The Institute for Safe Medication Practices recently received reports from two different health professionals who expressed concern about the way tablet strength is listed on certain phenobarbital and ferrous sulfate labels. The apothecary measure, grains (gr), is used on the products. Even though the US Pharmacopeial Convention (USP) has banned the use of the apothecary system, remnants of it continue to appear on container labels for these and several other products. For example, today you can still find aspirin tablets, sodium bicarbonate tablets, nitroglycerin tablets, and calcium gluconate tablets labeled in grains. The labeling on phenobarbital tablets, which lists the strength in both mg and gr, poses a particular hazard. A 1 gr (1 g) tablet could be misread and transcribed as 1 g (gram)! In June 30, 1999, a case was published in which a surgical resident read a patient’s prescription bottle labels and ordered phenobarbital 500 mg IV daily. The pharmacy label expressed the dose using the apothecary measurement 0.5 gr, which the resident thought meant 0.5 g (500 mg) instead of 0.5 grains (30 mg). The patient received phenobarbital 500 mg IV daily for three days. After the patient suffered respiratory difficulties, the dose was withheld and the patient recovered.

Use of the apothecary system can also lead to math errors. For example, years ago, when a nurse needed a 1/300 gr (0.2 mg) dose of nitroglycerin for a patient, she administered two 1/150 gr tablets (0.4 mg each) believing 1/150 + 1/150 = 1/150, not 1/75. The nurse was accurate in her thinking but not in her calculations. The patient received 0.4 mg nitroglycerin instead of the desired 0.2 mg dose. The patient was then given 12 1/150 gr tablets, which, when added up, would equal 1.2 mg nitroglycerin. Yet the nurse was not aware of the problem and continued to administer the two 1/150 gr tablets. She thought she was giving the correct dose. Had the nurse been more aware of the correct dose, she would have administered four 1/150 gr tablets for the correct dose of 0.8 mg.
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On the other hand, what is the best way to check the label of a high-alert drug when working alone, with no one available to perform an independent check? Use both hands, says Dr. John Senders, Principal Scientific Consultant, who has years of experience in the field. Once you have both hands, read the label aloud while holding it in the right hand and perhaps also while holding the container in the left hand.
New Extended-Release Namenda Compared to Immediate-Release Formulation

In June 2013, it was announced that the once-daily extended-release formulation of memantine (Namenda XR) would be available to pharmacies in the United States. The FDA has approved Namenda XR for the treatment of moderate to severe dementia caused by Alzheimer’s disease. The safety and efficacy of Namenda XR were determined in a randomized trial of 677 outpatients already on a cholinesterase inhibitor by comparing Namenda XR to a placebo in addition to their previous medication. Results from the trial indicated significant benefits in terms of behavior, and clinical global status in patients treated with Namenda XR compared to those that received the placebo.

Titrating and Switching from Immediate-Release to Namenda XR

Patients naive to memantine should be started on 5mg per day of Namenda XR and titrated up weekly in 5mg increments to the target dose of 28mg per day. When switching from Namenda to the XR formulation, it is recommended for a patient on a 10mg twice daily regimen of Namenda tablets should begin taking the 28mg Namenda XR capsules the day after the last 10mg dose of Namenda. In patients with severe renal impairment (Ccr<30), it is recommended to switch from the recommended dose of 3mg twice immediate-release Namenda to 14mg once daily XR capsules the day after the last 5mg dose of the immediate-release.

Daliresp (roflumilast) is a phosphodiesterase-4 inhibitor indicated for the treatment of bronchitis and chronic obstructive pulmonary disease, and is currently the only medication of its kind. It was approved early in 2011 by the FDA and is therefore approximately $207 per month daily supply. Daliresp has shown to provide significant improvement in lung function measured by spirometry and quality of life while significantly reducing the number of COPD symptoms and exacerbations. Daliresp even showed improvement in asthma symptoms. Calverley et al. showed that prebronchodilator FEV1 increased by 48 milliliters with Daliresp compared to placebo. The same study showed that patients with severe to moderate COPD using Daliresp had about 1.14 COPD exacerbations per patient per year compared to 1.37 exacerbations per patient per year for placebo patients. Tsung et al even went as far to suggest Daliresp only provides a net benefit to patients at high risk for exacerbations. Rabe et al. showed similar results as well as significant improvements in health-related quality of life. The most common side effects that were seen in multiple different studies included headache, diarrhea, nausea, and weight loss. Therefore, Daliresp has labeled warnings for gastrointestinal effects which include weight loss and/or diarrhea and neuropsychiatric effects (depression, sleep disturbance) which are common with COPD exacerbations. During the studies, diarrhea was experienced about ten percent of the time and weight loss was experienced from eight to twenty percent of the time. One study showed that most patients who experienced weight loss typically observed weight loss within six months of starting therapy. A second placebo-controlled clinical trial, 20% of patients treated with Daliresp experienced weight loss which was classified as five to ten percent of original body weight compared to just seven percent of patients who received placebo reducing weight. Theophylline, 20% of patients receiving

Effective calcium supplements for treating hypocalcemia Many people do not consume anywhere near the recommended amount of calcium in their diets and regularly take vitamin D supplements to maintain normal calcium levels in the body (total calcium: 8.4-10.2 mg/dl; ionized: 3.6-5.3 mg/dl.) In order to prevent the problems caused by hypocalcemia (i.e. osteoporosis and broken bones). However, recent studies have indicated the questionable efficacy of calcium supplements in preventing bone fractures and they have also been found to potentially cause an increased risk of heart attacks and death. This has not been thoroughly studied and requires further research to confirm these claims. However, it is not necessary to use calcium supplementation treatment to avoid the potentially serious symptoms of hypocalcemia. Symptoms of hypocalcemia are usually observed when calcium levels are ~7.5 mg/dl (or <2.8 mg/dl ionized calcium) and can vary in severity from asymptomatic to severe QT prolongation, and life-threatening tachycardia, so it is important to address low calcium levels. However, there are many causes of hypocalcemia and supplements may not necessarily be needed to correct the problem. Other imbalances that can cause hypocalcemia should be addressed before supplemental calcium is given. A few common causes are listed below.

1. Vitamin D deficiency: causes decreased calcium absorption
   Treatment: 50,000 IU 25-hydroxyvitamin D or 0.25-0.5mg 1,25-hydroxyvitamin D
2. Low magnesium: makes it difficult to normalize calcium and potassium levels and should be corrected in every patient
   Treatment: saline + 10-15mg/kg acetazolamide every 3-4 hours
3. Hemodialysis may be needed (especially if impaired renal function)
4. Alkalosis: increases calcium binding to albumin and decreases ionized calcium available; increases severity of symptoms
5. Treatment of metabolic acids can have the same effect

Acute symptomatic hypocalcemia (total calcium <7.0 mg/dl or ionized calcium <0.8 mmol) should be treated immediately due to the risk of severe symptoms. The most appropriate treatment (unless there is low magnesium levels) is IV calcium in the form of calcium gluconate. Calcium chloride is not preferred because it causes more tissue necrosis if extravasated.

- IV dosing: 100-200mg of elemental calcium (1-2g calcium gluconate diluted in saline or dextrose) initially over 10-20 min, then a slow infusion at 0.5-1.5 mg/kg/hr
- Continue slow infusion until the patient is receiving effective doses of oral calcium + vitamin D

Chronic hypocalcemia should be treated with oral calcium supplement therapy with a target calcium level of 8.0 because most patients will be asymptomatic and higher levels can cause hypercalcemia. Oral vitamin D supplementation may be needed as well if calcium supplements alone do not achieve the desired calcium level.

- Oral dosing ~1-2 g/day (elemental calcium) in 2-4 divided doses with food
- or 500-1000mg of CaCO3 (200-400mg elemental calcium) four times a day

When adequate blood levels of calcium are reached with supplementation, it is important to measure urinary calcium excretion and a thiazide diuretic may be added if hypercalcuria is detected to prevent complications including kidney stones and renal impairment. Serum calcium levels should also be monitored closely at first and then every 3-6 months when controlled.

In conclusion, the best way to maintain normal calcium levels in the body and prevent all of the potential complications caused by hypocalcemia (or treatment of hypocalcemia) is to consume the recommended amount of dietary calcium every day from foods/drinks such as milk, yogurt, almonds, kale, broccoli, and calcium-fortified orange juice, etc. However, symptomatic hypocalcemia should be treated as described. The varied severity of hypocalcemia, calcium supplementation should be used as recommended until further studies prove that it is not beneficial or that the potential risks of the treatment outweigh the potential benefits.

REFERENCES:
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Conclusion

Compared to target dose of immediate-release Namenda (10mg twice daily), the extended-release formulation of Namenda allows for an increased daily dose and a simplified dosing regimen. This can result in increased compliance and reduced caregiver burden due to the convenience of the once-daily administration of Namenda XR.

There have been no studies comparing the efficacy of the immediate-release Namenda versus the extended release formulation at this time. Until there is adequate research to determine how the efficacy of Namenda XR compares to standard dosing of immediate-release Namenda, it is not possible to determine if one is superior to the other. The XR formulation provides increased convenience for the caregiver and should be considered for any patient with compliance concerns that could cause a high caregiver burden due to their condition and/or the complexity of their medication regimen.

REFERENCES


Continued on Page 4 see Daliresp

Daliresp

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REFERENCES


