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Can Exenatide be Substituted for Insulin?

Source: Davis SN, et al. *Diabetes Care.* 2007;30(11):2767-2772.

Historically, insulin (INS) is the only agent that can consistently attain glycemic goals once patients have failed oral antidiabetic agents (OADA). Even when patients readily accept INS treatment, weight gain and hypoglycemia sometimes remain daunting obstacles. Hence, another highly-efficacious agent is very desirable.

Exenatide (EXNT) is a member of the class of OADA known as incretins. While providing a substantial glucose-lowering effect, EXNT is not associated with weight gain; indeed, weight reduction is commonly seen in patients treated with EXNT. Previous non-inferiority trials have shown comparable glucose control in patients failing OADA to whom either insulin or EXNT are added.

Davis, et al studied type 2 diabetes patients who were already on a combination of INS + OADA. Half of the study subjects (n=45) were switched to EXNT instead of INS, and the other half continued on INS. No changes were made in oral agents, diet, or exercise, although if hypoglycemia occurred, sulfonylurea dose was cut in half.

At the 16-weeks endpoint of the study, the change in A1C between the groups was not statistically significant. Although the incidence of hypoglycemia was similar in the EXNT and INS treatment groups, weight loss was significantly more common in the EXNT group. This small study is encouraging for patients who find insulin utilization problematic. EXNT might provide equally favorable control. ■

Treatment of Osteoporosis Saves Bones AND Lives

Source: Lyles KW, et al. *N Engl J Med.* 2007;357:1799-1809.

Hip fracture (HPFx) portends risk: mortality rates as high 25% in the year following HPFx have been reported. Once a HPFx has occurred, the risk of new fracture is 2.5 times greater than in persons without such history. Zoledronic acid (ZOL), a parenteral bisphosphonate (like oral alendronate, risedronate, ibandronate, but parenterally administered) is an intervention that could potentially change the balance of these negative outcomes.

The HORIZON trial (Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly Recurrent Fracture Trial) randomized 2,137 patients who had sustained a HPFx to either a once-yearly ZOL injection or placebo. All subjects (both groups) received supplementation with vitamin D and calcium.

At 1.9 years of follow-up, the ZOL recipients enjoyed not only a 35% relative risk reduction in new fractures, but also a 28% relative risk reduction in mortality.

Some earlier data has reported a meaningful incidence of atrial fibrillation in persons receiving ZOL, as well as (rarely) osteonecrosis. Neither was seen in this trial, nor was the rate of stroke increased (as would be anticipated were ZOL to induce occult atrial fibrillation). No serious adverse events were attributed to ZOL, though transient systemic malaise-like symptoms were seen. ZOL holds promise in persons with very-high-risk osteoporosis, such as those who have already sustained a HPFx. ■

Incidentalomas: It's All In Your Head

Source: Vernooij MW, et al. *N Engl J Med.* 2007;357:1821-1828.

One of the downstream "consequences" of our ever more-sophisticated quiver of diagnostic arrows—CT, MRI, etc—is the discovery of incidental findings. Sometimes these "incidentalomas" are important new findings that are ultimately lifesaving. Most often, however, the findings are benign entities which sometimes nonetheless require additional followup and added expense. Studies of abdominal CT report a 12% frequency of incidentalomas. A retrospective study among an age-diverse population (3-83 years) of brain MRI reported a 1% incidence of incidentalomas.

Vernooij, et al performed MRI of the brain on 2000 persons who are participating in the population-based Rotterdam Study. This study group is comprised of persons age 45 or greater (mean age = 63 years). All MRIs were read by one of two reviewers, neither of whom had clinical information about the subjects.

The most common incidental finding was asymptomatic ischemic CVA (7.2%). Aneurysms were the next most frequent (1.8%), most of which were <7 mm in size. Benign brain tumors were almost as common as aneurysms (1.6%), most of which were meningiomas.

It is generally recommended that asymptomatic meningiomas be followed for growth, even though most will not require any intervention. Aneurysms of the size discovered in this trial also generally no not merit intervention. Secondary stroke prevention strategies (eg, ASA, clopidogrel) are predicated upon a pre-existing symptomatic

stroke or TIA; little guidance is available as to the propriety of secondary stroke prevention driven by incidentally identified CVA. Outcome followup of incidentalomas will help guide future management strategies. ■

MRSA in These United States

Source: Klevens HM, et al. *JAMA.* 2007;298(15):1763-1771.

MRSA (methicillin-resistant *staphylococcus aureus*) has attained sufficient notoriety that it is not uncommon these days for patients to walk in, display their ill part, and ask "Do you think it's MRSA?" As recently as 10 years ago, MRSA might often be considered an infectious etiologic afterthought, and certainly only in persons who had been hospitalized. Today, it represents the most common etiology of cellulitis and cutaneous abscess presenting to Emergency Rooms.

To gain a better perspective on the population burden of MRSA, 9 US communities participated in surveillance for MRSA from July, 2004 to December 2005. Although admittedly sometimes a 'hazy line', MRSA infections were subclassified as either health care associated (MRSA-h) or community associated (MRSA-c).

Over the 18-month surveillance period, almost 9,000 MRSA cases were identified, the slight majority of which (58.4%) were MRSA-h. The incidence was substantially greater in blacks (over 2-fold) and women (1.4 fold). The mortality of invasive MRSA was 17.8%. If these data are extrapolated to the entire USA, it would be estimated that 94,360 MRSA infections occur, including 18,650 deaths. MRSA is a burgeoning public health issue. Clinicians are encouraged to continue to make a presumptive diagnosis of MRSA in appropriate clinical settings and promptly institute currently recommended treatment. ■

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Skin Cancer Screening: Our Patients Want It!

Source: Rodriguez GL, et al. *J Am Acad Dermatol.* 2007;57:775-781.

The statistics of skin cancer (Sk-Ca) are stark: not only does Sk-Ca overall outnumber all other cancers combined in the US, melanoma diagnosis is anticipated in upwards of 60,000 individuals in the US in 2007. Discouragingly, since only modest progress in survival for melanoma sufferers has been made, we must rely upon early diagnosis to make an impact.

In 2006, the National Center for Health Statistics reported that for adults over age 18, only 14.5% reported ever having undergone screening for skin cancer; only 8% said they had had a "recent" skin cancer screen. Further insights come from this study performed at University of Miami in 2006. Questionnaires administered to patients seeing both primary care and dermatology health professionals included whether patients received FBSE (Full Body Skin Examination), whether they would be embarrassed to receive such an examination, whether their PCP should perform FBSE on a regular basis, and if FBSE was done, had the clinician performed it with thoroughness.

Only 20% of PCP patients reported regular FBSE, with slightly fewer women than men (19% vs 22%). More than three times as many women reported feeling embarrassed by FBSE (15% vs 4%), but still the majority did not report embarrassment. Most patients (men 74%, women 67%) reported that an annual FBSE would be regarded by them as "thorough."

Sk-Ca screening is different than almost all other cancer screenings, in that the clinician may well be performing such an examination without formally noting to the patient that it is being done. Hence, patient perception of the frequency of screening may be a marked underestimate. In any case, it is clear that patients endorse Sk-Ca screening, and that it may be necessary to either increase our frequency of FBSE, or make our involvement in the process more evident to our patients. ■

Bell's Palsy: Steroids, Acyclovir, Both, or Neither?

Source: Sullivan FM,et al. *N Engl J Med.* 2007;357:1598-1607.

Of the thousands of persons afflicted each year with Bell's Palsy, the majority will recover without sequelae. As many as 30%, however, are left with some degree of facial paresis, pain, or both. Best evidence supports an etiologic role for herpes virus infection, although vascular and inflammatory disorders have also been implicated. Based upon the putative herpes virus etiology, coupled with the belief that perineural swelling contributes to nerve palsy, it has been commonplace to treat with steroids, antivirals, or both. The evidence supporting such practice is not robust. Indeed, a Cochrane review found insufficient evidence to endorse the use of either intervention. Sullivan, et al has now published the results of a Department of Health (England) commissioned study to ascertain the effects of prednisolone (PRED), acyclovir (ACYC), or both in Bell's palsy (BELL).

Scottish patients (n = 551) with BELL of duration <72 hours were randomized to PRED, ACYC, both, or placebo. The proportion of patients with recovered full facial function was evaluated at 3 and 9 months after intervention.

At three months, there was a statistically significant difference in full recovery for patients who received PRED compared vs those who did not (83% vs 63.6%) which persisted at 9 months (94.4% vs 81.6%). No evidence of benefit was seen in those receiving ACYC, whether in comparison to placebo, or when added to PRED. This is the largest study on treatment of Bell's palsy, and supports only the utilization of PRED. ■