Melatonin effective for some sleep disorders


Clinical Question
Is melatonin effective for insomnia and other sleep problems?

Bottom Line
Melatonin in doses from 0.1 mg to 10 mg is effective in helping adults and children who have difficulty falling asleep. It is particularly helpful in patients whose circadian rhythm is permanently off-kilter (delayed sleep phase syndrome). It increases sleep length, but not sleep quality, in patients who perform shift work or who have jet lag. (LOE=1a)

Study Design
Meta-analysis (randomized controlled trials)

Setting
Outpatient (any)

Synopsis
The authors of this systematic review evaluated the role of melatonin in the treatment of different types of sleep problems in different types of patients. They performed a thorough search of the literature though they limited the research to English-language publications. Potential research was screened by 2 independent reviewers and the data were abstracted by 1 reviewer and then checked for accuracy by another. They included controlled clinical trials and reviewed all studies for quality using the established Jadad criteria.

In normal sleepers, melatonin had a clinically insignificant effect on the time to sleep onset (sleep onset latency) or the amount of time actually spent asleep (sleep efficiency). Melatonin in doses of 1 mg to 3 mg caused an average 12.7-minute delay in rapid eye movement onset (REM latency) as compared with placebo.

In patients with simple insomnia, melatonin helped adults to fall asleep an average 10.7 minutes faster (95% CI, 3.7–17.6 min). Children had a better response, falling asleep an average 17 minutes faster. It was particularly effective in patients with delayed sleep phase syndrome, a condition in which we might say that a person’s circadian rhythm is misaligned without an external cause such as jet lag or shift work. In these patients, sleep onset was an average 38.8 minutes faster (95% CI, 27.3–50.3 min). Melatonin had no effect on sleep quality, wakefulness, total sleep time, or percent time spent in REM sleep.

In patients suffering from jet lag, melatonin did not decrease sleep onset latency or increase sleep efficiency, sleep quality, or the time spent in REM sleep, though it was effective in increasing the total sleep time. It had an effect similar to zolpidem (Ambien) in patients with jet lag in one study. Melatonin is not effective in patients with a secondary sleep disorder.

What is a POEM?
Each month, the POEMs (Patient-Oriented Evidence that Matters) editorial team reviews 105 research journals in many specialties, and selects and evaluates studies that investigate important primary care problems, measure meaningful outcomes, and have the potential to change the way medicine is practiced. Each POEM offers a Bottom Line observation and summarizes the study’s objective, patient population, study design and validity, and results. InfoPOEMs, InfoRetriever and POEMS for Primary Care are registered trademarks of InfoPOEM, Inc. POEMS and Patient-Oriented Evidence that Matters are trademarks of InfoPOEM, Inc. These POEMs are copyrighted by, and published with the express permission of InfoPOEM, Inc. and may not be copied or otherwise reproduced without the prior written consent of InfoPOEM, Inc.
Antibiotic choice makes little difference in CAP


Clinical Question
In the treatment of patients with community-acquired pneumonia, is there a difference among antibiotics?

Bottom Line
Strange, but true: Oral beta-lactam antibiotics—amoxicillin, amoxicillin/clavulanate (Augmentin), or a cephalosporin—are as effective in the treatment of community-acquired pneumonia as antibiotics active against atypical pathogens, even in patients infected with *Mycoplasma pneumoniae* or *Chlamydia pneumoniae*. These old standbys can be used instead of the more expensive drugs for most patients.

*Legionella* infection still requires treatment with an antibiotic effective against atypical pathogens, but in these studies only 1.1% of the patients with nonsevere pneumonia had *Legionella*. These results are backed up by similar findings from clinical practice (Hedlund J, et al. Scand J Infect Dis 2002; 34:887–892). (LOE=1a)

Study Design
Meta-analysis (randomized controlled trials)

Setting
Various (meta-analysis)

Synopsis
We have to treat some patients with community-acquired pneumonia (CAP) for atypical bacteria, just in case, don’t we? This question was answered by the authors of this meta-analysis. They identified 18 studies comparing a beta-lactam antibiotic with an antibiotic active against the atypical pathogens *M pneumoniae*, *Legionella* species, and *C pneumoniae*: macrolides, fluoroquinolones, or ketolides (eg, telithromycin [Ketek]). They used rigorous methods to identify the studies, searching 3 databases for articles published in any language, searching the reference lists of review articles and retrieved studies, and including unpublished research conducted by pharmaceutical companies. Two reviewers independently screened the studies for inclusion. On average, the 6749 patients in the clinical trials were younger than the typical patient with pneumonia (in most studies the average age was between 40 and 55 years) and had a better risk profile.

Neither macrolides, ketolides, or fluoroquinolones were superior to beta-lactam antibiotics. When analyzed separately by type of antibiotic, neither macrolides nor fluoroquinolones were superior, either with regard to cure or mortality rates at the time specified in the study, usually end of treatment or at 10 days. The speed of response, relapse, or length of stay were not compared.

Here’s a surprising outcome: There was no difference between beta-lactams and the other drugs in patients who had *M pneumoniae* or *C pneumoniae*. The numbers of patients in these subgroups was small: 211 patients had *Mycoplasma* infections and 115 had *Chlamydia* infections. The antibiotics active against atypical pathogens were significantly better at producing clinical cures in the treatment of 75 patients with *Legionella* (relative risk=0.4; 95% CI, 0.19–0.85).

The investigators used a combined endpoint of success, including cure of pneumonia, absence of adverse drug reactions, absence of medical complications, no need for additional visits, no changes in initial treatment, and no hospital admission or death within 30 days. This outcome was achieved by 83.6% of outpatients and 80.7% of hospitalized patients. Readmission rates were similar in the 2 groups (6%–7%). Health-related quality-of-life scores measured at 7 and 30 days were similar in both groups. More outpatients than inpatients reported satisfaction with their overall care (91.2% vs 79.1%; *P*=.03).
Anemia does not predict iron deficiency among toddlers


Clinical Question
Does screening toddlers for anemia identify those with iron deficiency?

Bottom Line
These study results present a quandary: We cannot feel assured that a young child doesn’t have anemia if they show a normal hemoglobin level, and we can’t be sure that he or she has anemia if the hemoglobin level is low. Screening for iron deficiency in toddlers by checking serum hemoglobin misses most children with a deficiency, and most of the children with anemia do not have an iron deficiency. As the author of this study suggests, it might make more sense to continue low-dose supplementation of iron in all children rather than use a policy of screen and treat. (LOE=1c)

Study Design
Cohort (prospective)

Setting
Population-based

Synopsis
An insufficient level of iron (which is used in more than 200 enzymes in the body) is associated with developmental disabilities in young children. Measuring serum hemoglobin as an indicator of anemia is used to screen for iron deficiency in young children.

The author of this study evaluated the correlation between anemia and iron deficiency by examining the findings of the National Health and Nutrition Survey (NHANES) conducted between 1988 and 1994. The NHANES is a stratified population sample performed across the US. The survey included 1289 toddlers between the ages of 12 and 35 months, and all of these children underwent complete blood counts, as well as measures of iron stores: ferritin, transferrin saturation, and free erythrocyte protoporphyrin. Iron deficiency, identified in 10.9% of the children studied, was defined as at least 2 of the iron indices being below normal. Anemia was defined as a hemoglobin level of less than 11.0 g/dL. There was little relation in this sample between the presence of iron deficiency and anemia.

Children with iron deficiency had an average hemoglobin level of 11.5 g/dL, which, although statistically lower than the average 12.1 g/dL in nondeficient toddlers, was still above the cutoff for anemia. Only 28% (95% confidence interval [CI], 20–38) of toddlers with low hemoglobin actually had iron deficiency. The ability of anemia to rule out iron deficiency was also low: the sensitivity of the test was only 30% (95% CI, 20–40). In other words, for every 100 toddlers studied, 9 will have anemia, and 9 will have iron deficiency, but only 3 of the children with iron deficiency will be anemic and only 3 of the children with anemia will be iron deficient; not a great overlap. Similar results have been shown in data from New Zealand, Britain, and Europe (see the Discussion section of this study).

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CONTINUED
Once-daily topical steroid dosing effective for atopic eczema


Clinical Question
Is dosing topical corticosteroids more than once a day better than once-daily dosing for atopic eczema?

Bottom Line
Patients should begin with once-daily dosing of topical corticosteroids for atopic eczema, increasing to twice or 3 times per day only if symptoms are not well controlled. (LOE=1a–)

Study Design
Meta-analysis (randomized controlled trials)

Setting
Outpatient (any)

Synopsis
The authors searched the literature for randomized controlled trials (RCTs) comparing once-daily with more frequent dosing of topical corticosteroids for atopic eczema. They excluded studies of seborrheic eczema, varicose eczema, discoid eczema, and contact dermatitis. The 2 primary outcomes consistent between most studies was “at least a good response or 50% improvement” and “eczema rated as cleared or controlled.” The meta-analysis was well executed with a comprehensive search, a good description of inclusion criteria, careful abstracting of data, and an appropriate analysis.

Of the 10 RCTs enrolling a total of 1819 patients, 1 studied a very potent steroid, 8 studied potent steroids, and 1 studied a moderately potent steroid. Results between studies were heterogeneous, so it was inappropriate to combine the results—which is frustrating for clinicians who want an answer, but it’s good policy for a meta-analysis.

Review of the individual studies shows little support for dosing more than once a day: only 1 of
Early intrathecal analgesia does not increase cesarean sections


Clinical Question
Does early administration of neuraxial analgesia in labor increase the risk of cesarean delivery?

Bottom Line
Intrathecal fentanyl followed by epidural bupivacaine plus fentanyl, if needed for pain relief, in early labor is not associated with a higher cesarean delivery rate than systemic hydromorphone for early labor. The neuraxial approach also provides more effective analgesia and a shorter mean duration of first-stage labor. (LOE=1b)

Study Design
Randomized controlled trial (nonblinded)

Allocation
Concealed

Setting
Inpatient (ward only)

Synopsis
Epidural analgesia, when given before a cervical dilatation of 4 cm, has been associated with higher cesarean delivery rate. Systemic narcotics are often used for women requesting analgesia in early labor.

In this trial, 750 women with cervical dilatation of less than 4 cm were randomized at the first request for analgesia to a neuraxial analgesia group that received intrathecal fentanyl 25 mg or to a control group that received 1 mg intravenous hydromorphone plus 1 mg intramuscular hydromorphone. At the second request for analgesia, even with cervical dilatation still less than 4 cm, the neuraxial group received epidural analgesia with bupivacaine at half the usual strength plus fentanyl, while the control group received the same dosing of hydromorphone.

The cesarean delivery rate was a similar 18% to 20% in the 2 groups. The mean time from first administration of analgesia to complete dilatation was 90 minutes shorter in the neuraxial group (295 minutes vs 385 minutes). Pain control after the first dose of analgesia was better in the neuraxial group (mean = 2 vs 6, on a 0–10 scale).