Drug Monitor

Timing IG Therapy

Guidelines recommend that interventions included in the "resuscitation bundles" used to treat septic patients are timely, but what constitutes "timely" is difficult to establish, given that the onset of sepsis and septic shock may be hard to determine. That means, say researchers from the Cattinara University Hospital in Trieste, Italy, that the real window of opportunity for interventions such as intravenous immunoglobulins (IVIGs) may be much narrower than expected, especially for patients who are not in the intensive care unit (ICU) when they develop sepsis and whose signs and symptoms may not be immediately recognized.

The researchers conducted a retrospective study to find the best timing for IgM and IgA enriched immunoglobulins (eIgs). They looked at data from 129 patients admitted to the ICU for severe sepsis or septic shock over 5 years. Treatment included antibiotic therapy and selective decontamination of the digestive tract. The eIgs were administered at the dose of 250 mg/kg on the day of the diagnosis; the infusion lasted 10 hours and was repeated for 3 days. Ten patients received recombinant human-activated protein C, and 6 patients were treated with coupled plasma filtration adsorption.

Forty-two patients (32%) died during the ICU stay. Survivors received eIg significantly earlier than nonsurvivors (23 hours vs 63 hours; $P < .05$). The delay in administration of eIg was a significant predictor of the odds of dying during the ICU stay and was independent from the Simplified Acute Physiology Score II and other variables. A 24-hour delay in administering eIg nearly tripled the probability of dying during the ICU stay, independent of sex, diagnosis at admission, presence of septic shock before admission, administration of recombinant human-activated protein C, treatment with coupled plasma filtration adsorption, and propensity score. Among survivors, a 24-hour delay almost doubled the length of stay in the ICU (likelihood ratio test vs the null model, $P < .001$).

The researchers note that the role of IVIGs and eIg in the treatment of sepsis and sepsis-related conditions remains less clearly defined than other measures and is still not "universally accepted," even though meta-analyses have demonstrated their effectiveness.

Source: Berlot G, Vassallo MC, Busetto N, et al. *J Crit Care.* 2012;27(2):167-171. doi:10.1016/j.jcrc.2011.05.012.

A Safe Choice for OA Pain

When oral nonsteroidal anti-inflammatories are too risky for patients with joint pain, topical diclofenac gel may be a safe option, according to researchers from the Center for Rheumatology and Bone Research in Wheaton, Maryland.

The researchers analyzed data from 5 randomized, double-blind, placebo-controlled trials involving 2,209 patients with mild-to-moderate osteoarthritis (OA) of the knee or hand. Patients applied 4 g of diclofenac sodium 1% gel (DSG) or placebo to affected knees qid for 12 weeks or 2 g of DSG or placebo to affected hands qid for 8 weeks.

Adherence was high in both groups, with most participants applying at least 3 of 4 prescribed doses every day. DSG treatment was well tolerated by all patients, regardless of age and comorbidities, such as hypertension, diabetes, and cerebrovascular or cardiovascular disease.

In all the subgroups, patients using DSG were slightly more likely to experience adverse events (AEs) and to stop treatment because of the AEs, which were usually application site reactions (particularly dermatitis).

In the subset of patients treated for knee problems, 2.9% of patients aged < 65 years and 3.6% of those aged > 65 years had AEs. Treatment-related gastrointestinal AEs were rare with 3 DSG patients and 2 placebo patients, respectively, experiencing symptoms; serious AEs were also rare. The only cardiovascular AE considered potentially related to treatment occurred in an 80-year-old woman with hypertension and type 2 diabetes. The patient developed deep vein thrombosis and pulmonary embolism but was treated successfully with heparin and warfarin.

Safety results were similar among patients being treated for OA of the hand. Older patients were more likely to discontinue the treatment because of AEs (4.3% of the DSG patients vs 1.2% of placebo patients), again usually because of application site reactions or allergic dermatitis.

The researchers note that 1 limitation of their analysis is that the pooled data were from short trials—8 or 12 weeks. Longer studies are needed to determine whether tolerability is maintained. Moreover, they add, because patients with clinically significant diseases (such as severe renal, hepatic, or cardiovascular disease) were excluded from the analysis, closer monitoring may be warranted for patients with severe comorbidities. ●

Source: Baraf HSB, Gold MS, Petruschke RA, Wieman MS. *Am J Geriatr Pharmacother.* 2012;10(1):47-60 doi:10.1016/j.amjopharm.2011.12.002.

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