Clinical Briefs in Primary Care

Evidence-based updates in primary care medicine

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Online Supplement to *Clinical Cardiology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Integrative Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports*

Volume 22, Number 1 January 2017

Topical Agent for Premature Ejaculation

SOURCE: Mark KP, Kerner I. Event-level impact of Promescent on quality of sexual experience in men with subjective premature ejaculation. *Int J Impot Res* 2016;28:216-220.

Premature ejaculation (PEJ) reportedly is the most common sexual dysfunction in men, even outstripping the prevalence of erectile dysfunction. This may surprise clinicians, since patients do not present often with that complaint, nor is it routine — except when encounters specifically are focused on sexual health — for clinicians to inquire about PEJ.

Currently, there are no drugs specifically approved for PEJ; instead, clinical trials documenting the efficacy of selective serotonin reuptake inhibitors (SSRIs) and tramadol for PEJ have led to their off-label use as often effective treatments.

In this open label trial in which patients (n = 91) were their own control, investigators invited study subjects who self-designated as PEJ and fulfilled criteria of a PEJ diagnostic tool to try topical Promescent (trade name) spray on their penis prior to intercourse. The active ingredient in Promescent is lidocaine.

According to the pre-set parameters of the study, Promescent was efficacious in that it essentially doubled the time to ejaculation; additionally, study subjects believed that the product was easy to use, with minimal interruption of sexual activity.

On the other hand, the latency time (time from intromission until ejaculation) was quite atypical compared to most of the PEJ trials in the literature. That is, in the Promescent trial, baseline ejaculatory latency time was 6.81 minutes, increasing to 11.16 minutes with treatment. Previous trials with SSRIs enrolled PEJ subjects with an ejaculatory latency time of 30 seconds, which would typically increase to three to four minutes with treatment. In any case, Promescent was effective in prolonging time to ejaculation, and was well tolerated. ■

Lung Cancer Screening at a VA Medical Center

SOURCE: Okereke IC, Bates MF, Jankowich MD, et al. Effects of implementation of lung cancer screening at one Veterans Affairs medical center. *Chest* 2016;150:1023-1029.

Thanks to favorable results from a very large clinical trial of low-dose CT lung cancer screening (n > 53,000) that showed not only a reduction in lung cancer mortality but also all-cause mortality, it is incumbent on clinicians to offer screening to appropriately selected patients. Experience at a VA medical center in Providence, RI, appears to favorably reflect some of the track record of the aforementioned National Lung Screening Trial.

When Okereke et al compared identification of lung nodules in a pre-screening period (2011-2013) to the 2013-2014 screening interval, they noted a distinct "downgrading" of lung cancer staging achieved through screening; that is, prior to screening, 37% of lung cancers were early stage (Stage I or Stage II). During the screening interval, 60% of identified lung cancers were early stage.

The prevalence of smoking usually is higher in VA medical center settings than the general public. Lung cancer screening in this population assists in identifying lung cancer at an earlier, more survivable stage. ■

Are We Using Novel Oral Anticoagulants Wisely?

SOURCE: Barra ME, Fanikos J, Connors JM, et al. Evaluation of dose-reduced direct oral anticoagulant therapy. *Am J Med* 2016;129:1198-1204.

There is little dispute over whether the so-called novel oral anticoagulants (NOACs), currently comprised of apixaban, dabigatran, edoxaban, and rivaroxaban, are as efficacious as warfarin, as well as simpler to use, since food interactions are minimal.

NOACs individually include labeling that calls for potential dose adjustments for chronic kidney disease, low body weight, and interacting substances (agents with p-glycoprotein and/or P450 interactions). Have clinicians performed dose-adjustments appropriately?

Barra et al retrospectively analyzed data from 224 patients who had been prescribed reduced-dose NOACs to determine if the dose reductions had been according to appropriate indications (as per labeling) as well as appropriate in amount of dose reduction.

Less than half the patients who had been

prescribed reduced-dose NOACs matched labeling criteria for such dose reduction. It may have been that concern over bleeding risk prompted prescribers to choose dose reduction; however, bleeding rates even within this group of patients receiving reduced-dose NOAC actually were higher than had been seen in clinical trials of NOACs.

How dose adjustment based on clinician judgment, as opposed to specific FDA labeling, will affect long-term outcomes remains to be determined. ■

Placebo for Osteoarthritis Pain

SOURCE: Dieppe P, Goldingay S, Greville-Harris M. The power and value of placebo and nocebo in painful osteoarthritis. *Osteoarthritis Cartilage* 2016;24:1850-1857.

Terminology about placebo, according to Dieppe et al, might be more useful if divided into placebo response ("a change seen in response to a sham intervention") and placebo effect ("the difference between doing nothing ... and giving a sham treatment"). The authors chose to focus on the symptomatic improvements that can occur for patients simply as a result of an encounter with a health professional.

By comparing pain reduction achieved in placebo groups of randomized, controlled osteoarthritis trials with treatment arms that received no treatment (not even placebo), the authors determined that an effect size of about 0.5 is seen with placebo, comparable to that seen with many "active" interventions. Context also may be important. For instance, injection placebos were particularly powerful.

The physiologic underpinnings of placebo response for pain indicate it is not "imaginary." For instance, the pain reduction of placebo can be blocked by pre-administration of naloxone, suggesting that such responses may be reflective of activation of endogenous endorphins.

The authors concluded that positive placebo response from patients occurs most fruitfully when patients feel safe, calm, and validated by their clinician. ■

New Tools for Glucose Monitoring

SOURCE: Bolinder J, Antuna R, Geelhoed-Duijvestijn P, et al. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: A multicentre, non-masked, randomised, controlled trial. *Lancet* 2016;388:2254-2263.

The inconvenience of frequent finger-stick testing to assess control of diabetes is particularly problematic for type 1 diabetics. The FreeStyle Libre (trade name) is a sensor the size of a human hair that is inserted in the skin of the upper arm and attached to a patch that records glucose readings over eight hours. The reading device can be downloaded and has the capacity to store up to 90 days of readings. Does the FreeStyle Libre outperform traditional fingerstick methodologies?

To test this hypothesis, Bolinder et al randomized participants with already well-controlled type 1 diabetes (n = 328) to use the "flash glucose monitoring system" or typical finger-stick monitoring. The primary outcome of the trial was amount of time in hypoglycemia during six months of follow-up. Time in hypoglycemia was reduced by 38% with the Freestyle Libre device, compared to "traditional" methods. A small number of participants (n = 10) experienced local reactions at the site of insertion of the sensor.

The device recently received FDA approval. A FreeStyle Libre "starter kit" currently is advertised at $359. ■

Dietary Supplement Trends, 1999-2012

SOURCE: Kantor ED, Rehm CD, Du M, et al. Trends in dietary supplement use among US adults from 1999-2012. *JAMA* 2016;316:1464-1474.

According to results from in-home interviews with 37,859 U.S. adults, 52% reported use of a supplement within the 30 days prior to the interview. Included under the canopy of "supplements" were multivitamins, fish oil, and individual supplements (such as vitamin D). Of concern (depending on your personal philosophical-scientific position on the issue), the use of supplements has remained essentially stable during the 1999-2012 interval.

Although some major players have declined over the past decade (multivitamin/multimineral use decreased from 37% to 31%), others have increased substantially: fish oil use increased from 1.3% in 1999 to 12% in 2012, and vitamin D increased from 5.3% to 19%. The authors reported that approximately 25% of supplement use had been recommended by a healthcare provider.

With the exception of folate supplementation for women, support for the benefits of supplements, in the absence of predefined deficiency, is scant.

The item that provided me that greatest reason for pause was not in the article itself but an editorial about this article in the same issue of *JAMA*, which I believe deserves to be quoted in full (reader discretion is advised): "... even after high-quality studies that show no meaningful clinical differences between supplements and placebos are published, the law provides [supplement] manufacturers latitude to continue advertising their products based on earlier, low-quality data. For example, Ginkgo biloba continues to be sold 'to support mental sharpness' despite a large, high-quality, NIH-funded study that found evidence to the contrary."

I am already reasonably supple. In the absence of strong evidence, I will continue to eschew supplements. ■

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is published monthly by AHC Media, LLC.

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