Cochrane for Clinicians

Putting Evidence into Practice

Exercise vs. No Exercise for the Occurrence, Severity, and Duration of Acute Respiratory Tract Infections

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Clinical Question

Does regular exercise reduce the occurrence, severity, or duration of acute respiratory tract infections?

Evidence-Based Answer

For adults, regular exercise may reduce the overall severity of acute respiratory tract infections and the number of days with symptoms, but there is no evidence that exercise reduces the overall occurrence or duration of these infections.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Acute respiratory tract infections (i.e., infections of the respiratory tract lasting less than 30 days) are a common cause of morbidity each year.[2] In 2016 in the United States, 9.6% of all medical office visits were for respiratory diseases.[3] A 2015 Cochrane review of 11 trials involving 904 adults did not determine whether exercise could affect the occurrence, severity, or duration of acute respiratory tract infections and called for larger, higher-quality studies.[4]

For this updated review, the authors added three new trials for a total of 1,377 adults; nine trials were from the United States and the remainder were from Brazil, Canada, Portugal, Spain, and Turkey.[1] Participants were 18 to 85 years of age. Study duration ranged from seven days to 12 months, and the most common intervention was supervised aerobic exercise for 30 to 45 minutes per session for three to five days each week. All studies compared exercise with no exercise. The review authors relied on the definition of acute respiratory tract infections used by the trial authors. The studies in this review were assessed as being at low risk of reporting bias; low, unclear, or high risk of attrition bias; unclear risk of selection bias; and high risk of performance and detection bias.

Low-certainty evidence demonstrated that aerobic exercise vs. no exercise does not reduce the number of acute respiratory tract infection episodes per year or the proportion of individuals who will experience at least one acute respiratory tract infection over 12 to 52 weeks of follow-up.

The effect of exercise vs. no exercise on severity of acute respiratory tract infection symptoms was measured in two studies.[5,6] The studies calculated global severity using scores on the Wisconsin Upper Respiratory Symptom Survey (WURSS), a validated tool used to determine the severity of upper respiratory tract infections in study participants.[7] When combined, these two studies found that over eight weeks of follow-up, participants who exercised scored a mean total of 236 points on the WURSS tool, whereas those who did not scored a mean total of 342 points, for a mean difference of 106 points.[5,6] This finding was rated low certainty because of a lack of blinding and the wide CIs for the results.

The reviewers also found that exercise reduced the overall number of symptomatic days over 12 weeks of follow-up (mean difference = –2.24 days; 95% CI, –3.50 to –0.98), but they did not note a reduction in symptomatic days per illness episode; these findings were rated low certainty because of the risk of selection bias and inconsistency of results between studies. Exercise did not impact quality of life or disease cost and did not seem to cause more exercise-related injury. The evidence supporting these conclusions remains of low certainty, and future high-quality studies are needed to provide further clarity on the benefits of exercise for acute respiratory tract infections.

The practice recommendations in this activity are available at http://www.cochrane.org/CD010596.

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, assistant medical editor.

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CME **This clinical content** conforms to AAFP criteria for CME. See CME Quiz on page 141.

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Topical and Device-Based Treatment of Toenail Onychomycosis

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Clinical Question

Are topical and device-based therapies safe and effective in the treatment of toenail onychomycosis?

Evidence-Based Answer

Topical antifungal drugs, including efinaconazole 10% solution (Jublia), tavaborole 5% solution (Kerydin), and ciclopirox 8% lacquer and hydrolacquer, are beneficial in treating mild to moderate toenail onychomycosis.[1,2] Potential adverse effects are mild and include dermatitis and vesicles.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Onychomycosis, a fungal infection of the nail caused by dermatophytes, nondermatophyte molds, and yeasts, is the most common nail disorder encountered in primary care.[1,3] Aside from its cosmetic impact, toenail onychomycosis may cause pain and discomfort.[1] Oral antifungal medications are considered the most effective treatment; however, they are associated with drug interactions and systemic adverse effects.[1] The authors of this review sought to determine the safety and effectiveness of topical and device-based therapies to treat toenail onychomycosis.

This Cochrane review included 56 randomized controlled trials (published between 1993 and 2019) involving 12,501 participants.[1] The primary outcomes were complete cure rate (defined as mycologic cure and resolution of all clinical symptoms) and treatment-related adverse effects. Secondary outcomes at follow-up included mycologic cure rate (negative mycologic testing) and clinical cure rate (0% nail plate involvement). Ultimately, 12 studies involving 4,269 participants were included in the quantitative meta-analysis.[1] Most studies addressed mild to moderate onychomycosis without matrix involvement and with more than one toenail affected. Participants were 27 to 68 years of age, on average, with a treatment duration of 36 or 48 weeks, and clinical outcomes were measured up to four weeks after treatment completion.

High-quality evidence demonstrated that efinaconazole 10% solution was superior to placebo at achieving clinical cure (relative risk [RR] = 3.07; 95% CI, 2.08 to 4.53; two studies, 1,655 participants) and complete cure (RR = 3.54; 95% CI, 2.24 to 5.60; three studies, 1,716 participants). Moderate-quality evidence demonstrated that efinaconazole 10% solution produced mycologic cure (RR = 2.31; 95% CI, 1.08 to 4.94; three studies, 1,716 participants).

In two studies involving 1,198 participants, tavaborole 5% solution was superior to placebo at achieving mycologic cure (RR = 3.40; 95% CI, 2.34 to 4.93; high-quality evidence) and complete cure (RR = 7.40; 95% CI, 2.71 to 20.24; moderate-quality evidence). Finally, ciclopirox 8% lacquer was superior to placebo at achieving mycologic cure (RR = 3.15; 95% CI, 1.93 to 5.12; two studies, 460 participants; moderate-quality evidence) and complete cure (RR = 9.29; 95% CI, 1.72 to 50.14; two studies, 460 participants; low-quality evidence). Additional studies reviewed by the authors were very low quality and did not demonstrate effectiveness for 1064-nm Nd:YAG (neodymium:yttrium-aluminum-garnet) laser

(three studies) or luliconazole 1% solution (Luzu; one study).[1]

When compared with ciclopirox 8% lacquer and amorolfine 5% lacquer, ciclopirox 8% hydrolacquer was more effective at achieving complete cure (RR = 2.43; 95% CI, 1.32 to 4.48; two studies, 490 participants; moderate-quality evidence). However, there was no difference between these treatments in mycologic cure or risk of adverse effects, including erythema, rash, and burning.[1]

Adverse effects such as dermatitis and vesicles were associated with use of efinaconazole (RR = 1.10; 95% CI, 1.01 to 1.20; three studies, 1,701 participants; high-quality evidence), and adverse effects at the application site occurred in studies of tavaborole (RR = 3.82; 95% CI, 1.65 to 8.85; two studies, 1,186 participants; moderate-quality evidence). Use of ciclopirox 8% lacquer did not seem to increase the risk of rash or nail alteration.[1]

Current clinical practice guidelines recommend using oral antifungal agents as first-line treatment for onychomycosis; however, this may not be feasible for patients with limited access to care, potential drug interactions, contraindications to oral therapy, or a preference for topical treatment.[4,5] Of note, oral terbinafine (Lamisil; $8 to $72 for 30 tablets) costs the same as or less than topical agents (e.g., ciclopirox 8% lacquer, which ranges from $16 to $45 per bottle).[6]

The practice recommendations in this activity are available at http://www.cochrane.org/CD012093.

This article reflects the opinions of the authors alone and does not reflect the opinion of the Department of the Army, the Department of the Air Force, the Department of the Navy, the Defense Health Agency, the Department of Defense, or the U.S. government.

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