POEMs

Patient-Oriented Evidence That Matters

Short-Term Clopidogrel Plus Aspirin Prevents Second Ischemic Stroke Better Than Aspirin Alone

Clinical Question

Does clopidogrel (Plavix) add benefit to aspirin treatment in patients with acute minor ischemic stroke or transient ischemic attack?

Bottom Line

Combined treatment with clopidogrel and aspirin, started within 24 hours of the first event, will decrease the likelihood of a recurrent stroke in an additional 2% of patients compared with aspirin alone, with a slight increase in the risk of extracranial bleeding. The greatest additional benefit is in the first 10 days with little additional benefit after 21 days of combined treatment. (Level of Evidence = 1a)

Synopsis

The authors searched several databases, including the Cochrane Central Register of Controlled Trials and reference lists of retrieved studies. They included studies that enrolled patients with a diagnosis of an acute minor ischemic stroke or high-risk transient ischemic attack for whom treatment was started within three days. Two researchers independently abstracted data from the studies and evaluated study quality. They identified three high-quality studies of 10,447 patients. When started within 24 hours of symptoms, combination treatment with clopidogrel and aspirin, compared with either treatment alone, had no additional effect on reducing all-cause mortality but reduced the risk of nonfatal recurrent stroke by 1.9% (a reduction of 20 per 1,000 patients treated). Stroke reduction benefit was most prominent in the first 10 days of treatment with the combination; there was little additional benefit after 21 days. The likelihood of major extracranial bleeding was slightly higher with the combination (0.2% absolute increase).

Study design: Systematic review

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Hao Q, Tampi M, O'Donnell M, et al. Clopidogrel plus aspirin versus aspirin alone for acute minor ischaemic stroke or high risk transient ischaemic attack: systematic review and meta-analysis.* BMJ. *2018;363:k5108.*

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5% Fluorouracil Is the Preferred Treatment for Actinic Keratoses

Clinical Question

What is the best approach to treat multiple actinic keratoses in a single field?

Bottom Line

The use of topical 5% fluorouracil is most likely to result in successful elimination of actinic keratoses in a field on the head or face. Treatment is once weekly for four weeks, which may create a barrier to adherence for some patients (even in this trial, where adherence should be optimal, 12% of patients were nonadherent). The impact of treatment on longer term outcomes, such as progression to squamous cell carcinoma, is not reported in this one-year study. (Level of Evidence = 1b)

Synopsis

The best field treatment for actinic keratoses (treatment of multiple lesions in a single continuous field) has not been established. Investigators recruited 1,174 patients from four Dutch dermatology clinics, of whom 624 met eligibility criteria (at least five actinic keratoses in a 25-cm to 100-cm contiguous area of the head or neck). The median age of participants was 73 years, 89% were men, and approximately half the lesions were on the face with the other half on the top of the head or vertex. The patients were randomized to receive one of four treatments: fluorouracil, imiquimod (Aldara), ingenol mebutate (Picato), or methyl aminolevulinate (Metvixia) with photodynamic therapy. Patients in the imiquimod group were evaluated at one month and were retreated if they were classified as a treatment failure (less than 75% lesion response). This retreatment of treatment failure was also done for the other three treatment groups at three months. Those who failed a second course of treatment were classified as treatment failures for the final assessment of outcomes, which occurred at 12 months. Only two to five patients in each group withdrew. A modified intention-to-treat analysis found that fluorouracil had the best results, with a cumulative success rate of 75% (compared with 54% for imiquimod, 38% for methyl aminolevulinate with photodynamic therapy, and only 29% for ingenol mebutate). The per-protocol analysis had similar findings, as did an analysis of patients limited to grade I or II actinic keratoses. Adverse events were common and similar across groups, with early severe burning pain much more common among those undergoing methyl aminolevulinate with photodynamic therapy. U.S. pricing based on GoodRx (http://www.goodrx.com, April 12, 2019) was $83 for fluorouracil, $23 for imiquimod, and $1,037 for ingenol mebutate.

Study design: Randomized controlled trial (single-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Jansen MH, Kessels JP, Nelemans PJ, et al. Randomized trial of four treatment approaches for actinic keratosis.* N Engl J Med. *2019;380(10):935-946.*

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