

# Complementary and Alternative Medicine in Clinical Practice Guideline for Insomnia

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**Objectives:** The aim of this review was to investigate whether evidence of complementary and alternative medicine (CAM) was reflected in clinical practice guidelines (CPGs) for insomnia based on relevant clinical trials.

**Methods:** We conducted a systematic search on domestic and international CPG databases and medical databases. In addition, we conducted manual searches of relevant articles. Three authors independently searched and selected relevant studies; any disagreement was resolved by discussion. We extracted and analyzed the following data: published language, country, development group, participants, interventions, presence or absence of recommendations for CAM, level of evidence, grade of recommendation for CAM, and methods of development.

**Results:** We identified 8,241 records from domestic and international databases, and 22 CPGs were included. Eleven of the 22 CPGs mentioned CAM interventions including herbal medicine, relaxation, acupuncture moxibustion, Tai Chi, meditation, hypnosis, biofeedback, Tuina, and external herbal medicine. However, most of the CPGs indicated 'no recommendation' or 'weak recommendation' for CAM interventions. Only *Valeriana dageletiana Nakai* and relaxation were considered to have experimental evidence. *Valeriana dageletiana Nakai* was recommended for improvement of sleep latency, sleep maintenance, total sleeping time, and sleep cycle. Relaxation was recommended as effective intervention for relieving physical and psychological arousal.

**Conclusions:** Despite systematic reviews and randomized controlled trials on CAM for insomnia, most of the CPGs for insomnia did not reflect the evidence obtained. Further CPGs for insomnia should be developed by considering the current advanced studies in the field of CAM.

**Key Words:** Insomnia, Complementary and Alternative Medicine, Korean Medicine, Clinical Practice Guideline.

## I. INTRODUCTION

Insomnia is one of the most popular neuropsychiatric disorders all over the world, which causes significantly impaired quality of life and enormous societal costs<sup>1,2</sup>. In recent population-based epidemiological study, according to diagnostic standard including DSM (the Diagnostic and Statistical Manual), ICD (International Classification of Diseases), and ICSD (International Classification of Sleep Disorder), 4~22% of adults in Hong Kong are suffering from insomnia<sup>3</sup>. In other epidemiological studies in Japan and Korea, 13% and 23% of adults are reported to suffer from insomnia, respectively<sup>4,5</sup>. In traditional concept of insomnia, it was considered as a secondary pathological condition rather than a disease. But as insomnia has been better understood, now it is considered that insomnia can be caused as an independent disease as well as secondary product from other diseases<sup>6</sup>.

Generally CBT-I (Cognitive Behavioral Therapy for Insomnia) consisted of sleep education, stimulus control, sleep restriction, and cognitive therapy is recommended primarily as a conventional treatment of insomnia<sup>7</sup>. And medications including benzodiazepines, nonbenzodiazepine hypnotics, melatonin agonists, and antidepressants are used to shorten sleep latency and to improve the quality of sleep<sup>8</sup>. However the pharmacotherapy will not contribute to a fundamental solution in patients of insomnia, and it has some limitations including poor adherence, drug dependency, tolerance, and side effects like daytime drowsiness, or dizziness<sup>9,10</sup>. These limitations of pharmacotherapy turned some insomnia patients and relevant health care providers on to CAM (Complementary and Alternative Medicine) to find effective alternative treatment for insomnia and to compensate those limitations.

CAM is defined as 'a broad set of health care practices that are not part of that country's own tradition and are not integrated into the dominant health care

system'<sup>11</sup>. According to an analysis study of 2007 National Health Interview Survey conducted in USA, about 45% among adults who suffered from insomnia symptoms were estimated to receive CAM therapies in a year<sup>12</sup>.

Catching up with this growing interest in CAM, studies on CAM therapy of insomnia have been actively conducted<sup>13-19</sup>. Based on these evidences, some systematic reviews and meta-analyses about acupuncture<sup>13-15</sup>, natural products including herbs and herbal remedies based on TCM (Traditional Chinese Medicine)<sup>16,17</sup>, valerian<sup>18</sup>, L-tryptophan and kava<sup>19</sup> to treat insomnia were published. Moreover these evidences about CAM therapy on insomnia have been mentioned in some CPGs (Clinical Practice Guidelines), which is one of the most effective and powerful method to apply EBM (Evidence-Based Medicine) in clinical practice, and they allowed patients and doctors to consider broader treatment options on insomnia.

However recommendations of CPG varied from nation to nation or society to society, as the recommendations are presented not only by the evidences, but also the social circumstances, medical resources, economic feasibilities, and so on. In this review, we performed systematic search of CPGs on insomnia, and investigated the evidence level and recommendations of CAM therapy to assess current status of CAM therapy in CPGs on insomnia.

## II. METHODS

### 1. Study selection

CPGs on insomnia which are corresponding to the definition of CPG in this review and described treatments on insomnia were included. The screening process was performed by 3 authors (CY, HW, EJ) independently, and every disagreement was solved by discussion.

## 1) Definition of CPG in this review

We defined CPG in this review as below, considering a precedent study<sup>20</sup>. Review article, systematic review without recommendation, medical information for patient, education manual, literal translation of CPG, assessment of medical technology, clinical pathway, or CPG developed by one researcher were not considered as CPGs and were excluded in this review<sup>21</sup>.

(1) Literature which meets the definition of ‘CPG’<sup>22</sup>: ‘Statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.’

(2) Literature which contains recommendations.

(3) Final version of literature when it has been updated.

## 2) Classification of CAM in this review

The category of CAM includes the following, considering the NCCIH (National Center for Complementary and Integrative Health) and Cochrane Collaboration classification system for CAM<sup>23</sup>.

(1) Whole medical system (e.g. traditional Chinese medicine, naturopathy, homeopathy, and ayurveda)

(2) Mind-body interventions, biology-based practices (e.g. herbs, foods, vitamins, and other natural substances)

(3) Manipulative and body-based practices (e.g. chiropractic and osteopathic manipulation)

(4) Energy medicine

(5) Biofield therapies

(6) Bioelectromagnetic based therapies (e.g. pulsed fields, alternating-current, and direct-current fields)

## 2. Search strategy

### 1) CPG DBs

We searched several CPG-related DBs to find relevant CPGs. In domestic DB, KoMGI (Korean Medical Guideline Information Center) was used, whereas in foreign DBs, G-I-N International Guideline Library, AHRQ (Agency for Healthcare Research and Quality, National Guideline Clearinghouse), NICE (National Institute for Health and Care Excellence), SIGN (Scottish Intercollegiate Guideline Network), NHMRC (National Health and Medical Research Council), CGC (China Guideline Clearinghouse) and MINDS (Medical Information Network Distribution Service) were used. The keywords were ‘insomnia’ and ‘sleep disorder’. The search performed at March 9, 2016, and CPGs published before the date were investigated.

### 2) Medical DBs

We conducted searches on several medical DBs to investigate comprehensively. In foreign DBs, PubMed, CNKI (China National Knowledge Infrastructure), and J-STAGE (Japan Science and Technology Information Aggregator, Electronic) were used. The keywords were ‘insomnia’, ‘sleep disorder’, ‘practice guideline’, and ‘CPG’. Given that CPG is usually not published on general DBs, manual search on Google Scholarship with the keywords was also conducted.

The following search strategies were used that (‘insomnia’ or ‘sleep disorder’) and (‘practice’ or ‘guideline’ or ‘CPG’) in PubMed, (‘临床实践指南’ or ‘guideline’) and (‘失眠’ or ‘不眠’ or ‘不寐’ or ‘睡眠障碍’ or ‘insomnia’ or ‘sleep disorder’) in CNKI, and ‘ガイドライン’ and ‘眠’ in J-STAGE.

## 3. Analysis

With CPGs which met our inclusion criteria, we investigated basic characteristics of the CPGs including

language, country, type of developer, target population, intervention, presence of CAM therapy, evidence levels and recommendations of CAM therapy, and method of grading recommendations by reviewing full-text of CPGs. The analysis was performed by 3 authors (CY, HW, EJ) independently, and every disagreement was solved by discussion.

### III. RESULTS

#### 1. Selection of CPGs

Totally 8,241 records were searched, among them 631 records were searched from CPG DBs and 7,610 records from medical DBs. After 3 duplicates removed, 8,208 records, which were not CPG or not related with insomnia, were excluded by title and abstract, and 30 records were screened. The 30 records were

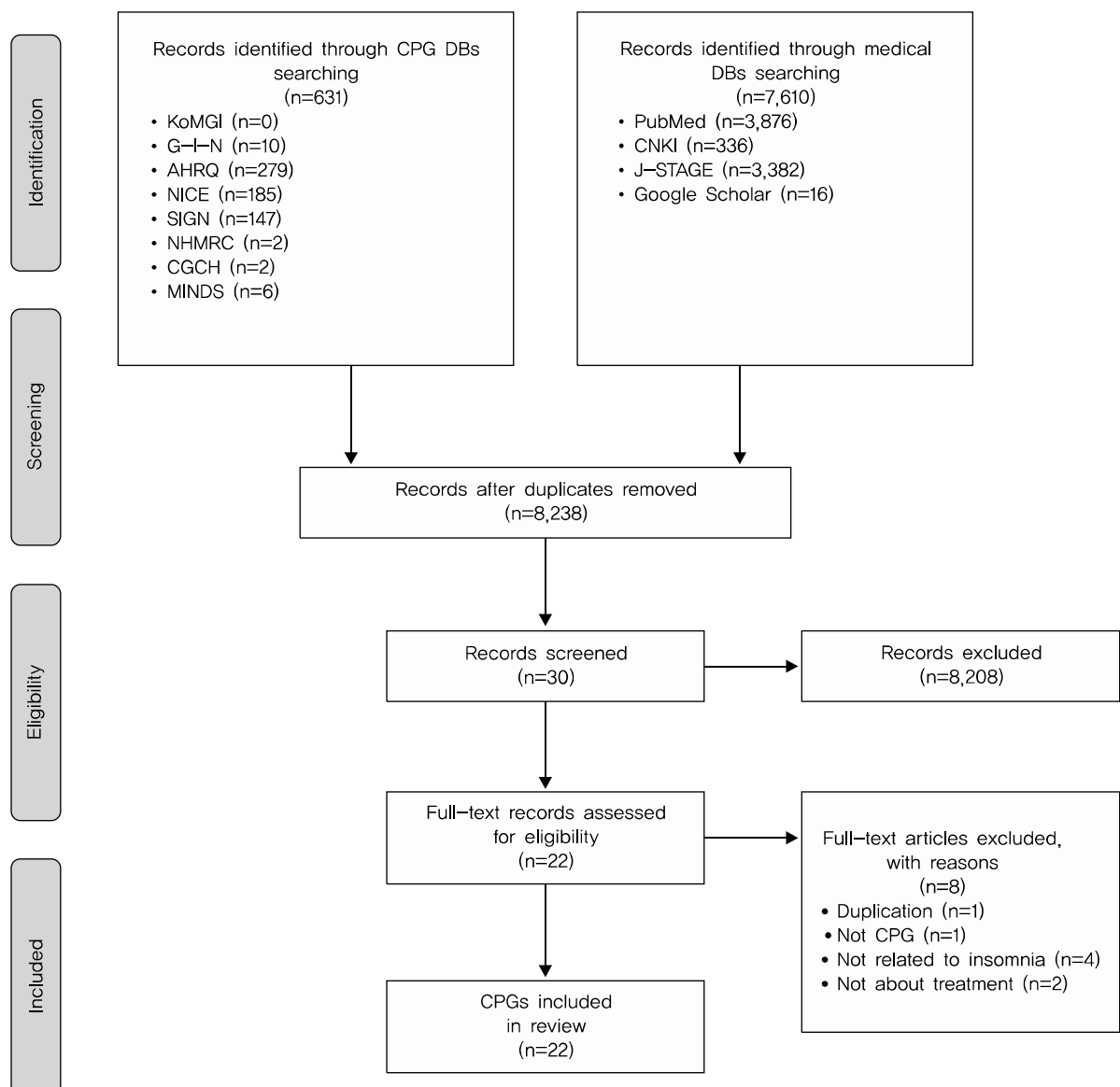


Fig. 1. PRISMA flow diagram.

reviewed by full text to find relevant CPGs. 1 record of duplication, 1 record not corresponding to the definition of CPG, 4 records not related with insomnia, and 2 records not about treatment of insomnia were excluded. Finally 22 CPGs which met our inclusion criteria were selected (Fig. 1).

## 2. The basic characteristics of included CPGs

When analyzing the 22 included CPGs in terms of DBs, 5 CPGs<sup>24-28)</sup> were obtained from PubMed, 3 CPGs<sup>29-31)</sup> from AHRQ, 1 CPG from NICE<sup>32)</sup> and CGC<sup>33)</sup> respectively, and 12 CPGs<sup>34-45)</sup> from manual search.

Publication year varied from 2004 to 2016, and 8 CPGs<sup>25,26,28,29,31,35,36,38)</sup> were conducted in USA, 5 CPGs<sup>32,37,40-42)</sup> in UK, 3 CPGs in Canada<sup>24,34,39)</sup> and Japan<sup>44,45)</sup> respectively, and 1 CPG in Ireland<sup>43)</sup>, Spain<sup>30)</sup>, Brazil<sup>27)</sup>, and China<sup>33)</sup> respectively. When analyzing the CPGs in terms of type of developer, 10 CPGs<sup>27,28,31,33-37,39,43)</sup> were developed by academic societies, 6 CPGs<sup>26,30,32,40-42)</sup> by governments, 1 CPG by government and academic society<sup>45)</sup>, 3 CPGs<sup>25,38,44)</sup> by expert groups, and 1 CPG by university<sup>29)</sup> and non-profit medical institution<sup>24)</sup> respectively. In terms of development method, bibliographic search and assessment which are considered as evidence-based method in this review was used in 12 CPGs<sup>24,25,27-29,33-35,37-39,45)</sup>, expert consensus in 6 CPGs<sup>26,30-32,36,44)</sup>, and no mention of the method in 4 CPGs<sup>40-43)</sup>.

The included CPGs recommended various interventions on insomnia including sleep hygiene education, cognitive behavior therapy, pharmacological treatment, and nonpharmacological treatment. Among 11 CPGs<sup>25,26,28-30,33-35,38,44,45)</sup> which described CAM therapies, herbal medicine was stated in 7 CPGs<sup>25,30,33,35,38,44,45)</sup>, relaxation in 5 CPGs<sup>26,28,34,35,38)</sup>, acupuncture (including acupressure) and moxibustion in 4 CPGs<sup>26,29,33,35)</sup>, Tai-Chi<sup>26,29)</sup>, meditation<sup>26,34)</sup>, yoga<sup>29,34)</sup> and biofeedback<sup>28,34)</sup> in 2 CPGs respectively,

tuina<sup>33)</sup>, herbal external application<sup>33)</sup>, and hypnosis<sup>34)</sup> in 1 CPG respectively.

There were 'no recommendation' or 'weak recommendations' for the most of CAM therapies stated, except for relaxation<sup>28,38)</sup>. In all CPGs<sup>25,26,28-30,33-35,38,44,45)</sup> which stated CAM therapies, CAM therapies were considered as complementary treatment to Western medicine (Table 1).

## 3. Analysis of CAM therapy on included CPGs

### 1) Herbal medicine

An evidence-based CPG which was conducted in USA, 2007<sup>38)</sup>, mentioned several herbs and dietary supplements including Valeriana dageletiana Nakai, Lavandula, Passiflora caerulea, Ecklonia cava, Hypericum perforatum, melatonin, glutamine, niacin, and 1-tryptophan in treatment of insomnia. Among them Valeriana dageletiana Nakai and melatonin were considered to have some evidences and the other herbs and dietary supplements were not considered to have sufficient evidence to recommend.

An evidence-based CPG which was conducted in USA, 2008<sup>25)</sup>, didn't recommend herbal medicine considering insufficient evidence of its efficacy and safety, except for Valeriana dageletiana Nakai. The CPG mentioned that there are some evidences of Valeriana dageletiana Nakai to improve on sleep latency, sleep maintenance, total sleeping time, and sleep cycle.

An expert consensus based CPG conducted in Spain, 2011<sup>30)</sup>, mentioned that Valeriana dageletiana Nakai alone or Valeriana dageletiana Nakai combined with Humulus lupulus have insufficient evidence to recommend on insomnia of children and adolescents. The CPG mentioned that using herbs requires caution due to insufficient evidence.

An evidence-based CPG conducted in China, 2012<sup>33)</sup>, summarized the pattern identifications of in-

**Table 1.** Characteristics on Included CPGs

No.	DB (language)	Country/Group (published year)	Target population (age group)	Intervention	Presence of CAM	Methods of grading recommendation
1	PubMed (English)	Canada/The Sleep Disturbance Expert Panel on behalf of the Cancer Journey Advisory Group of the Canadian Partnership Against Cancer (2013) <sup>24)</sup>	Sleep disturbances with cancer (adults)	1. Non-Pharmacological intervention 2. Pharmacological intervention	None	ADAPTE methodology, AGREE II <sup>47)</sup>
2	PubMed (English)	USA/Expert group (2008) <sup>25)</sup>	Chronic insomnia (adults)	1. Psychological and behavioral therapies 2. Pharmacological treatment 3. Combined treatments	1. Herbal substance	AASM Levels of Recommendations
3	PubMed (English)	USA/NIH (2009) <sup>26)</sup>	Sleep disorders (including insomnia) (older persons)	1. Behavioral treatment 2. Sleep hygiene and sleep education 3. Sleep restriction-sleep compression 4. Stimulus control 5. Relaxation therapy 6. CBT-I 7. Exercise and CAM treatment modalities 8. Pharmacologic treatment 9. Combination therapy	1. Relaxation therapy (PMR, diaphragmatic breathing, meditation) 2. CAM therapy (Tai-Chi, acupressure)	Expert consensus
4	PubMed (English)	Brazil/Brazilian Sleep Association (2010) <sup>27)</sup>	Insomnia (NS)	1. CBT 2. Pharmacological treatment	None	Evidence-based method
5	PubMed (English)	USA/Standards of Practice Committee of the American Academy of Sleep Medicine (2006) <sup>28)</sup>	Chronic insomnia (NS)	1. Psychological and behavioral interventions	1. Relaxation training 2. Biofeedback	AASM Levels of Recommendations
6	AHRQ (English)	USA/University of Texas at Austin School of Nursing, Family Nurse Practitioner Program (2014) <sup>29)</sup>	Primary insomnia (middle-aged and older adults)	1. Sleep hygiene education 2. CBT 3. Pharmacological intervention 4. Non-pharmacological intervention	1. Tai-Chi 2. Acupressure/Acupuncture 3. Yoga	Subjective review weighting according to a rating scheme
7	AHRQ (English)	Spain/Guia Salud Lain Entralgo Agency (2011) <sup>30)</sup>	Sleep problems (including insomnia) (children and adolescents)	1. Sleep hygiene education 2. Psychological intervention 3. Pharmacological management 4. Health supplement food	1. Herbal medicine	Expert consensus
8	AHRQ (English)	USA/American Medical Directors Association (2006) <sup>31)</sup>	Sleep disorders (including insomnia) in the long-term care setting (elderly)	1. Non-pharmacological intervention 2. Pharmacological intervention	None	Expert consensus
9	NICE (English)	UK/NICE appraisal committee & project team (2004) <sup>32)</sup>	Insomnia (NS)	1. Pharmacological intervention	None	Expert consensus

Table 1. Continued 1

No.	DB (language)	Country/Group (published year)	Target population (age group)	Intervention	Presence of CAM	Methods of grading recommendation
10	CGC (Chinese)	China/Sleep Disorder Group of Chinese Society of Neurology (中華醫學會神經病學分會睡眠障礙學組) (2012) <sup>33)</sup>	Insomnia (NS)	1. Sleep hygiene 2. CBT 3. Pharmacological treatment 4. CAM	1. Herbal medicine 2. Acupuncture, moxibustion 3. Tuina 4. External application of herbal medicine	Evidence-based method
11	GoogleScholar (English)	Canada/Clinical Practice Guidelines Working Group (2010) <sup>34)</sup>	Primary insomnia (adults)	1. Behavioral and cognitive non-pharmacologic strategies	1. Yoga, PMR, biofeedback, hypnosis, meditation	Basis of recommendations was formed based on major literatures
12	GoogleScholar (English)	USA/American College of Physicians (2016) <sup>35)</sup>	Chronic insomnia disorder (adults)	1. Psychological treatment 2. Pharmacological treatment 3. CAM	1. Relaxation therapy 2. Acupuncture 3. Chinese herbal medicine	ACP grading system based on the GRADE approach
13	GoogleScholar (English)	USA/Group Health (2015) <sup>36)</sup>	Insomnia, Obstructive sleep apnea, Restless legs syndrome	1. Behavioral treatment 2. Pharmacologic treatment	None	Expert consensus
14	GoogleScholar (English)	UK/British Association for Psychopharmacology (2015) <sup>37)</sup>	Insomnia, parasomnias and circadian rhythm disorders (NS)	1. Psychological treatment 2. Pharmacological treatment	None	Evidence-based method
15	GoogleScholar (English)	USA/Expert group (2007) <sup>38)</sup>	Insomnia (NS)	1. Sleep hygiene measures and exercise 2. Non-pharmacologic therapy 3. Pharmacologic treatment	1. Relaxation therapy 2. Herbs and supplements	SORT evidence rating system
16	GoogleScholar (English)	Canada/Guidelines and Protocols Advisory Committee (2004) <sup>39)</sup>	Non-respiratory sleep disorders (adults)	1. Sleep hygiene 2. Behavioral intervention 3. Hypnotics	None	Evidence-based method
17	GoogleScholar (English)	UK/Cheshire and Merseyside Palliative and End of Life Care Network Audit Group (2014) <sup>40)</sup>	Insomnia (NS)	1. Drugs which may contribute to insomnia should be reviewed and discontinued where possible 2. Psychological and behavioral therapy 3. Hypnotic drugs	None	Unclear
18	GoogleScholar (English)	UK/Drugs and Therapeutics Group (2015) <sup>41)</sup>	Insomnia (adults)	1. Sleep hygiene 2. Pharmacological treatment	None	Unclear
19	GoogleScholar (English)	UK/Pharmacy Department Medicines Management Services (2014) <sup>42)</sup>	Insomnia (NS)	1. Non-pharmacological management 2. Pharmacological treatment	None	Unclear
20	GoogleScholar (English)	Ireland/Irish Sleep Society (2015) <sup>43)</sup>	Insomnia (NS)	1. Sleep hygiene 2. Pharmaceutical treatment 3. CBT	None	Unclear

Table 1. Continued 2

No.	DB (language)	Country/Group (published year)	Target population (age group)	Intervention	Presence of CAM	Methods of grading recommendation
21	GoogleScholar (Japanese)	Japan/Guideline Working Group for Diagnosis and Treatment of Insomnia (睡眠障害の診断・治療ガイドライン研究会 (2012) <sup>44)</sup>	Sleep disorder (NS)	1. Pharmacological treatment. 2. Non-pharmacological management	1. Herbal medicine	Expert consensus
22	GoogleScholar (Japanese)	Japan/Welfare Labor Science Laboratory & Japan Sleep Association (厚生労働科学研究班・日本睡眠学会) (2013) <sup>45)</sup>	Insomnia (NS)	1. Sleep hygiene 2. Pharmacological treatment 3. CBT	1. Herbal medicine	GRADE

AASM: American Academy of Sleep Medicine, ACP: American College of Physicians, AGREE: Appraisal of Guidelines for Research and Evaluation, AHRQ: Agency for Healthcare Research and Quality, CAM: Complementary and Alternative Medicine, CBT: Cognitive Behavioral Therapy, CBT-I: Cognitive Behavioral Therapy for Insomnia, CGC: China Guideline Clearinghouse, DB: database, GRADE: Grading of Recommendations, Assessment, Development and Evaluations, NICE: National Institute for Health and Care Excellence, NIH: National Institutes of Health, NS: not specified, PMR: Progressive Muscle Relaxation, Ref: reference, SORT: Strength of Recommendation Taxonomy.

somnia into six types, but didn't mention any recommendations: pattern of depressed liver qi transforming into fire (肝鬱化火), pattern of internal harassment of phlegm-heat (痰熱内擾), yin deficiency with effulgent fire (陰虛火旺), dual deficiency of the heart-spleen (心脾兩虛), heart-gallbladder qi deficiency pattern (心膽氣虛), and heart-kidney non-interaction pattern (心腎不交). The CPG listed to use herbal medicine by these pattern identifications, and listed the frequently used herbs: Ziziphus jujuba Mill (酸棗仁), Thuja orientalis Linne (柏子仁), Poria cocos (茯苓), Polygala tenuifolia (遠志), Schizandra chinensis Baili (五味子), Caulis polygoni multiflori (夜交藤), Curcuma longa Linne (鬱金), Gardenia jasminoides for. grandiflora (梔子), Pinellia ternata (半夏), Liliun longiflorum Thunb. (百合), and Dimocarpus longan Lour. (龍眼肉).

An expert consensus based CPG developed by Guideline working group for diagnosis and treatment of insomnia, 2012<sup>44)</sup>, listed some herbal medicines on insomnia which are covered by insurance in Japan: Da Chai Hu Tang (大柴胡湯), Chai Hu Gui Zhi Gan Jiang Tang (柴胡桂枝乾薑湯), Ban Xia Hou Pu Tang (半夏厚朴湯), Yi Gan San (抑肝散), Gui Pi Tang (歸脾湯), Suan Zao Ren Tang (酸棗仁湯), and Wen Dan Tang (溫膽湯). Additionally the CPG mentioned that these herbal medicines are effective on several neurosis and meno-

pause syndrome as well as insomnia by regulating autonomic nervous system and relaxing mood of patients.

An evidence-based CPG conducted in Japan, 2013<sup>45)</sup>, didn't recommend herbal medicine due to insufficient evidence of its efficacy. However The CPG mentioned that when comorbidity with insomnia is improved by herbal medicine the symptom of insomnia can be alleviated too.

An evidence-based CPG conducted in USA, 2016<sup>35)</sup>, mentioned that there is insufficient evidence of efficacy and safety of herbal medicine to recommend it on insomnia.

## 2) Relaxation

An evidence-based CPG conducted in USA, 2006<sup>28)</sup>, mentioned that relaxation is effective on chronic insomnia and strongly recommended relaxation on it. In this updated CPG, the recommendation level of relaxation was increased from previous version<sup>46)</sup>, as 4 RCTs (randomized controlled trials) of relaxation on insomnia had conducted since then.

An evidence-based CPG conducted in Canada, 2010<sup>34)</sup>, mentioned that relaxation is effective on insomnia as it relieves physical and psychological arousal. The CPG listed some specific measures of relaxation: deep breathing, light exercise, stretching, and



yoga. And also it mentioned that progressive muscle relaxation, biofeedback, and meditation can be provided by experts to manage stress.

An evidence-based CPG conducted in USA, 2007<sup>38)</sup>, recommended exercise, cognitive behavioral therapy, and relaxation as effective non-pharmacological therapies on insomnia.

An expert consensus based CPG conducted in USA, 2009<sup>26)</sup>, mentioned that relaxation can be used to keep stable state when patient is trying to go to sleep. The CPG listed some measures of relaxation; meditation, progressive muscle relaxation, and abdominal breathing.

An evidence-based CPG conducted in USA, 2016<sup>35)</sup>, mentioned that there is insufficient evidence to judge the efficacy of relaxation on senile chronic insomnia patients.

### 3) Acupuncture and moxibustion

An expert consensus based CPG conducted in USA, 2009<sup>26)</sup>, mentioned and assessed that some studies reported that acupuncture may improve insomnia, but the efficacy of acupuncture on insomnia is still unclear.

An evidence-based CPG conducted in China, 2012<sup>33)</sup>, mentioned that herbal medicine and acupuncture can be helpful on insomnia patients.

An evidence-based CPG conducted in USA, 2014<sup>29)</sup>, mentioned that some studies reported acupuncture, especially ear acupuncture, improved senile insomnia, but further studies were needed.

A CPG evidence-based CPG conducted in USA, 2016<sup>35)</sup>, mentioned that there is insufficient evidence to judge the efficacy and safety of acupuncture on insomnia.

### 4) Tai-Chi

An expert consensus based CPG conducted in USA, 2009<sup>26)</sup>, mentioned and assessed that some studies reported Tai-Chi improved insomnia, but the efficacy of Tai-Chi on insomnia is still unclear.

An evidence-based CPG conducted in USA, 2014<sup>29)</sup>, mentioned that Tai-Chi can be recommended as a non-pharmacological intervention by expert to improve senile insomnia.

### 5) Meditation and hypnosis

An evidence-based CPG conducted in Canada, 2010<sup>34)</sup>, mentioned meditation and hypnosis as measures of relaxation.

An expert consensus based CPG conducted in USA, 2009<sup>26)</sup>, mentioned meditation as a part of relaxation.

### 6) Yoga

An evidence-based CPG conducted in Canada, 2010<sup>34)</sup>, mentioned yoga as a measure of relaxation.

An evidence-based CPG conducted in USA, 2014<sup>29)</sup>, mentioned that yoga is known to improve senile insomnia, but the clinical evidence is limited.

### 7) Biofeedback

An expert consensus based CPG conducted in USA, 2006<sup>28)</sup>, mentioned that biofeedback is effective on chronic insomnia, and recommended biofeedback on it.

An evidence-based CPG conducted in Canada, 2010<sup>34)</sup>, mentioned biofeedback as a measure of relaxation.

### 8) Tuina and herbal external application

An evidence-based CPG conducted in China, 2012<sup>33)</sup>, mentioned that herbal medicine, tuina, and herbal external application can be helpful on insomnia patients.

### 9) Safety and economic evaluation

An expert consensus based CPG conducted in USA, 2007<sup>38)</sup>, mentioned that Valeriana dageletiana Nakai can cause daytime drowsiness and rarely liver injury. An expert consensus based CPG developed by Guideline working group for diagnosis and treatment of insomnia, 2012<sup>44)</sup>, mentioned that herbal medicines has few side effects as it contains a few medicinal

properties, but overindulgence of *Glycyrrhiza uralensis* (甘草) can cause renal injury, hypokalemia, and pseudoaldosteronism. And the CPG also mentioned that manufacturing processes of herbal medicine can affect the safety.

In 11 CPGs<sup>25,26,28-30,33-35,38,44,45</sup> which stated CAM therapies, there's no statement about economic evaluation (Table 2).

## IV. DISCUSSION

We performed systematic search, and investigated the current of evidence level and recommendations of CAM therapy on insomnia.

As a result, 22 CPGs were included in this review, and among them 11 CPGs<sup>25,26,28-30,33-35,38,44,45</sup> stated CAM therapies. The most frequently stated CAM ther-

**Table 2.** TCM Therapy Described in Included CPGs

No.	Country/Group (published year)	CAM therapy	Evidence level/Recommendation of the CAM therapy	Side effects of the CAM therapy
1	USA/Expert group (2008) <sup>25</sup>	1. Herbal substance	1. NR/Consensus (not recommended)	NR
2	USA/NIH (2009) <sup>26</sup>	1. Relaxation therapy (PMR, diaphragmatic breathing, meditation) 2. CAM therapy (Tai-Chi, acupressure)	NR (insufficient)	NR
3	USA/Standards of Practice Committee of the American Academy of Sleep Medicine (2006) <sup>28</sup>	1. Relaxation training 2. Biofeedback	1. I&II (good quality)/Standard (high degree of clinical certainty) 2. -/Guideline (moderate degree of clinical certainty)	NR
4	USA/University of Texas at Austin School of Nursing, Family Nurse Practitioner Program (2014) <sup>29</sup>	1. Tai-Chi 2. Acupressure/Acupuncture 3. Yoga	1. Low (insufficient)/C (recommended selectively) 2. Low (insufficient)/I (balance of benefits and harms cannot be determined) 3. Low (insufficient)/I (balance of benefits and harms cannot be determined)	NR
5	Spain/Guia Salud Laín Entralgo Agency (2011) <sup>30</sup>	1. Herbal medicine	1. NR/B (insufficient) or D (not recommended)	NR
6	China/Sleep disorder group of Chinese society of neurology (中華醫學會神經病學分會睡眠障礙學組) (2012) <sup>33</sup>	1. Herbal medicine 2. Acupuncture & moxibustion 3. Tuina 4. External application of herbal medicine	NR	NR
7	Canada/Clinical Practice Guidelines Working Group (2010) <sup>34</sup>	1. Yoga, PMR, biofeedback, hypnosis, meditation	NR	NR
8	USA/American College of Physicians (2016) <sup>35</sup>	1. Relaxation therapy 2. Acupuncture 3. Chinese herbal medicine	1. Insufficient 2. Insufficient 3. Insufficient	NR
9	USA/Expert group (2007) <sup>38</sup>	1. Relaxation therapy 2. Herbs and supplements	1. A (good quality)/- (recommended) 2. Not stated (insufficient)	Valerian root: Residual daytime sedation and hepatotoxicity Glycyrrhizae Radix: renal dysfunction Calcium: urinary stone
10	Japan/Guideline working group for diagnosis and treatment of insomnia (睡眠障害の診断・治療ガイドライン研究会) (2012) <sup>44</sup>	1. Herbal medicine	NR	Glycyrrhizae Radix: renal dysfunction Calcium: urinary stone
11	Japan/Welfare Labor Science Laboratory&Japan Sleep Association (厚生労働科学研究班・日本睡眠学会) (2013) <sup>45</sup>	1. Herbal medicine	1. NR (insufficient)/C2 (not recommended)	NR

CAM: Complementary and Alternative Medicine, NIH: National Institutes of Health, NR: not recorded, PMR: Progressive Muscle Relaxation, Ref: reference.

apy was herbal medicine, and relaxation, acupuncture and moxibustion, Tai-Chi, meditation, yoga, biofeedback, tuina, herbal external application, and hypnosis followed. However most recommendations of CAM therapy was on relaxation and *Valeriana dageletiana* Nakai, and there was weak recommendations or no recommendation for the other CAM therapies.

In herbal medicines, statement on the efficacy of *Valeriana dageletiana* Nakai was a majority, and some CPGs<sup>25,30,38</sup> mentioned that it may be effective to improve insomnia. Two CPGs which were conducted in China<sup>33</sup> and Japan<sup>44</sup> respectively classified herbal medicine based on pattern identification, and 1 CPG<sup>44</sup> listed some herbal medicines on insomnia which are covered by insurance in Japan. In relaxation, except for 1 CPG<sup>35</sup> of senile insomnia, the other 4 CPGs<sup>26,28,34,38</sup> recommended relaxation on insomnia or mentioned the relaxation is effective on insomnia. In acupuncture and moxibustion, most of CPGs<sup>26,29,35</sup> mentioned that the efficacy of acupuncture on insomnia is still unclear due to insufficient evidence. In Tai-Chi, 1 CPG<sup>29</sup> mentioned that Tai-Chi can be recommended as a non-pharmacological intervention by expert to improve senile insomnia, while in yoga, 1 CPG<sup>29</sup> mentioned that the clinical evidence of yoga on senile insomnia is limited. In biofeedback, 1 CPG<sup>28</sup> mentioned that biofeedback is effective on chronic insomnia, and recommended biofeedback on it. In tuina and herbal external application, 1 CPG<sup>33</sup> mentioned that they can be helpful on insomnia patients.

Sometimes CPG is used as a part of health care policy, so not only clinical efficacy of the intervention and safety but also the economic evaluation are important. In included CPGs, there were 2 CPGs<sup>38,44</sup> which mentioned adverse effect of CAM therapy, about *Valeriana dageletiana* Nakai and *Glycyrrhiza uralensis* (甘草) respectively. However there was no CPG which performed economic evaluation.

We can suggest several reasons why CPGs included

in this review omitted or underestimated CAM, especially about traditional oriental medicine such as herbal medicine and acupuncture.

First, although development groups were consisted of insomnia experts, most of them were developed in western countries where traditional oriental medicine was not used as major treatment except for three<sup>33,44,45</sup>. These factors are thought to make the CPGs have no mention of traditional oriental medicine, such as herbal medicine and acupuncture, as a therapeutic option. Also, even if traditional oriental medicine including herbal medicine and acupuncture was mentioned in the CPGs, they may not be evaluated properly because developers were not experts of tradition oriental medicine. When they formulated recommendations, especially during process for consensus, they couldn't consider clinical effectiveness or circumstance of traditional oriental medicine properly because of a lack of deep understanding.

Second, most of the evidences in the CPGs, except for three<sup>33,44,45</sup>, were studies conducted in western countries. Current evidences that assess effectiveness of CAM on sleep disorders<sup>13-17</sup> were not considered in CPGs included in this review. For evaluating CAM, it is necessary to search and include studies conducted in East Asia. Because CAM is used as major treatment options in Korea, China, Japan, Taiwan, etc., CAM was actively investigated in these countries.

Finally, current evidences of traditional oriental medicine have quantitative and qualitative limitations. Because there was an opinion that traditional oriental medicine needed a different approach from western medicine<sup>48</sup>, it can be thought that studies based on evidence-based medicine have not been conducted actively in this field. Moreover, the methodological golden standard suitable for clinical trials of herbal medicine and acupuncture was not established. Therefore, clinical trials evaluating traditional oriental medicine were usually graded as low-quality due to

limitation of the methodology. As a result, CAM, including traditional oriental medicine, couldn't be reflected in CPGs based on EBM, and it was recommended weakly with low-quality of evidence.

Nevertheless given the increasing interest in CAM<sup>12)</sup> and the limitations of conventional treatments<sup>9,10)</sup>, clinical studies and evidences of CAM on insomnia seem to be increased consistently. As analyzed above, assessments of the efficacy of CAM therapy in CPG are very limited, and there's little evidence of economics evaluation and safety. However, high quality clinical evidences like systematic review and RCT on CAM therapy including herbal medicine, acupuncture, moxibustion, and meditation have been accumulated recently<sup>13-17,48)</sup>. We think that these clinical evidences should be considered when new CPG will be developed or previous CPGs will be updated to follow the growing interest in CAM and the current level of evidence on treating insomnia by CAM therapies. Especially, systematic review and meta-analysis which evaluate efficacy of traditional oriental medicine need to collect expert opinions on subgroup analysis. By conducting well-designed subgroup analysis, we can identify the sources of heterogeneity as well as we can figure out the clinical differences among herbal medicines, methods of acupuncture therapies, acupoints, and duration of treatment.

In terms of economic evaluation, given the project of KMCPG (Korean Medicine Clinical Practice Guideline) development is going on in Korea from 2016 and the Ministry of Health and Welfare pronounced that they'll support to perform clinical trials and economic evaluations to develop KMCPGs, in pre-arranged insomnia KMCPGs economic evaluation of CAM therapy on insomnia would be performed.

## V. CONCLUSION

We investigated the trend of CPG on insomnia by

systematic search and the current of evidence level and recommendations of CAM therapy in the CPGs. According to our inclusion criteria, 22 CPGs were included in this review, and the following conclusions were obtained.

1. Among 22 CPGs on insomnia, 11 CPGs stated CAM therapy.
2. The most frequently stated CAM therapy was herbal medicine, and statement on the efficacy of *Valeriana dageletiana* Nakai was a majority.
3. In acupuncture and moxibustion, most of CPGs mentioned that the efficacy of acupuncture on insomnia is still unclear due to insufficient evidence.
4. The reasons why CPGs for insomnia didn't mention CAM or recommended it weakly can be considered that most developers of CPGs included in this review were western researchers, the latest CAM researches were not reflected, and the quantitative and qualitative limitations of CAM researches were existed.
5. Further CPGs have to address CAM therapies as alternative and complementary therapeutic options on insomnia, and to evaluate the practical effectiveness of CAM its experts should be included in development group as well as latest CAM researches need to be considered.

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