Shift Workers at Risk for Metabolic Syndrome
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In this highly digitalized era, sleep disorders are becoming more common and are associated with an increased burden of chronic disease. Shift workers are at an increased risk for both sleep disorders and metabolic syndrome. In this article, the authors outline the connection between circadian discordance, hormonal imbalance, and the development of metabolic syndrome in shift workers. Based on a literature review of animal model studies, observational studies, and clinical trials conducted between August and October of 2018, the authors offer several clinical interventions, including work schedules, light therapy, medications, and dietary habits to improve the circadian synchronicity of shift workers and reduce their risk of morbidity and mortality. It is important for physicians to be familiar with the consequences of shift work and ways to mitigate the risks for this patient population.

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Many of the human body’s neurohormonal cascades, including key metabolic cascades and the sleep-wake cycle, follow 24-hour rhythms. These circadian rhythms evolve in response to a light-dark cycle established by sunrise and sunset along with the daily rhythm of other external factors, such as temperature and noise. Today, people are exposed to synthetic light, heat, and other stimulating cues that do not follow a 24-hour cyclic pattern. These synthetic factors interfere with the carefully coordinated interplay between external regulators and the endogenous maintenance of circadian rhythms.1 Shift workers are increasingly affected by this phenomenon.2 This discordance among shift workers has been linked to disruption in the sleep-wake cycle and metabolic pathways, leading to sleep deprivation and an increased risk of metabolic syndrome.3

In this review, we discuss the relationship between metabolic syndrome and shift work. We completed PubMed searches in August and October 2018 using the following keywords: “shift worker demographics,” “metabolic syndrome and shift workers,” “risk factors associated with metabolic syndrome in shift work,” “circadian rhythm and shift work,” “cortisol release and shift work,” “shift work and exercise habits,” “shift work and nutrition habits,” “circadian rhythm discordance and metabolic syndrome,” “sleep hygiene and shift work disorder,” “nutrition and sleep hygiene,” “exercise and cortisol release,” “sleep disorders and shift work,” “sleep disorders and metabolic syndrome,” “osteopathic manipulation and sleep latency,” “shift work and heart rate variability,” and “osteopathic manipulation and heart rate variability.” Of the literature reviewed, 38 articles were experimental studies (animal model or clinical trials), 35 were review articles, and 17 were observational studies. Based on this literature
review, we provide clinical recommendations to improve circadian rhythm in shift workers.

Demographics of Shift Workers

Previous research indicates that 17.7% of the US labor force is engaged in work outside the hours of 6 AM to 6 PM. The industries with the largest portion of their workforce engaged in shift work are leisure/hospitality, arts, entertainment, mining, transportation, and warehousing. Shift workers are more likely to work in lower-paying industries. One article highlighted that people tend to work outside of 6 AM to 6 PM before acquiring their college education. A study of retired shift workers found that a history of shift work remained an independent risk factor for diabetes and hypertension, even though sleep quality improved upon retirement. Nearly 6.5% of shift workers are assigned either irregular shift work or rotating shift work. These workers are at an even greater risk of circadian rhythm discordance.

The Relationship Between Metabolic Syndrome and Circadian Desynchrony

Research shows that shift workers have an increased incidence of metabolic syndrome, which increases their risk for the metabolic trifecta of cardiovascular disease, strokes, and type 2 diabetes mellitus. Initially, it was believed that unhealthy lifestyle choices and lower socioeconomic status were largely responsible for increased risk among this population, but the data do not support this belief. For example, studies have found that night shift workers are not exercising less than the general population. They may even be exercising more than their day-shift counterparts.

A growing body of research suggests that discordance with the circadian rhythm is an independent risk factor for the development of metabolic syndrome. Circadian rhythm is a bimolecular mechanism that keeps time for the body through both neural and hormonal signaling. When the circadian rhythm does not match the sleep-wake cycle, as seen in shift workers, it causes opposing signaling, termed circadian desynchrony. This desynchrony disrupts the suprachiasmatic nucleus network rhythm and the patterned hormonal release for which it keeps time, leading to disturbances in sleep and metabolism. Shift workers sleep less than non-shift workers and report feeling more tired than their day-working counterparts, all signs of circadian desynchrony. Some shift workers’ circadian rhythms become so disrupted as to cause shift work sleep disorder—a sleep disorder characterized by insomnia and the inability to stay alert at work.

People subject to circadian desynchrony exhibit several disturbances in hormonal levels, including increased cortisol and ghrelin and decreased thyroid-stimulating hormone, growth hormone, insulin, leptin, and serotonin. For example, circadian desynchrony results in increased insulin and glucose levels and has been shown to occur independently of behavioral choices. Qian et al found that circadian desynchrony is specifically associated with decreased insulin sensitivity, which could explain the innately worse glycemic ranges found in shift workers. Circadian desynchrony has a similar effect on ghrelin, increasing the appetite for energy-dense foods and post-prandial ghrelin levels.

These relationships substantiate the link between sleep disturbances and metabolic dysregulation. Hormonal cascades linked to the development of metabolic syndrome, such as the regulation of insulin, have a reciprocal relationship with our circadian rhythms. In a rat study, diet-induced insulin resistance led to circadian desynchrony, but insulin release has also been shown to cause reproducible phase-shift responses in circadian clock genes. The reciprocal relationship has also been seen with hormones such as cortisol and melatonin, as well neurotransmitters such as serotonin. Other hormones, including ghrelin, leptin, and adiponectin, could prove to have similar reciprocal relationships with circadian rhythm regulators.
This information is key in determining current intervention recommendations.

Clinical Assessments and Interventions

Sleep Hygiene

Table 1 presents a sleep hygiene screening tool for shift workers. To maintain circadian synchrony and normal sleep architecture, shift workers should sleep in a single 7- to 8-hour block each 24 hours. Patients should choose a time to go to sleep each day, as close to the same time of day as possible.20,21 Tracking sleep has also been shown to be an effective way to maintain a consistent sleep schedule.22 Patients should be encouraged to use a sleep journal or phone application to track their sleep.

Because sleeping during the day is not practical for many night shift workers on off days, night shift workers can follow the phasic sleep schedule developed by Smith et al.23 This sleep schedule has been shown to improve circadian synchrony and increase total sleep time for shift workers23 (Table 2). Shift workers who sleep in the evenings rather than mornings report fewer circadian disruptions.24 To increase the quantity of sleep, shift workers can take 20- to 120-minute naps.1,25 Recuperative naps have been linked to decreased total sleep time, so shift workers can be encouraged to take prophylactic naps before the start of shifts.26

Table 1. Sleep Hygiene Screening Tool for Shift Workers

<table>
<thead>
<tr>
<th>Question</th>
<th>Clinical Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>How many meals do you eat a day?</td>
<td>Patients should eat ≥3 meals per day; meals should consist of fresh produce and lean protein.</td>
</tr>
<tr>
<td>How much sleep do you get a night?</td>
<td>Patients should sleep ≥7 hours per night.</td>
</tr>
<tr>
<td>What is your shift schedule like?</td>
<td>Patients should minimize rotating schedules.</td>
</tr>
<tr>
<td>Do you take naps?</td>
<td>Patients should be encouraged to take prophylactic naps.</td>
</tr>
<tr>
<td>What hours of the day do you typically sleep?</td>
<td>Patients should be encouraged to sleep in the evening if working the night shift.</td>
</tr>
<tr>
<td>What is your sleeping pattern on off days?</td>
<td>Patients who work nights should shift their sleep cycle by 5 hours instead of by 12; patients who work early-morning or late-evening shifts should attempt to adhere to a regular sleep schedule.</td>
</tr>
<tr>
<td>How is your commute home from work? Do you ever feel you are falling asleep behind the wheel?</td>
<td>Patients should be educated on driver safety; driving drowsy is as dangerous as driving drunk.</td>
</tr>
<tr>
<td>How long after waking do you feel hungry?</td>
<td>Not feeling hungry within 1 hour of waking may indicate circadian dysrhythmia and cortisol imbalance.</td>
</tr>
<tr>
<td>Do you feel you are overeating or feel hungry all the time?</td>
<td>This is a sign of circadian desynchrony; possible causes include elevated cortisol, insulin insensitivity, sleep deprivation, elevated progesterone, and elevated ghrelin.</td>
</tr>
<tr>
<td>Do you have any of the following symptoms?</td>
<td>Any of these symptoms may indicate a circadian sleep disorder.</td>
</tr>
<tr>
<td>▪ difficulty falling asleep</td>
<td></td>
</tr>
<tr>
<td>▪ maintaining sleep</td>
<td></td>
</tr>
<tr>
<td>▪ feeling tired when awake</td>
<td></td>
</tr>
<tr>
<td>▪ feeling unrested after sleeping</td>
<td></td>
</tr>
<tr>
<td>▪ headaches</td>
<td></td>
</tr>
<tr>
<td>▪ difficulty concentrating</td>
<td></td>
</tr>
<tr>
<td>▪ slowed psychomotor coordination</td>
<td></td>
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</tbody>
</table>
Types of Shift Work
To maintain a consistent sleep pattern, it is better to work night shifts consistently rather than switch between night and day shifts to avoid constant circadian rhythm disruption. Working 11 hours or less and starting night shifts before midnight both reduce sleep drive. For those shift workers required to work a rotating shift schedule, the literature discusses 2 different transition techniques: (1) night-to-morning to evening-to-night and (2) night-to-evening to morning-to-night. Some research indicates that the first option reentrains sleep cycles more efficiently and leads to lower cortisol release. However, a 2018 study found no significant difference between these 2 strategies. Consistent schedules, work that begins before midnight, and shifts that last up to 11 hours can all optimize shift work to improve circadian reentrainment. Physicians should screen patients for rotating shift work and other maladaptive schedules. This knowledge can serve to identify patients who may benefit from other interventions and would be of educational value to patients. Suggested workplace modifications are presented in Table 3.

Light
Exposure to light promotes wakefulness. Light exposure upon waking will cause phase shift advance, promoting transition in circadian rhythm. Conversely, exposure before sleep will cause phase shift delay, delaying circadian sleep drive. Shift workers can use this phenomenon to their advantage by increasing light exposure just before and throughout work shifts. Reminding shift workers to control light exposure is a simple but effective tool to promote timely sleep.

The intensity of lighting can also affect circadian phase shifts. Normal indoor light intensity is 150 lux. High-intensity light can suppress melatonin production to an extent. Exposure to 3000-lux light was found to be near equivalent to 12,000 lux (daylight range, 10,000-25,000 lux) in facilitating circadian

<table>
<thead>
<tr>
<th>Event</th>
<th>Evening Sleep Schedule</th>
<th>Morning Sleep Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedtime</td>
<td>1:30 PM-8:30 PM</td>
<td>8:30 AM-3:30 PM</td>
</tr>
<tr>
<td>Last day of night shift</td>
<td>1:30 PM-6:30 PM</td>
<td>8:30 AM-1:30 PM</td>
</tr>
<tr>
<td>Off day</td>
<td>6:30 PM-2:30 AM</td>
<td>3:30 AM-10:30 AM</td>
</tr>
</tbody>
</table>

* These proposed schedules are examples for patients working a 10:30 PM to 7 AM shift with 2 days off per week, a schedule in which patients will most likely prefer to be awake during the daytime. Patients should be encouraged to find a sleep schedule that fits with their personal routine while minimizing adjustments between off days and on days of shift work.

Table 2. Suggested Sleep Schedules for Overnight Shift Workers to Reduce Circadian Desynchrony

<table>
<thead>
<tr>
<th>Event</th>
<th>Recommendation</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease blue light exposure</td>
<td>Provide Redshift application for digital screens</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Use lightbulbs that block blue lights</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Apply blue light filter to head/eye gear</td>
<td></td>
</tr>
<tr>
<td>Provide meals</td>
<td>Recommend lean proteins and fresh fruits and vegetables</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Provide highest calorie meal midway through shift</td>
<td></td>
</tr>
<tr>
<td>Promote health screenings</td>
<td>Provide benefits that cover yearly or biannual health screening for metabolic syndrome and circadian desynchrony</td>
<td></td>
</tr>
<tr>
<td>Create health program that promotes healthy behavior</td>
<td>Provide incentive to use health tracking applications that track health parameters like sleep, diet, and exercise</td>
<td></td>
</tr>
<tr>
<td>Modify shift schedules to ease burden of sleep debt</td>
<td>Avoid rotating shift schedules</td>
<td></td>
</tr>
<tr>
<td>Modify break times to allow for earlier meal times</td>
<td>Ensure that employees can have the same break time each day</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Employer Workplace Modifications for Shift Workers
adaptation. Blue light (460–480 nm) has the greatest effect on melanopsin receptors to delay melatonin production. This light is especially prominent in electronic screens that have high blue light content. Gooley et al. showed that green light exposure can also delay melatonin production through cone photoreceptors (eg, red, blue, green). However, green light melatonin suppression decayed faster than blue, lasting half as long. If they intend to sleep directly after their shift, workers can decrease exposure to bright or high-wavelength light near the end of their shift. For example, orange-tinted goggles have been shown to block the melatonin-suppressing effect of light significantly more than neutral gray density goggles. Other tools include red visor caps, lighting changes in the work environment, or the Redshift application for digital screens.

To our knowledge, no studies have been conducted to determine the optimal length of time needed with minimal blue light exposure to promote adequate melatonin production. Most sleep education entities recommend minimizing blue light exposure at least 2 hours before going to sleep. A 2009 randomized control trial showed that blocking blue light for 3 hours before sleeping improved sleep quality.

In a 2008 study, participants who were exposed to bright light pulses during shift work wore dark sunglasses while leaving work in the daylight and then were exposed to outdoor light in the afternoon after waking, showed equal performance and duration of sleep as they had during day shifts. We recommend using orange-tinted goggles during the commute home and wide-spectrum blue lights during work hours to promote wakefulness. We also recommend increasing blue light exposure during the beginning of the shift and decreasing blue light exposure 2 to 3 hours before the end of the shift. Last, we recommend intermittent alternating of green and blue light exposure during work shifts to entrain the circadian cycle.

**Chronotypes**

Two major human chronotypes, morning chronotype and evening chronotype, are distinguished by the time of day that melatonin level begins to increase. For persons with the evening chronotype, melatonin increase begins several hours later than the morning chronotype (approximately 12 AM vs 9 PM, respectively). People with an evening chronotype have been found to adjust to shift work better than people with a morning chronotype. However, chronotype does not change the effectiveness of light therapy interventions. Helping patients to identify chronotype allows physicians to discuss sleep hygiene practices with their patients.

Shift workers should focus on creating a sleep environment that promotes sleep and reduces sensory stimuli. It may be helpful if they eat and exercise at similar times of day. The exogenous entrainment of these external factors has the potential to improve synchrony of peripheral and central clock genes. Table 4 presents further examples of sleep hygiene practices that can improve circadian synchronicity.

**Table 4. Tools to Improve Daytime Sleep in Shift Workers**

<table>
<thead>
<tr>
<th>External Regulators</th>
<th>Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darkness</td>
<td>Eye pillows; blackout curtains</td>
</tr>
<tr>
<td>Noise</td>
<td>Television turned off; cellular phones silenced; earplugs; white noise machine</td>
</tr>
<tr>
<td>Temperature</td>
<td>Cold environment</td>
</tr>
</tbody>
</table>

**Sleep Disorder Comorbidities**

While shift workers are at risk for shift work sleep disorder, they are also at a heightened risk for other sleep disorders, such as sleep apnea. Shift workers with sleep deprivation and sleep apnea were found to be twice as likely to experience adverse cardiovascular events than shift workers without sleep disturbances. Shift workers should be screened for sleep duration, sleep apnea, and other sleep disorders to reduce the risk of adverse outcomes. Barger et al recommend the 10-item Berlin Questionnaire to screen for sleep apnea. Other sleep disorders, such as restless legs...
syndrome, periodic limb movement disorder, and rapid eye movement sleep disorder could also compound the risk of stroke and other adverse outcomes of metabolic syndrome.38

Nutrition
Shift work may also be associated with lifestyle behaviors known to increase the risk of developing metabolic syndrome. A 2016 meta-analysis found that night shift workers do not consume more calories.39 Bonham et al36 theorized that misalignment of the circadian rhythm, food choice, and the timing of meals may partly explain why metabolic syndrome is more likely to develop in shift workers despite average caloric intake.

One review40 summarized the reciprocal relationship between nutritional intake and circadian rhythm disturbance. While light is the main external influencer of clock genes, which govern the central circadian rhythm, eating patterns can have a significant influence on the genes that govern the peripheral circadian rhythm of various organs. For this reason, timing meals with activity cycles and maintaining regular eating patterns have been found to reduce the development of obesity and metabolic syndrome.40 Specifically, people who eat more of their calories earlier in the day have been found to lose significantly more weight than those who eat the majority later in the day.41,42 Peripheral circadian rhythms dictate higher insulin sensitivity and diet-induced thermogenesis earlier in the morning for diurnal humans.40 In addition, high-fat diets have been found to dampen peripheral circadian rhythms, leading to worse metabolic outcomes.43 These combined findings underline the importance of regular timing of meals and timing meals in accordance with circadian rhythm and activity cycles for shift workers.

Night shift workers are significantly more likely not to follow a daily eating pattern than those who work day shifts.44 Several studies have also shown that shift workers are more likely to eat snacks higher in sugar and saturated fat while consuming less protein and vegetables.45,46 One study42 found that shift workers were more likely to skip meals. Those who skipped meals (≤2 meals per day) had a higher body mass index.42

Based on these findings, health professionals should screen shift workers for their eating patterns and the nutritional quality of their food. Shift workers should be encouraged to eat at similar times each day and to eat 3 meals or more per day to decrease the risk for metabolic syndrome.36,47 In addition, shift workers should be encouraged to eat more calories in the beginning of their wake cycle. Shift workers should be counseled on dealing with nighttime cravings of high-fat snacks by choosing protein-rich options.47 They should also be counseled to limit alcohol intake.40 To assist with establishing regular eating patterns, employers can cater meals and offer midnight snacks.48 Employers may also consider ensuring that employees have access to regularly timed breaks early in the shifts.

Cortisol and Exercise
Cortisol plays a key role in inflammation, which is a major factor in metabolic syndrome. However, its effects are dualistic, determined by timing and concentration. Basal cortisol levels and cortisol spikes without inflammatory stimuli do not contribute to inflammatory response. But spikes close to a stimulus will produce anti-inflammatory effects, such as decreasing leukocyte migration and monocytopenia.49

Cortisol becomes proinflammatory via increasing cytokine release and cyclooxygenase enzymes when there is a delay between the stimulus and elevation of cortisol levels. Increased cyclooxygenase enzyme levels can lead to platelet hypersensitivity and increased risk for atherosclerotic diseases.50 Shift workers in particular have been shown to have increased cortisol levels and increased serum cyclooxygenase enzyme levels, which have both been linked to the development of metabolic syndrome and disruption of the circadian rhythm.50 Yeager et al49 found that mild spikes in cortisol were anti-inflammatory, whereas intermediate elevation in cortisol levels was proinflammatory.49 High levels of cortisol were found to be neither.52
showed that a 12-hour delay between the onset of the stimulus and elevated cortisol levels produced a proinflammatory state lasting for 6 days.49

Metabolic syndrome can promote proinflammation by both creating moderate elevation in cortisol and increasing inflammatory stimuli that are more likely to be delayed from the time of peak concentration spike. Metabolic syndrome has been associated with functional hypercortisolism.51 Because cortisol is linked to the circadian rhythm by the hypothalamic-pituitary-adrenal axis, modulation of cortisol may be a mechanism through which physical activity could synchronize the circadian rhythm and improve sleep quality. Physical activity has been shown to improve reentrainment of the circadian rhythm, the ability to fall asleep, and quality of sleep.20,52 Exercise has also been shown to reduce morning cortisol levels in individuals with metabolic syndrome.52

Physical activity can reestablish the circadian rhythm and decrease inflammation in shift workers, so it is important for physicians to understand night shift workers’ current exercise habits and desire to exercise. Physicians can help develop a physical activity plan that is functional for shift workers’ schedules. For example, shift workers should be advised to exercise at a similar time each day, at least 5 hours before they go to bed.36 In addition, they should be counseled to incorporate aerobic exercise into their physical activity, as it has specifically been indicated to improve sleep quality.

Melatonin
Prolonged exposure to light in the work environments of shift workers leads to changes in peaks and troughs of melatonin levels. When people experience these abnormal fluctuations in melatonin levels, they report poorer quality of sleep and increased need to nap.53 The use of melatonin supplements promotes phase shift advance and has been shown in a meta-analysis to improve sleep onset, efficiency, and duration.54 Exogenous melatonin administration works better when endogenous levels are low, as is often the case for elderly persons and persons who experience jet lag, insomnia, and circadian desynchrony disorders.55,56

For exogenous administration, melatonin can be bought over the counter as pills, liquid drops, or sublingual tablets. It is believed that excess doses of melatonin can worsen sleep cycles, with best effects reported to be at 0.3 to 0.5 mg.57 Oral pills are the most commonly used; however, sublingual tablets have more consistent and overall increased bioavailability58 because they are not subject to the first-pass effect.59

Melatonin has been shown to inhibit the harmful effects of fructose on clock genes and protect against reactive oxygen species.50 Melatonin has also been shown to regulate leptin and adiponectin secretion cycles, further underlying the reciprocal relationship of these hormonal cascades.61 Addressing these hormonal changes in hunger signaling and food cravings may offer therapeutic benefit for the prevention of metabolic syndrome in shift workers. Therefore, melatonin may also have benefits in weight management, which is also a concern for shift workers. Further research is needed to elucidate the relationship between weight management, insulin sensitivity, and exogenous melatonin.

Pharmacologic Interventions
Medications may be useful in promoting circadian balance (Table 5). Anything that can affect hormone equilibrium can be beneficial to patients with metabolic syndrome. Using medications to regulate sleep and wake cycles can reciprocally benefit metabolic disorders.

Osteopathic Manipulative Treatment
Shift work has been linked to poor regulation of the autonomic nervous system, as measured by heart rate variability.62 This poor regulation could play a role in shift workers’ increased risk for metabolic syndrome. One study of emergency medical technicians found that those working a 24-hour shift were more likely to have low heart rate variability and a higher risk of cardiovascular disease.63 Osteopathic manipulative treatment
Table 5. Possible Pharmacologic Interventions to Improve Circadian Balance in Shift Workers

<table>
<thead>
<tr>
<th>Drug Class or Names</th>
<th>Mechanism of Action</th>
<th>Indications</th>
<th>Common Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melatonin, ramelteon</td>
<td>Melatonin agonist</td>
<td>▪ Daytime insomnia ▪ Jet lag</td>
<td>▪ Headache ▪ Somnolence ▪ Dizziness ▪ Insulin suppression</td>
</tr>
<tr>
<td></td>
<td>Note: most effective in elderly patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypnotics, benzodiazepines (zolpidem, zaleplon, eszopiclone)</td>
<td>GABA agonists</td>
<td>▪ Daytime insomnia Note: These medications do not increase performance and alertness when awake. Short-term use is recommended.</td>
<td>▪ Headache ▪ Drowsiness ▪ Dizziness ▪ Sinusitis ▪ Depression ▪ Tolerance, symptoms include difficulty staying asleep</td>
</tr>
<tr>
<td>Antidepressants (SSRIs, SNRIs, trazodone, mirtazapine)</td>
<td>Serotonergic receptor agonist</td>
<td>▪ Insomnia ▪ Depression</td>
<td>▪ Headache ▪ Sexual dysfunction ▪ Abdominal discomfort ▪ Decreased metabolism/weight gain ▪ Increased blood pressure</td>
</tr>
<tr>
<td>Valerian root</td>
<td>GABA agonists</td>
<td>▪ Day time insomnia ▪ Jet lag</td>
<td>▪ Headache ▪ Excitability/uneasiness ▪ Abdominal discomfort</td>
</tr>
<tr>
<td>First generation antihistamines (diphenhydramine, doxylamine)</td>
<td>Histamine antagonists</td>
<td>▪ Insomnia</td>
<td>▪ Drowsiness ▪ Dizziness ▪ Headache ▪ Impaired coordination ▪ Decreased absorption of potassium</td>
</tr>
<tr>
<td>Orexin antagonists</td>
<td>Orexin antagonists</td>
<td>▪ Insomnia ▪ Weight loss with long-term use</td>
<td>▪ Somnolence ▪ Headache ▪ Dizziness ▪ Abnormal dreams</td>
</tr>
<tr>
<td>Orexin agonists</td>
<td>Orexin agonists Note: Orexin neurons fire during wake and REM phase.</td>
<td>▪ Increased alertness ▪ Weight loss ▪ Improved mood</td>
<td>N/A</td>
</tr>
<tr>
<td>Modafinil, armodafinil</td>
<td>Unclear; inhibits dopamine reuptake</td>
<td>▪ Increased night time alertness</td>
<td>▪ Headaches ▪ Nervousness ▪ Abdominal discomfort ▪ Increased blood pressure</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Adenosine antagonist</td>
<td>▪ Increased night time alertness</td>
<td>▪ Insomnia ▪ Palpitations ▪ Tremors ▪ Dependency ▪ Rebound sleepiness</td>
</tr>
</tbody>
</table>

Abbreviations: GABA, γ-aminobutyric acid; NA, not applicable; NREM, non–rapid eye movement; REM, rapid eye movement; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
(OMT) has been shown to improve both heart rate variability and sleep latency.\textsuperscript{64,65} For these reasons, OMT should be considered as part of the treatment plan for shift workers at risk for metabolic syndrome. These techniques can be used to both reset autonomic tone and to immediately improve sleep quality.

**Conclusion**

Shift workers should be screened for signs of circadian discordance. Early identification of circadian discordance in this population is essential to reduce the risk of developing metabolic syndrome. Primary prevention through lifestyle modifications (eg, sleep hygiene practices, light therapy, eating and exercise habits, pharmaceuticals, and OMT) is the best way to address both the quality of life and the long-term health care burdens in shift workers.

In addition, workplace adjustments may have an even greater effect on improving sleep quality, hormonal balance, and overall health. Systemic changes in shift-work scheduling, light exposure, and better nutrition offerings may be the best ways to improve circadian rhythm disorders and reduce mortality associated with metabolic syndrome. As physicians, we should discuss these concerns with patients, local employers, and within the community.

With few clinical trials conducted to evaluate clinical and workplace interventions directed at shift workers with a nocturnal or rotational sleep-wake pattern, future research on the influence of lifestyle factors and pharmaceutical interventions should be done to determine the most effective strategy to reduce the burden of metabolic syndrome in this population.

**References**


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