 day washout)	Valerian (400 mg), hops (375 mg), lemon balm (160 mg) Valerian (4 mg), hops (375 mg), lemon balm (160 mg)	1
Oxman[21]	2007	405	43.7	RCT, DB Multicentre	Valerian (600 mg)	14
Schulz[22]	1994	14	61.6	RCT, DB Pilot study	Valerian (405 mg in aq, 3 times/day)	7
Taibi[23]	2009	16	69.4	RCT, DB, C/O (13 day washout)	Valerian (300 mg)	14
Ziegler[24]	2002	202	52.4	RT, DB Multicentre	Valerian (600 mg in eth) Oxazepam (10 mg)	42
Valerian and hops combination						
Dimpfel[25]	2008	42	Not disclosed	RCT, DB	Valerian, hops (460 mg, 460 mg in eth)	1
Fussel[26]	2000	30	57.6	SB One group, pre- and post-test	Valerian, hops (500 mg, 120 mg in eth)	14
Koetter[27]	2007	30	37.8	RCT, DB	Valerian (500 mg in eth) Valerian, hops (500 mg, 120 mg in eth)	28
Morin[28]	2005	184	44.3	RCT, DB Multicentre	Valerian, hops (374 mg, 83.8 mg in eth) Diphenhydramine (50 mg)	28

* Most studies explained how the herbal extracts were made, ie. using either an ethanol (eth) or aqueous (aq) solvent. This information was not reported for four studies[14,20,21,23]

** The aim of these studies was to test the effectiveness of valerian, not the hops component. As such, they will be analysed and compared to other valerian trials

Washout period = between treatment duration in crossover studies; RCT = randomised placebo controlled trial; RT = randomised trial (no placebo control); DB = double blind; SB = single blind; C/O = crossover

Table 2. Key findings in relation to sleep parameters in the 16 studies of the use of valerian and hops in primary insomnia included in this review

Study (first author)	Sleep parameters					Study limitations
	Total sleep time	Time to fall asleep (sleep latency)	Slow wave sleep	Nocturnal awakenings	Sleep quality	
Valerian						
Balderer[13]	X (laboratory group, objective only)	√ (home group, subjective only)	X (laboratory group, objective only)	√ (home group, subjective only)	X	Baseline differences in age of participants in the home and laboratory groups
Coxeter[14]*	X	X	–	X	X	43% of subjects withdrew Control treatment = 3% active valerian N = 1 study design
Diaper[15]	X	X	X	X	X	1 day treatment duration
Donath[16]	X	√ (subjective improvement only)	√	X	X	
Herrera-Arellano[17]	X	X	√	√	√	No placebo control group
Leathwood[18]	X	√	–	X	√	Ceiling treatment effects observed with higher valerian dose
Leathwood[19]*	–	√	–	X	√	
Lindahl[20]*	–	–	–	–	√	Control treatment = 1% active valerian
Oxman[21]*	X	X	–	√	X	
Schulz[22]	X	X	√	X	X	All female subjects Baseline differences in sleep parameters (eg. total sleep time, sleep efficiency, sleep latency) of participants in the placebo and treatment groups
Taibi[23]	X	X	X	X	X	All female subjects
Ziegler[24]*	√	–	–	–	√	No placebo control group Baseline differences in age of participants in the two groups
Valerian and hops combination						
Dimpfel[25]	√	–	–	–	√	
Fussel[26]	X	√	X	√	√	No placebo control group
Koetter[27]	–	√	√	X	X	Baseline differences in age, gender and sleep parameters (eg. sleep latency) between treatment and control groups
Morin[28]	X	X	–	–	X	Baseline differences in sleep latency between treatment and control groups, and across treatment centres

√ = benefit seen, X = no benefit seen, – = parameter results not reported, * = only subjective data recorded

that valerian and hops did not significantly improve sleep for any of the parameters measured.

Discussion

In total, nine studies (six of which were randomised, double blind, placebo controlled trials) that assessed the efficacy of valerian alone, and three studies (two of which were randomised, double blind, placebo controlled trials) that assessed the efficacy of valerian in combination with hops in the treatment of primary insomnia, found that subjects reported improvement in at least one sleep parameter, often sleep latency and sleep quality. Valerian, singularly or in combination with hops, may be suitable as a trial in patients wanting an alternative to current treatment, but better quality studies are needed before physicians can confidently promote the use of these herbs as an effective, reliable approach to treating primary insomnia.

Study design limitations

There were numerous inconsistencies between the studies that make comparison and interpretation of the results difficult. These study design differences include variations in the following:

- how sleep disorders were defined and measured
- the inclusion and exclusion criteria used to select subjects, and
- the dosage and duration of treatment.

Furthermore, differences in the concentration of active constituents in the different herbal preparations, according to the extraction method used, might explain some of the inconsistencies in the findings. Plant constituents can vary according to the method of cultivation, plant species, climate and season, geographical location and extraction techniques.[12]

This review also identified that many of the studies were limited by:

- short treatment durations, eg. 1 day
- small sample sizes
- insufficient washout times in crossover studies
- differences in herbal extract preparation methods, ie. ethanol versus aqueous preparations
- variations in dosage of herbal preparations
- variations in tools used to measure sleep parameters
- lack of placebo control.

Conclusion

As this review has found, herbal medicines may improve sleep latency and quality of sleep. However, methodological problems of studies included in this review, weaken the conclusions of these findings and their application to clinical practice. Further studies with robust design are needed before the efficacy of herbal treatment for the treatment of primary insomnia in clinical practice can be established with confidence.

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