POEMs

Patient-Oriented Evidence That Matters

Platelet-Rich Plasma Is Equal to Saline for Patients with Patellar Tendinopathy

Clinical Question

Are platelet-rich plasma injections effective in patients with patellar tendinopathy?

Bottom Line

In this study, platelet-rich plasma injections were no better than saline injections in improving pain or activity in patients with patellar tendinopathy. It did not matter whether the plasma was leukocyte rich or leukocyte poor. The study was too small to detect potential harms of the intervention. (Level of Evidence = 2b)

Synopsis

In this multicenter (Seattle, Oslo, Bologna) trial, the authors enrolled 61 adults, 18 to 50 years of age, with at least six months of clinically diagnosed patellar tendinopathy confirmed by ultrasonography with persistent symptoms in spite of a minimum of six weeks of exercise-based rehabilitation. The authors randomized patients to receive ultrasound-guided injections of either leukocyte-rich platelet-rich plasma, leukocyte-poor platelet-rich plasma, or saline. One week later, all patients engaged in a supervised gym-based rehabilitation program three times weekly for six weeks. Using standardized scales, the researchers evaluated each patient's pain, function, and activity limitations at baseline, and at 12, 24, and 52 weeks after the injections. They asked the patients for their own overall rating of change at the subsequent assessments. They had nearly complete (93%) follow-up at 12 weeks but only 79% at the end of a year. At no point in the study did the authors find any differences in the three groups as to any of the outcomes or patient global assessment of improvement. Six weeks after the intervention, five patients, none of whom received saline, reported overall worsening compared with their baseline. The authors report one patient experienced localized patellar tendon pain following the injection, enough to prevent activity. No other harms are reported, possibly because of the small sample size. The study was large enough to detect clinically meaningful differences in pain and functional limitations.

Study design: Randomized controlled trial (single-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Scott A, LaPrade RF, Harmon KG, et al. Platelet-rich plasma for patellar tendinopathy: a randomized controlled trial of leukocyte-rich PRP or leukocyte-poor PRP versus saline.* Am J Sports Med. *2019;47(7):1654-1661.*

Henry C. Barry, MD, MS
Professor
Michigan State University
East Lansing, Mich.

Augmentation of Antidepressant Treatment Offers Little Benefit

Clinical Question

Is augmentation of antidepressant treatment effective for patients with treatment-resistant depression?

Bottom Line

The available evidence that treatment-resistant depression (depression that is unresponsive to two different treatments of adequate dose and length) responds well to augmentation treatment (i.e., adding psychotherapy, lithium, or aripiprazole [Abilify] to current treatment) is weak. The available evidence shows no benefit with lithium and small benefit with psychotherapy or aripiprazole. (Level of Evidence = 1a–)

Synopsis

The authors searched two databases (but not the Cochrane Library) for randomized studies of augmentation treatment for patients who did not respond to at least two courses

of treatment for major depressive disorder. Two authors selected studies for inclusion and independently extracted the data. Most of the 28 studies of 5,461 patients had low to moderate risk of bias (i.e., studies were of medium to high quality) and included both drug treatment and psychological therapies. Instead of comparing directly across treatments (the benefit in one group vs. the other), the authors compared the before-after change in results within each group. In three low-quality studies, psychological treatment showed a moderate benefit. In four studies of aripiprazole, there was a small likelihood of benefit after short-term treatment (effect size = 1.33; 95% CI, 1.23 to 1.44) compared with placebo. Lithium produced an effect size similar to placebo.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Various (meta-analysis)

Reference: *Strawbridge R, Carter B, Marwood L, et al. Augmentation therapies for treatment-resistant depression: systematic review and meta-analysis.* Br J Psychiatry. *2019;214(1):42-51.*

Allen F. Shaughnessy, PharmD, MMedEd
Professor of Family Medicine
Tufts University
Boston, Mass.

Baloxavir Reduces Symptom Duration Similar to Oseltamivir, Primarily Within 24 Hours of Symptom Onset

Clinical Question

Is baloxavir (Xofluza) a safe and effective for treatment of influenza?

Bottom Line

Baloxavir has similar efficacy to oseltamivir (Tamiflu) (33-hour reduction in duration of symptoms compared with placebo) and, like oseltamivir, is most effective when given within 24 hours of the onset of symptoms. If given 24 to 48 hours after symptom onset, symptom duration was reduced by only 13 hours (which is almost identical to what we found in our meta-analysis of oseltamivir [*Fam Pract*. 2013;30(2):125-133]). It does not seem worth the extra cost in the United States: $160 for baloxavir vs. $50 for oseltamivir (www.goodrx.com). There are no data regarding the effect on complications or mortality, nor any data for patients younger than 12 years, older than 64 years, or with serious comorbidities. The major advantages of baloxavir over oseltamivir for those who choose to use it are convenience because it is a single dose and fewer adverse drug reactions (number needed to treat = 25). (Level of Evidence = 1b)

Synopsis

Baloxavir inhibits polymerase acidic protein, which is involved in viral replication. This report summarizes the results of a phase two (dose-ranging) trial and a phase three trial comparing baloxavir with oseltamivir and placebo (baloxavir is now U.S. Food and Drug Administration approved). We will focus on the phase three trial, which recruited patients 12 to 64 years with an influenza-like illness for less than 48 hours. The authors randomized patients 20 to 64 years of age into one of three groups in a 2:2:1 ratio: baloxavir in a single dose (40 mg for patients weighing less than 80 kg [176 lbs] and 80 mg for patients weighing at least 80 kg); oseltamivir, 75 mg twice daily for five days; or matching placebos. The patients 12 to 19 years of age were randomized in a 2:1 ratio to baloxavir or placebo. Influenza-like illness was defined as the presence of fever 100.4°F (38°C) or higher, at least one respiratory symptom that was moderately severe, and at least one systemic symptom. The median age of patients was 32 to 38 years among the different treatment groups, 77% of the patients were recruited in Japan (the remainder in the United States), and 53% were recruited within 24 hours of the onset of symptoms. Groups were well balanced at randomization. Patients were followed up for 14 days, and the primary outcome was time to symptom alleviation, which was defined as all symptoms being absent or mild for at least 21.5 hours. Of the 1,436 patients who were randomized, 1,064 had influenza confirmed by polymerase chain reaction. In the intention-to-treat population (patients with influenza-like illness), the median time to symptom alleviation was 88.6 hours for placebo and 65.4 hours for baloxavir (median difference = 23.2 hours; 95% CI, 14.0 to 34.2 hours). When limiting the analysis to only those who later were determined by polymerase chain reaction to have influenza, the median duration of symptoms was 80.2 hours for placebo, 53.7 hours for baloxavir, and 53.8 hours for oseltamivir. The benefit was much greater among patients recruited within 24 hours of onset of symptoms than in those recruited between 24 and 48 hours (32.8 hours vs. 13.2 hours; $P = .008$). Nausea and vomiting were more common with oseltamivir (4.8%), diarrhea was more common with baloxavir (1.8%), but overall the drugs were well tolerated. The number needed to treat to prevent an adverse drug reaction with baloxavir compared with oseltamivir was 25.

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Uncertain

Setting: Outpatient (any)

Reference: *Hayden FG, Sugaya N, Hirotsu N, et al.; Baloxavir Marboxil Investigators Group. Baloxavir marboxil for uncomplicated influenza in adults and adolescents.* N Engl J Med. *2018;379(10):913-923.*

Mark H. Ebell, MD, MS
Professor
University of Georgia
Athens, Ga.

One Month of Dual Antiplatelet Therapy Followed by Clopidogrel Alone Is Superior to 12 Months of Dual Antiplatelet Therapy After Percutaneous Coronary Intervention

Clinical Question

Is one month of dual antiplatelet therapy followed by clopidogrel (Plavix) monotherapy noninferior or superior to 12 months of dual antiplatelet therapy in adults undergoing percutaneous coronary intervention?

Bottom Line

This study found that one month of dual antiplatelet therapy (aspirin plus clopidogrel or prasugrel [Effient]) followed by clopidogrel monotherapy for up to five years is both noninferior and superior to 12 months of dual antiplatelet therapy followed by aspirin for up to five years for reducing the risk of adverse cardiovascular outcomes and major bleeding complications in adults undergoing successful percutaneous coronary intervention with a drug-eluting stent. Another study of similar patients in the same journal also reported noninferior rates of major adverse cardiovascular events and significantly fewer adverse bleeding events after three months of dual antiplatelet therapy followed by P2Y12 inhibitor monotherapy (e.g., clopidogrel, prasugrel, ticagrelor [Brilinta]) compared with 12 months of dual antiplatelet therapy. (Level of Evidence = 1b)

Synopsis

The optimal duration of dual antiplatelet therapy after percutaneous coronary intervention with drug-eluting stents remains uncertain, especially because the mortality associated with a bleeding event is comparable with cardiovascular mortality following acute myocardial infarction. The investigators identified consenting adults (N = 3,045) who underwent successful percutaneous coronary intervention with a cobalt-chromium everolimus–eluting stent. Before hospital discharge, eligible patients randomly received (concealed allocation assignment) one month of dual antiplatelet therapy with either aspirin (81 to 200 mg per day) and clopidogrel (75 mg per day) or aspirin and prasugrel (3.75 mg per day) followed by clopidogrel monotherapy for up to five years, or dual antiplatelet therapy with aspirin and clopidogrel for up to 12 months, followed by aspirin monotherapy for up to five years. The primary end point was a composite of cardiovascular death, myocardial infarction, stent thrombosis, stroke, or bleeding. Individuals masked to treatment group assignment adjudicated all clinical events. Complete follow-up occurred for 98.8% of participants at 12 months.

Using intention-to-treat and per-protocol analyses, one month of dual antiplatelet therapy was both significantly noninferior and superior to 12 months of dual antiplatelet therapy for the primary end point (2.36% vs. 3.70%; number needed to treat = 76.3; 95% CI, 39.0 to 1,128.6). Major bleeding occurred in significantly fewer patients in the one-month dual antiplatelet therapy group compared with the 12-month dual antiplatelet therapy group (0.41% vs. 1.54%; number needed to harm = 116.2; 65.4 to 334.0).

Study design: Randomized controlled trial (single-blinded)

Funding source: Industry

Allocation: Concealed

Setting: Inpatient (any location) with outpatient follow-up

Reference: *Watanabe H, Domei T, Morimoto T, et al.; STOPDAPT-2 Investigators. Effect of 1-month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy on cardiovascular and bleeding events in patients receiving PCI: The STOPDAPT-2 randomized clinical trial.* JAMA. *2019;321(24):2414-2427.*

David C. Slawson, MD
Professor of Family Medicine
UNC Chapel Hill
Charlotte, N.C.

Editor's Note: Dr. Ebell is deputy editor for evidence-based medicine for *AFP* and cofounder and editor-in-chief of Essential Evidence Plus, published by Wiley-Blackwell. Dr. Shaughnessy is an assistant medical editor for *AFP*. ■