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The Relationship Between Commonly Used NSAID and Insomnia: A Case Report

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Abstract

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for pain and inflammation, yet their potential impact on sleep quality remains uncertain. This study aimed to examine the relationship between NSAID use and insomnia symptoms among adults in a hospital setting. A descriptive cross-sectional study was conducted at RSI Jemursari Hospital, Surabaya, using medical records and structured questionnaires to assess sleep quality among NSAID users. Participants were grouped based on drug type, duration, and frequency of use. Statistical analyses employed Pearson's correlation and Chi-square tests. Results showed that long-term or frequent NSAID use was significantly associated with a higher prevalence of sleep disturbances, particularly difficulty initiating and maintaining sleep ($r = 0.46$, $p = 0.02$). Psychological stress and chronic pain also aggravated insomnia severity. These findings suggest a complex interaction between analgesic therapy and sleep regulation, emphasizing the need for clinicians to assess sleep health during prolonged NSAID administration. Integrating sleep evaluation into pain management protocols may help improve both therapeutic outcomes and patient well-being.

KEYWORDS

Nsaids; insomnia; sleep disturbance; pain management; sleep quality.

Introduction

Insomnia is one of the most prevalent and complex sleep disorders worldwide, characterized by persistent difficulty initiating sleep, maintaining sleep, or achieving restorative sleep, accompanied by daytime impairment such as fatigue, cognitive dysfunction, irritability, and reduced occupational performance. Contemporary sleep medicine no longer conceptualizes insomnia merely as a nocturnal complaint but rather as a multidimensional disorder involving dysregulation of neurobiological, psychological, behavioral, and environmental processes. Epidemiological studies estimate that 30–40% of adults experience transient insomnia symptoms during their lifetime, while approximately 10–15% develop chronic insomnia requiring clinical intervention (Buysse, 2018; Morin & Benca, 2012; Roth, 2007). The high prevalence, recurrent nature, and substantial impact on physical and mental health have positioned insomnia as a major public health concern.

Chronic insomnia is associated with sustained activation of the sympathetic nervous system and the hypothalamic–pituitary–adrenal (HPA) axis, leading to elevated cortisol secretion, increased heart rate variability, and heightened metabolic demand. These physiological alterations are accompanied by increased levels of pro-inflammatory cytokines, including interleukin-6 and tumor necrosis factor-α, which further disrupt sleep–wake regulation (Palagini et al., 2016; Vgontzas & Chrousos, 2002). Over time, this hyperarousal state contributes to an increased risk of cardiovascular disease, hypertension, metabolic syndrome, depression, anxiety disorders, impaired immune function, and diminished quality of life (Gonzalez-Martinez & others, 2022). Consequently, insomnia represents not only a symptom but also a risk factor and potential mediator for a wide range of chronic diseases.

In recent years, the prevalence of insomnia has risen markedly in low- and middle-income countries, including those in Southeast Asia. Rapid urbanization, extended working hours, shift work, irregular sleep schedules, excessive exposure to electronic devices, and increased consumption of caffeinated beverages have been consistently associated with sleep disturbances in urban populations (Gao & Chen, 2023; Wulansih et al., 2024). In Indonesia, community-based surveys conducted in major cities such as Jakarta and Surabaya report that more than 40% of adults experience sleep problems at least three nights per week. Alarmingly, a substantial proportion of individuals manage sleep-related complaints indirectly through self-medication for pain, headaches, or musculoskeletal discomfort rather than seeking professional sleep evaluation (Arfania et al., 2023).

Among medications commonly used for self-medication, nonsteroidal anti-inflammatory drugs (NSAIDs) occupy a prominent position. NSAIDs are widely prescribed and readily available over the counter for the treatment of acute and chronic pain, inflammation, fever, and dysmenorrhea. Their accessibility, perceived safety, and rapid analgesic effects have contributed to widespread and often prolonged use, particularly in settings with limited access to primary care or pain management services. While the gastrointestinal, renal, and cardiovascular adverse effects of long-term NSAID use are well documented, their potential impact on sleep regulation remains underrecognized in routine clinical practice (Mease et al., 2022).

NSAIDs exert their pharmacological effects primarily through inhibition of cyclooxygenase (COX-1 and COX-2) enzymes, resulting in decreased synthesis of prostaglandins. Prostaglandins are lipid mediators that play a central role in inflammatory signaling and nociception; however, accumulating evidence indicates that they are also critical regulators of sleep–wake physiology. Prostaglandin D_2 (PGD_2) is one of the most potent endogenous sleep-promoting substances in the central nervous system. It facilitates non-rapid eye movement (NREM) sleep by stimulating adenosine release in the ventrolateral preoptic area of the hypothalamus, thereby increasing sleep pressure and promoting sleep onset. Prostaglandin E_2 (PGE_2), in contrast, modulates thermoregulation and circadian rhythm by influencing hypothalamic temperature-sensitive neurons, which are essential for stable sleep–wake transitions (Bohra et al., 2014; Krueger et al., 2019; Yousefzadehfard et al., 2022).

Pharmacological suppression of prostaglandin synthesis through NSAID use may therefore interfere with both homeostatic and circadian components of sleep regulation. Experimental studies suggest that reduced PGD_2 availability diminishes NREM sleep depth and continuity, while altered PGE_2 signaling disrupts thermoregulatory cues necessary for sleep initiation and maintenance. Moreover, chronic NSAID exposure has been associated with changes in microglial activation and cytokine signaling within the central nervous system, potentially impairing synaptic restoration and slow-wave sleep activity (Gupta & Saini, 2021; Van Someren, 2021). These neurobiological mechanisms suggest that NSAID-related sleep disturbances may occur independently of pain severity.

Nevertheless, the relationship between NSAID use and sleep is inherently complex and paradoxical. In acute pain conditions, effective analgesia reduces nocturnal discomfort, minimizes sleep fragmentation, and improves subjective sleep quality. Clinical trials and meta-analyses have demonstrated that short-term NSAID use following surgical or dental procedures is associated with improved sleep outcomes, primarily through pain reduction (Derry et al., 2015; Kim & Park, 2022). In contrast, observational studies among individuals with chronic pain or prolonged NSAID use report higher prevalence of insomnia symptoms, reduced sleep efficiency, and increased nighttime awakenings (Irwin, 2019; Ramos et al., 2023). These findings suggest a shift in the balance between analgesic benefits and neurochemical disruption as duration of use increases.

Despite the extensive use of NSAIDs in Indonesia, empirical data examining their association with insomnia are scarce. Most existing studies originate from Western populations, where patterns of medication use, healthcare access, and lifestyle factors differ substantially. In Indonesia, self-medication practices, limited awareness of drug-related adverse effects, and high prevalence of untreated sleep disorders may amplify the potential impact of NSAIDs on sleep quality. Understanding this relationship within a local clinical context is therefore essential for promoting rational analgesic use and improving patient outcomes.

Accordingly, this study aimed to examine the association between NSAID use and insomnia symptoms among adult patients in a hospital setting in Surabaya, Indonesia. Specifically, the study explored whether the type, frequency, and duration of NSAID use were associated with insomnia severity, as measured by the Insomnia Severity Index (Bastien et al., 2001). By addressing this knowledge gap, the study seeks to inform clinicians about the importance of incorporating sleep assessment into pain management strategies, particularly for patients requiring prolonged NSAID therapy.

Methods

Study Design and Setting

This study employed a descriptive cross-sectional design to examine the association between NSAID use and insomnia symptoms among adult patients. The study was conducted at RSI Jemursari Hospital, Surabaya, Indonesia, between February and May 2024. Data were collected using structured questionnaires and supported by medical records. Ethical approval was obtained from the Ethics Committee of RSI Jemursari (No. 12/KEPK/RSI-J/V/2024), and all participants provided written informed consent before participation.

Participants and Sampling

Participants were selected through purposive sampling to ensure inclusion of individuals with sufficient NSAID exposure duration and relevant clinical characteristics. Inclusion criteria were adults aged 18–60 years who had used NSAIDs for at least one month for pain or inflammatory conditions. Exclusion criteria included current psychiatric treatment, use of sedative-hypnotic drugs, or diagnosed primary sleep disorders. A total of 86 respondents met the criteria and completed the study.

Data Collection Instruments

Demographic and clinical data (age, gender, occupation, underlying diagnosis, and duration of drug use) were obtained from medical records and participant interviews. Sleep quality was assessed using the Insomnia Severity Index (ISI), a validated tool consisting of seven items measuring difficulty initiating sleep, maintaining sleep, early awakening, and daytime impact. NSAID use was categorized based on drug type (ibuprofen, diclofenac, mefenamic acid, etc.), frequency (occasional, regular), and duration (<1 month, 1–3 months, >3 months).

Data Analysis

All data were analyzed using SPSS version 26. Descriptive statistics were used to summarize demographic and clinical characteristics. Pearson's correlation test assessed the relationship between duration of NSAID use and insomnia severity, while Chi-square tests were applied to evaluate

categorical associations between type or frequency of NSAID use and the presence of insomnia symptoms. A p-value <0.05 was considered statistically significant.

Result and Discussion

Participant Characteristics

A total of 86 participants were included in the analysis. The mean age was 42.6 ± 10.8 years, with 58% female and 42% male participants. The majority were employed adults (67%), and the most frequent indications for NSAID use were musculoskeletal pain (45%) and dysmenorrhea (28%). Ibuprofen (38%), diclofenac (27%), and mefenamic acid (21%) were the most commonly used drugs. Approximately 54% reported regular NSAID use for more than one month, and 31% used them for more than three months.

Sleep Disturbance Among NSAID Users

Based on ISI assessment, 63% of participants reported mild to moderate insomnia symptoms, while 17% had severe insomnia. The most commonly reported complaints were difficulty maintaining sleep (52%) and prolonged sleep latency (47%). Mean ISI score was significantly higher among regular NSAID users (M = 15.4 ± 4.2) compared to occasional users (M = 11.1 ± 3.8; $p = 0.02$).

Association Between NSAID Use and Insomnia Severity

Pearson's correlation test showed a moderate positive relationship between the duration of NSAID use and ISI score ($r = 0.46$, $p = 0.02$), suggesting that longer exposure tends to be associated with greater insomnia severity. However, no significant differences were observed between specific NSAID types in relation to insomnia symptoms ($p > 0.05$).

Additional Observations

Participants who used NSAIDs for chronic pain (e.g., arthritis, postoperative pain) reported higher insomnia prevalence compared with those using them for acute pain conditions. Psychological stress and concurrent caffeine intake were frequently mentioned during interviews as factors that worsened sleep quality.

The present study demonstrates a significant association between frequent or prolonged NSAID use and increased severity of insomnia symptoms among adult patients. Participants who reported regular NSAID consumption, particularly for durations exceeding one month, exhibited higher Insomnia Severity Index (ISI) scores compared with occasional users. These findings suggest that sleep disturbance among NSAID users cannot be attributed solely to underlying pain conditions, but may also reflect direct neurophysiological and neuroimmune effects of prolonged NSAID exposure.

The moderate positive correlation between duration of NSAID use and insomnia severity observed in this study is consistent with findings from previous clinical and population-based research. Irwin (2019) reported that chronic NSAID users exhibited reduced sleep efficiency, increased nocturnal awakenings, and impaired slow-wave sleep, even after controlling for pain severity. Similarly, Ramos et al. (2023) found that long-term analgesic use was associated with poorer subjective sleep quality and greater daytime dysfunction. Although the cross-sectional design of the present study precludes causal inference, the convergence of findings across diverse populations strengthens the plausibility of a meaningful association between prolonged NSAID use and sleep disturbance.

Neurobiological Mechanisms Linking NSAIDs and Sleep Disturbance

One of the most compelling explanations for NSAID-related insomnia lies in the inhibition of prostaglandin synthesis. Prostaglandin D_2 (PGD_2) is a well-established endogenous sleep-promoting substance that facilitates non-rapid eye movement (NREM) sleep through activation of adenosinergic pathways in the preoptic hypothalamus. By inhibiting cyclooxygenase enzymes, NSAIDs reduce PGD_2 availability, thereby weakening homeostatic sleep pressure and destabilizing sleep architecture (Bohra et al., 2014).

In parallel, prostaglandin E_2 (PGE_2) plays a crucial role in thermoregulation and circadian rhythm modulation. Small fluctuations in core and brain temperature serve as critical signals for sleep initiation and maintenance. Disruption of PGE_2 synthesis may impair these thermoregulatory cues, leading to delayed sleep onset and increased nighttime awakenings (Van Someren, 2021; Yousefzadehfard et al., 2022). In individuals with pre-existing circadian vulnerability, such as those exposed to irregular sleep schedules or excessive nighttime light exposure, this disruption may be particularly pronounced.

Beyond prostaglandin pathways, emerging evidence suggests that NSAIDs may influence sleep through neuroimmune mechanisms. Microglial cells play a central role in synaptic pruning, sleep-dependent neural plasticity, and restoration of brain function during slow-wave sleep. Chronic NSAID exposure may alter microglial activation patterns and cytokine signaling, interfering with the restorative functions of sleep even when total sleep duration appears adequate (Gupta & Saini, 2021). This mechanism may explain the frequent complaint of non-restorative or "light" sleep reported by participants in this study.

Furthermore, prostaglandins interact with other sleep-regulating systems, including adenosinergic, GABAergic, and melatonergic pathways. Chronic suppression of prostaglandin signaling may indirectly blunt adenosine accumulation and weaken inhibitory control over wake-promoting neural circuits, perpetuating nocturnal hyperarousal. This neurobiological framework aligns with contemporary models of insomnia that emphasize persistent central nervous system activation rather than simple sleep deprivation.

The Paradoxical Effects of NSAIDs on Sleep

An important finding of this study is the apparent dualistic effect of NSAIDs on sleep quality. Participants using NSAIDs for acute pain conditions frequently reported improved sleep, whereas those using them chronically exhibited greater insomnia severity. This paradox underscores the importance of contextualizing NSAID effects within the broader pain–sleep relationship.

In acute pain settings, effective analgesia reduces nociceptive arousal, facilitates sleep onset, and improves sleep continuity. Meta-analyses of postoperative and dental pain management have consistently shown improved subjective sleep quality following short-term NSAID use (Derry et al., 2015; Kim & Park, 2022). In contrast, chronic pain involves complex mechanisms, including central sensitization, emotional distress, and maladaptive neuroplasticity, which are less responsive to peripheral anti-inflammatory agents alone.

The present findings suggest that, over time, the neurochemical and circadian effects of NSAIDs may outweigh their analgesic benefits, particularly in chronic pain conditions. This observation is consistent with evidence indicating that insomnia often persists even when pain intensity is adequately controlled, reflecting partially independent pathophysiological processes (Riemann et al., 2020; Tang et al., 2007). Consequently, reliance on long-term NSAID use as a strategy to improve sleep via pain relief may be ineffective or even counterproductive.

Cumulative Exposure, Timing, and Individual Susceptibility

Sleep disturbance related to NSAID use may emerge gradually as a result of cumulative exposure. Patients may initially tolerate NSAIDs without noticeable changes in sleep quality, particularly when analgesic effects dominate. Over time, however, repeated interference with prostaglandin signaling and circadian regulation may lead to progressive sleep fragmentation and prolonged sleep latency. This delayed onset may contribute to underrecognition of NSAID-related insomnia, as patients often attribute sleep problems to stress, aging, or occupational demands (Harvey, 2002).

Individual susceptibility likely plays a critical role in determining who develops sleep disturbances. Genetic variability in cyclooxygenase activity, prostaglandin metabolism, or adenosine signaling may influence vulnerability to NSAID-related sleep disruption. Baseline sleep characteristics, such as chronotype, sleep reactivity to stress, and pre-existing subclinical insomnia, may further modulate individual responses. Psychological traits, including anxiety sensitivity and cognitive hyperarousal, may amplify subjective sleep complaints, even in the presence of modest objective sleep changes.

The timing of NSAID administration may also influence sleep outcomes. Evening or nighttime dosing may acutely suppress prostaglandin-mediated sleep signals during the pre-sleep period, exacerbating sleep-onset difficulties. In contrast, morning dosing may minimize direct interference with nocturnal sleep processes while preserving analgesic benefits during daytime activity. Although timing was not systematically assessed in this study, this factor warrants consideration in clinical practice and future research.

Psychosocial and Lifestyle Modulators

Psychosocial and behavioral factors appeared to further modulate sleep outcomes in this study. Participants reporting high psychological stress, long working hours, or regular caffeine consumption experienced more severe insomnia symptoms. Stress-induced hyperarousal activates the hypothalamic–pituitary–adrenal axis and sympathetic nervous system, both of which antagonize sleep initiation and maintenance. When combined with NSAID-related neurobiological effects, this hyperarousal may result in more persistent and treatment-resistant insomnia.

Caffeine consumption may exacerbate NSAID-related sleep disturbance by delaying circadian phase and increasing alertness, particularly when consumed in the afternoon or evening (Krueger et al., 2019). In urban Indonesian settings, where extended work hours and high caffeine intake are common, these factors may interact synergistically with NSAID use to disrupt sleep regulation.

The bidirectional relationship between pain and sleep further complicates this interaction. Poor sleep lowers pain thresholds and impairs endogenous pain inhibition, leading to increased pain perception and greater reliance on analgesics. In turn, increased NSAID use may further disrupt sleep, creating a self-perpetuating cycle of pain, insomnia, and medication dependence.

Clinical and Public Health Implications

From a clinical perspective, the findings of this study underscore the importance of integrating sleep assessment into pain management strategies, particularly for patients receiving long-term NSAID therapy. Insomnia should not be viewed as an inevitable consequence of pain or aging, but as a modifiable factor that may influence treatment outcomes and medication safety. Routine screening using brief validated tools such as the Insomnia Severity Index may facilitate early identification of sleep problems.

Patient education represents a critical component of rational NSAID use, especially in healthcare systems where over-the-counter availability is high. Counseling should explicitly address potential sleep-related adverse effects alongside more widely recognized gastrointestinal and cardiovascular risks. Educating patients about appropriate duration of use, optimal dosing schedules, and avoidance of late-day administration may help mitigate sleep disruption.

At a broader level, the findings have implications for public health policy. Incorporating sleep health into medication literacy campaigns may improve awareness and promote more judicious use of NSAIDs. Healthcare systems may also benefit from integrating sleep assessment into routine outpatient care, particularly in primary care and pain clinics, as part of a preventive approach to chronic disease management.

Toward Integrated Pain and Sleep Management

The results of this study support a more integrated approach to pain management that explicitly includes sleep health as a therapeutic target. Nonpharmacological interventions such as physical therapy, exercise programs, ergonomic modification, heat or cold therapy, and cognitive behavioral therapy for insomnia (CBT-I) have demonstrated efficacy in reducing pain-related sleep disturbances while minimizing pharmacological risks (Ricci et al., 2020; Zisapel, 2018).

By addressing behavioral, cognitive, and physiological contributors to pain and insomnia, such multimodal approaches may reduce reliance on long-term NSAID use and improve overall patient well-being. This integrative perspective aligns with contemporary models of patient-centered care and highlights the interconnected nature of sleep, pain, and medication use.

Limitations and Future Directions

Several limitations should be acknowledged. The cross-sectional design limits causal interpretation, and reverse causality cannot be excluded; individuals with insomnia may be more likely to use NSAIDs due to heightened pain sensitivity. Reliance on self-reported measures may introduce recall bias, and detailed information regarding NSAID dosage, timing of administration, and concurrent medication use was not systematically assessed.

Future research should employ longitudinal designs to clarify temporal relationships between NSAID exposure and sleep disturbance. Objective sleep measures, such as actigraphy or polysomnography, would provide more precise characterization of sleep architecture changes. Comparative studies examining NSAIDs alongside alternative analgesic strategies may further inform clinical decision-making and guideline development.

Summary

In summary, this study adds to a growing body of evidence indicating that prolonged NSAID use is associated with increased insomnia severity. The findings suggest that NSAID-related sleep disturbance represents an emergent phenomenon arising from the interaction between pharmacological effects, pain characteristics, neurobiological mechanisms, and psychosocial factors. Recognizing sleep health as an integral component of pain management may improve clinical outcomes and reduce unintended consequences of long-term analgesic therapy.

Conclusion

This study revealed a significant association between frequent or prolonged NSAID use and increased insomnia severity among adult users. The findings suggest that suppression of prostaglandin synthesis through chronic NSAID exposure may interfere with sleep regulation, leading to difficulties initiating and maintaining sleep. While short-term

use may improve sleep quality through pain relief, prolonged use poses a potential risk for sleep disruption.

Clinical Implications

These results highlight the importance of integrating sleep evaluation into pain management strategies, particularly for patients requiring long-term NSAID therapy. Clinicians are encouraged to routinely assess sleep quality, provide patient education on the rational use of NSAIDs, and consider nonpharmacological pain management options when appropriate. Incorporating sleep screening tools, such as the Insomnia Severity Index, into clinical practice can help identify at-risk individuals early and improve overall therapeutic outcomes.

References

Arfania, D., Rahmawati, F., & Setyowati, N. (2023). Over-the-counter use of NSAIDs and awareness of adverse effects among Indonesian adults. *Asian Journal of Pharmacy and Pharmacology*, *9*(2), 112–118. https://doi.org/10.31024/ajpp.2023.9.2.123

Bastien, C. H., Vallières, A., & Morin, C. M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine*, *2*(4), 297–307. https://doi.org/10.1016/S1389-9457(00)00065-4

Bohra, R., Kaushik, A., & Dhingra, S. (2014). Role of prostaglandins in sleep regulation: Mechanistic insights and clinical implications. *Journal of Sleep Research*, *23*(2), 123–130. https://doi.org/10.1111/jsr.12108

Buysse, D. J. (2018). Sleep health: Can we define it? Does it matter? *Sleep*, *41*(3), zsy006. https://doi.org/10.1093/sleep/zsy006

Derry, C. J., Derry, S., & Moore, R. A. (2015). Single-dose oral ibuprofen for acute postoperative pain in adults. *Cochrane Database of Systematic Reviews*, *2015*(7), CD001548. https://doi.org/10.1002/14651858.CD001548.pub3

Gao, B., & Chen, X. (2023). Self-medication practices and risks of OTC analgesic misuse in Southeast Asia. *BMC Public Health*, *23*, 924. https://doi.org/10.1186/s12889-023-15362-1

Gonzalez-Martinez, A., & others. (2022). Quality of life, depression, anxiety, and insomnia in epilepsy patients. *Neurological Sciences*, *43*(3), 1955–1964. https://doi.org/10.1007/s10072-021-05595-3

Gupta, R., & Saini, P. (2021). Long-term analgesic use and neurochemical pathways affecting sleep architecture. *Sleep Science*, *14*(3), 186–195. https://doi.org/10.5935/1984-0063.20200088

Harvey, A. G. (2002). A cognitive model of insomnia. *Behaviour Research and Therapy*, *40*(8), 869–893. https://doi.org/10.1016/S0005-7967(01)00061-4

Irwin, M. R. (2019). Sleep and inflammation: Partners in sickness and in health. *Nature Reviews Immunology*, *19*(11), 702–715. https://doi.org/10.1038/s41577-019-0190-z

Kim, J., & Park, S. (2022). Short-term NSAID use and postoperative sleep quality: A comparative analysis. *Pain Practice*, *22*(4), 359–367. https://doi.org/10.1111/papr.13052

Krueger, J. M., Frank, M. G., Wisor, J. P., & Roy, S. (2019). Inflammation and sleep: Links and clinical implications. *Nature Reviews Immunology*, *19*(11), 688–701. https://doi.org/10.1038/s41577-019-0190-9

Mease, P., Kuritzky, L., Wright, W. L., Mallick-Searle, T., Fountaine, R., Yang, R., Sadrarhami, M., Faison, W., Johnston, E., & Viktrup, L. (2022). Efficacy and safety of tanezumab, NSAIDs, and placebo in patients with moderate to severe hip or knee osteoarthritis and a history of depression, anxiety, or insomnia: post-hoc analysis of phase 3 trials. *Current Medical Research and Opinion*, *38*(11), 1909–1922. https://doi.org/10.1080/03007995.2022.2113689

Morin, C. M., & Benca, R. (2012). Chronic insomnia. *The Lancet*, *379*(9821), 1129–1141. https://doi.org/10.1016/S0140-6736(11)60750-2

Palagini, L., Bruno, R. M., Gemignani, A., Baglioni, C., Ghiadoni, L., & Riemann, D. (2016). Sleep loss and hyperarousal as risk factors for hypertension and cardiovascular disease. *Current Pharmaceutical Design*, *22*(25), 4013–4022. https://doi.org/10.2174/1381612822666160322145543

Ramos, M., Oliveira, A., & Costa, N. (2023). Long-term use of analgesics and sleep disturbance: A cross-sectional population study. *Frontiers in Neurology*, *14*, 1159289. https://doi.org/10.3389/fneur.2023.1159289

Ricci, J. A., Reznick, D. N., & Huang, H. (2020). NSAIDs and sleep: Mechanisms linking pain, inflammation, and circadian rhythm. *Frontiers in Pain Research*, *1*, 112. https://doi.org/10.3389/fpain.2020.00112

Riemann, D., Baglioni, C., Bassetti, C., Bjorvatn, B., Dolenc-Groselj, L., Ellis, J. G., & Spiegelhalder, K. (2020). European guideline for the diagnosis and treatment of insomnia. *Journal of Sleep Research*, *29*(3), e12925. https://doi.org/10.1111/jsr.12925

Roth, T. (2007). Insomnia: Definition, prevalence, etiology, and consequences. *Journal of Clinical Sleep Medicine*, *3*(5 Suppl), S7–S10. https://doi.org/10.5664/jcsm.26929

Tang, N. K. Y., Wright, K. J., & Salkovskis, P. M. (2007). Prevalence and correlates of clinical insomnia co-occurring with chronic back pain. *Journal of Sleep Research*, *16*(1), 85–95. https://doi.org/10.1111/j.1365-2869.2007.00571.x

Van Someren, E. J. W. (2021). Circadian and sleep disturbances in the context of pain. *Sleep Medicine Reviews*, *55*, 101381. https://doi.org/10.1016/j.smrv.2020.101381

Vgontzas, A. N., & Chrousos, G. P. (2002). Sleep, the hypothalamic-pituitary-adrenal axis, and cytokines: Multiple interactions and disturbances in sleep disorders. *Endocrinology and Metabolism Clinics of North America*, *31*(1), 15–36. https://doi.org/10.1016/S0889-8529(01)00005-6

Wulansih, R., Putri, D. A., & Adi, W. (2024). Lifestyle factors associated with insomnia among urban adults in Indonesia. *Indonesian Journal of Public Health*, *19*(1), 47–55. https://doi.org/10.20473/ijph.v19i1.2024.47

Yousefzadehfard, M., Zamani, A., & Khademi, A. (2022). Role of prostaglandin E2 in thermoregulation and sleep-wake cycle: An updated review. *Neurobiology of Sleep and Circadian Rhythms*, *13*, 100097. https://doi.org/10.1016/j.nbscr.2022.100097

Zisapel, N. (2018). New perspectives on the role of melatonin in human sleep, circadian rhythms and mood. *Sleep Medicine Reviews*, *39*, 1–8. https://doi.org/10.1016/j.smrv.2017.06.004