

Digitalis glycosides exert a mild inotropic effect, attenuate carotid sinus baroreceptor activity, and are sympatho-inhibitory. These effects decrease serum norepinephrine levels, plasma renin levels, and possibly aldosterone levels. The Digitalis Investigation Group (DIG) trial demonstrated a reduction in HF hospitalizations in the treatment group (patients with HF and sinus rhythm) but no reduction in mortality or improvement in QOL. Importantly, treatment with digoxin resulted in a higher mortality rate and hospitalizations in women than men. It should be noted that low doses of digoxin are sufficient to achieve any potentially beneficial outcomes, and higher doses breach the therapeutic safety index. Although digoxin levels should be checked to minimize toxicity and although dose reductions are indicated for higher levels, no adjustment is made for low levels. Generally, digoxin is now relegated as late-line therapy for patients who remain profoundly symptomatic despite optimal neurohormonal blockade and adequate volume control.

■ ORAL DIURETICS

Neurohormonal activation results in avid salt and water retention. Diuretic therapy is typically required in patients with symptomatic HF to remedy congestive symptoms as a prelude to initiation and titration of neurohormonal therapy. Because of their potent effect on renal sodium excretion, loop diuretic agents are the preferred agents, with thiazide diuretics reserved for use in combination with loop diuretics for those with refractory volume overload. Frequent dose adjustments of loop diuretics may be necessary during longitudinal follow-up of patients with HF because of variable oral absorption and fluctuations in renal function. Patients who fail to respond to furosemide at high doses may benefit from transition to torsemide or bumetanide, which have greater oral bioavailability. Importantly, clinical trial data confirming efficacy are limited, and no data suggest that these agents improve survival. Since loop diuretics do enhance neurohumoral activation, dosing should be minimized as possible to maximize the balance of risk and benefit.

■ CALCIUM CHANNEL ANTAGONISTS