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Medical Reversals in Family Practice: A Review

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ABSTRACT

Background: Primary care physicians are challenged by the need to stay abreast of current research on a wide variety of topics in an environment of time constraints, evolving literature, and misinformation on health topics that are sometimes promulgated to the public.
Objective: We sought to identify and discuss common clinical situations encountered in primary care for which medical reversals have occurred.
Methods: We recently identified almost 400 medical practices that were used in clinical care before they were tested in well-done randomized controlled trials and subsequently were found to be ineffective or harmful.
Results: We review several of these practices commonly used in family medicine, which include arthroscopy for osteoarthritis of the knee, opioids for common causes of pain, and aspirin and continuous positive airway pressure for the prevention of cardiovascular disease.
Conclusions: Although these practices were implemented because of sound biologic plausibility or encouraging observational data, well done randomized controlled trials have failed to show evidence of effectiveness. These examples raise caution in introducing new clinical interventions into widespread clinical practice without sufficient high-quality evidence demonstrating efficacy.

Introduction

Primary care physicians treat a wide variety of conditions that require a broad knowledge base in the face of ever-evolving literature. Truisms that were taught in medical school and residency, or that are promulgated to the public, may not stand up to further research, and in fact, be reversed because of evidence from high-quality studies. Situations where medical practices are implemented and then are later found to be either ineffective or harmful (when compared against prior or lesser standards) through properly conducted randomized controlled trials (RCTs) are referred to as medical reversals.[1,2] Recent work has identified almost 400 of these medical practices in a variety of medical disciplines and conditions.[3] These practices were identified by reviewing RCTs in 3 high-impact medical journals (published 2003–2017), and represented almost all medical disciplines. Of 396 medical reversals identified in the original research, this article provides a focused summary of reversals of interest to primary care clinicians specifically, given the frequency of the conditions and persistent widespread use of the interventions. Here, we focus on 3 common clinical situations encountered in primary care for which medical reversals have occurred.[4] We have chosen to highlight these specific practices because of their relevance to primary care, the frequency of the conditions, the historical belief in the benefit of these interventions, and identified reversals that call into question the routine use of these medical practices.

Knee Pain

Millions of people in the United States have symptomatic knee osteoarthritis, affecting 10% to 13% of adults aged 60 years and older.[5] Guidelines strongly support participation in self-management programs, physical activity, strength training, and other low-impact exercises for those with symptomatic knee osteoarthritis.[6] However, despite inconsistent recommendations for more invasive treatments, hundreds of thousands in the United States are treated with corticosteroid injections and surgery.[7,8] Although these practices are common, randomized trials have failed to produce evidence for their effectiveness.

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For example, because corticosteroids have an anti-inflammatory effect and because osteoarthritis is an inflammatory condition, intra-articular corticosteroids have has been used for several decades, and as many as 95% of rheumatologists use them for osteoarthritis[9]; however, in a randomized trial of patients with symptomatic knee osteoarthritis, in which 140 patients were treated with an injection of either triamcinolone or saline every 12 weeks for 2 years, there were no differences in pain (difference = –0.6 on a scale of 0–20; 95% CI, –1.6 to 0.3) between patients treated with triamcinolone or saline.[10] Further, patients assigned to the triamcinolone treatment had a greater loss in cartilage thickness.

Many cases of osteoarthritis involve meniscal tears that are often treated with surgery to repair or remove the loose areas of degenerative cartilage, reduce swelling and pain, and preserve the knee from further damage.[11] More than 365,000 people were treated with knee arthroscopy in 2006 for a tear of the meniscus, an increase of about 25% from 10 years prior,[7] making it among the most commonly performed orthopedic surgeries.[12] Because it is unknown whether pain and other symptoms in patients with osteoarthritis come from meniscal tears, osteoarthritis, or both, there is question as to the effectiveness of knee arthroscopy in patients with osteoarthritis.

In 1 trial, patients with symptomatic and image-detected osteoarthritis and a meniscal tear (N = 351) were assigned to either surgery and postoperative physical therapy or a standardized physical therapy regimen.[13] After 6 months, there were no differences in physical function scores between the 2 groups (mean difference = 2.4 points on a 100-point scale; 95% CI, –1.8 to 6.5). Although there were a notable number of patients in the physical therapy only arm who also received surgery (30%), these results suggest that routine knee arthroscopy in all patients with osteoarthritis and meniscal tear is unwarranted.

Another trial has similarly cast doubt on the utility of meniscus surgery, even in the absence of arthritis. In this trial, 146 symptomatic patients with a meniscal tear but no evidence of osteoarthritis were assigned to either arthroscopic partial meniscectomy or sham surgery.[14] After 12 months of follow-up, there was no difference in physical functioning scores between the 2 groups (difference = –2.5 points on a 100-point scale; 95% CI, –9.2 to 4.1).

These studies collectively show that degenerative conditions of the knee do not benefit from routine invasive treatments such as corticosteroid injections and surgery. These patients are likely better off with a less-is-more approach of low-impact physical activity and strength training exercises.

Opioids for Pain

Pain is a common reason people visit the emergency department and patients are often prescribed an opioid medication to treat the pain.[15] Recent news has brought attention to the origins of the current opioid epidemic. The deception and downplaying of the addictiveness of these drugs is certainly a cause for concern,[16] but recent studies have provided evidence that opioids are no more effective in treating common conditions in the emergency setting than other less-addictive treatments. Back and neck pain are among the top reasons people are prescribed opioids,[17] and yet the superiority of opioids in treating these conditions over other common pain analgesics has not been established.

One trial randomized 323 patients in the emergency department with nontraumatic lower back pain to naproxen plus either oxycodone/acetaminophen, cyclobenzaprine, or placebo.[18] There were no differences in Roland-Morris Disability Questionnaire among the 3 treatment regimens (placebo = 8.9; 95% CI, 7.3–10.5; cyclobenzaprine = 8.2; 95% CI, 6.2–9.4; and oxycodone/acetaminophen = 7.8; 95% CI, 6.6–9.8).

Another trial randomized 416 patients who presented in the emergency department with acute extremity pain to aspirin plus 1 of 3 opioid treatments (5 mg oxycodone, 5 mg hydrocodone, or 30 mg codeine) or one nonopioid treatment (400 mg ibuprofen).[19] All groups had favorable changes in pain 2 hours after receiving treatment, but changes in pain intensity were no different between the aspirin plus ibuprofen group and any of the aspirin plus opioid groups (largest difference in pain was 0.8 on an 11-point scale; 95% CI, –0.2 to 1.7).

RCTs of in patients with chronic pain in the primary care setting have also failed to provide evidence of effectiveness. Patients (N = 240) in the Strategies for Prescribing Analgesics Comparative Effectiveness RCT who had chronic pain from back pain or hip or knee osteoarthritis and who were not responding to traditional analgesic use were assigned to either an opioid therapy or a nonopioid therapy.[20] After 12 months, there were no differences in pain-related function between the groups (difference = 0.1 on a scale of 0–10; 95% CI, –0.5 to 0.7), and pain intensity was better in the nonopioid group (difference = 0.5 on a scale of 0–10; 95% CI, 0.0–1.0).

The results from these trials show that, regardless of the potential addictiveness of these drugs, opioids are no better at controlling pain for common acute painful conditions than other nonopioid analgesics, and yet this practice became widely used before solid evidence of their effectiveness was established.

Cardiovascular Disease Prevention

Aspirin

Whether or not to take aspirin for the prevention of cardiovascular disease has been a heavily discussed topic. The US Preventive Services Task Force currently recommends aspirin for the prevention of cardiovascular disease in patients aged 50 to 59 years who are at an elevated risk of cardiovascular disease.[21] Other professional groups, including the American Heart Association and American Diabetes Association have made similar recommendations.[22] Perhaps because of extrapolation of these guidelines to other populations, many people have taken aspirin to prevent cardiovascular disease, even those who are average- or low-risk of cardiovascular disease.[23]

However, in the Japanese Primary Prevention Project, 14,464 patients aged 60 to 85 years with a history of hypertension, dyslipidemia, or diabetes were randomly assigned to either aspirin (100 mg/d) or no aspirin, in addition to any ongoing medications.[24] There were no differences in the composite outcome (death from cardiovascular causes, nonfatal stroke, and nonfatal myocardial infarction) between those assigned to the aspirin group and those assigned to the no aspirin group (2.77% vs 2.96%; $P = .54$) over 6 years.

Even in patients with other risk factors, aspirin for the prevention of cardiovascular disease does not seem to be effective. In a randomized trial of 2,539 patients with type 2 diabetes and no history of cardiovascular disease, patients were assigned to either 81 to 100 mg aspirin once daily or no regular use of aspirin.[25] After an average of 4.4 years follow-up, there was no difference in the rates of atherosclerotic events between the groups (hazard ratio =0.80; 95% CI, 0.58–1.10).

These results were just the beginning of studies showing a lack of benefit for the preventive nature of aspirin. The Aspirin to Reduce Risk of Initial Vascular Events study was an international RCT looking at the effects of aspirin in 12,546 patients with average cardiovascular risk and without diabetes.[26] Patients who received 100 mg aspirin daily did not have lower rates of the composite outcome (ie, cardiovascular death, myocardial infarction, unsta-

ble angina, stroke, or transient ischemic attack [HR = 0.96; 95% CI, 0.81–1.13]) after 5 years.

These results confirm that aspirin provides no benefit to patients who are at low or average risk of cardiovascular disease, and even suggests that aspirin does not benefit all patients who are at higher risk. Again, this practice has been regularly used despite of a lack of data to support its use in patients with average to low-risk likely because of overgeneralizing results of other studies in high-risk populations.

Obstructive sleep apnea and cardiovascular disease

Observational studies have shown an association between obstructive sleep apnea (OSA) and more cardiovascular events. This association is not necessarily direct, as individuals with OSA also often have other risk factors for cardiovascular disease, such as obesity and hypertension. Continuous positive airway pressure (CPAP) has been recommended for patients with moderate to severe sleep apnea because it was observed that OSA was associated with poor markers of cardiovascular disease (increased sympathetic activity and inflammatory mediators and decreased endothelial function),[27] but some recommend CPAP treatment for individuals with less-serious OSA and cardiovascular risk factors.[28]

In the Sleep Apnea Cardiovascular Endpoints RCT, the effectiveness of CPAP was evaluated in patients with OSA and either coronary artery disease or cerebrovascular disease and no severe daytime sleepiness.[29] Patients (N = 2717) were assigned to either CPAP care plus usual care or usual care only. After 3.7 years of follow-up, patients assigned to the CPAP group had fewer apnea or hypopnea events per hour but did not have improvements in the primary event (ie, death from cardiovascular causes; myocardial infarction; stroke; or hospitalization for unstable angina, heart failure, or transient ischemic attack [17.0% participants vs 15.4%; $P = 0.34$]). In another RCT of normotensive patients with OSA and no daytime sleepiness, 725 patients were randomized to either CPAP treatment or no CPAP treatment.[30] After a median of 4 years of follow-up, there were no differences in the incidence density rate between those assigned to CPAP and those assigned to no CPAP (9.20 vs 11.20 per 100 person-years; $P = 0.20$).

In this case, it appears that biologic plausibility may have spurred individuals to initially adopt this practice. Despite OSA being associated with cardiovascular disease, evidence to date has not supported that treatment of OSA with CPAP yields any improvement in cardiovascular outcomes.

Conclusions

We identified several common primary care conditions in which new, higher-quality evidence has reversed the prior understanding of effective treatments. In many situations, these interventions were adopted based on limited, lower-quality evidence, biologic plausibility, and expert opinion. These treatments have become widespread in clinical practice despite the lack of high quality supporting evidence. Even with RCTs demonstrating the inefficacy of some of these therapies, reversing these ineffective and/or harmful practices is still a major effort. These examples raise caution in introducing new clinical interventions into widespread clinical practice without sufficient high-quality evidence, as well as remind us of the continual need to appraise the evidence, even for time-honored clinical interventions.

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Author contributions

AH, CL, and VP selected and reviewed medical reversals to be included in this article; AH wrote the first draft and CL and VP reviewed and edited drafts.

Conflicts of Interests

Dr Prasad is host of Plenary Session podcast, which has Patreon backers. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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