

CLINICAL COMMENTARY**Thin-prep Pap smears can make workup of ASCUS easier for physician and patient**

The management of ASCUS Pap smears has often confused primary care doctors. This is confounded by the fact that it is often a challenge to ensure that patients follow our recommendations. How could we blame them—after all, who wants to undergo 4 Pap smears instead of 1? The advent of thin-prep Pap smears, with reflex HPV testing on the same specimen, has simplified our lives. By obtaining routine thin-prep Pap smears and then reflex HPV testing for only high-risk HPV types, fewer Pap smears and colposcopic exams are needed, without reducing the detection of HSIL. Best of all, fewer women are overtreated or lost to follow-up.

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LEVEL II CLINICAL INQUIRIES**Are ARBs or ACE inhibitors preferred for nephropathy in diabetes?****EVIDENCE-BASED ANSWER**

Angiotensin receptor blockers (ARBs) have been shown to reduce the progression of nephropathy in several consistent studies. While ACE inhibitors have not been as well studied for the endpoint of nephropathy, patients with nephropathy exhibit reduced mortality when treated with an ACE inhibitor (strength of recommendation: A, based on randomized controlled trials).

EVIDENCE SUMMARY

The RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) study¹—a multicenter, randomized, double-blind, placebo-controlled trial—followed 1513 patients with type 2 diabetes and nephropathy over a mean of 3.4 years. Patients were randomized to receive losartan (Cozaar) or placebo, both taken in addition to conventional anti-hypertensive therapy (but not including renin-angiotensin-aldosterone system antagonist medications). The primary outcome was a composite of a doubling of serum creatinine, end-stage renal disease, or death. The number needed to treat (NNT) for the composite outcome was 34. The NNT for a doubling of the serum creatinine was 25, and for end-stage renal disease was 17.

The 2-year IRMA (Irbesartan Microalbuminuria) study² a multicenter, randomized, double-blind, placebo-controlled trial, randomized 590 patients with type 2 diabetes, hypertension, and persistent microalbuminuria to receive 150 or 300 mg of irbesartan (Avapro) or placebo. Additional antihypertensive agents were allowed in each arm with the exception of ACE inhibitors, ARBs, and dihydropyridine calcium-channel blockers. The primary outcome was the development of overt

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The mortality benefit with ARBs has not been as consistent as that shown with ACE inhibitors

nephropathy defined by a urinary albumin excretion rate >200 µg/min that is at least 30% higher than the baseline rate. This trial showed that irbesartan delayed progression to nephropathy independent of its effect on blood pressure compared with conventional therapy (NNT=16 at the 150-mg dose and NNT=11 at the 300-mg dose).

A third double-blind, placebo-controlled trial—IDNT (Irbesartan Diabetic Nephropathy Trial)³—randomized 1715 patients to irbesartan, amlodipine (Norvasc), or placebo for a median follow-up of 2.6 years. Each group could also use other conventional antihypertensive therapy (but again excluding ACE inhibitors, ARBs, and calcium-channel blockers). Irbesartan reduced progression of nephropathy (defined by doubling of the serum creatinine) and the onset of end-stage renal disease more effectively than amlodipine (NNT=12) or placebo (NNT=16). Irbesartan did not decrease cardiovascular mortality, nonfatal myocardial infarction, heart failure resulting in hospitalization, neurologic deficit caused by a cerebrovascular event, or above-ankle lower-limb amputation.

The mortality benefit with ARBs has not been as consistent as that shown with ACE inhibitors. Both classes of drugs conferred reduced mortality as seen with ramipril in the HOPE (Heart Outcomes Prevention Evaluation) trial⁴ and losartan in the LIFE (Losartan Intervention For Life) trial.⁵ However, a survival benefit was not seen with irbesartan in the RENAAL and IDNT trials.

RECOMMENDATION FROM OTHERS

The American Diabetes Association recommends both ACE inhibitors and ARBs for the treatment of early nephropathy in hypertension to delay the progression of microalbuminuria to macroalbuminuria and overt nephropathy.⁶

CLINICAL COMMENTARY

ARBs not yet shown to be as good as ACE inhibitors at reducing mortality

The evidence is good that ARBs delay the progression of type 2 diabetic nephropathy. Although more studies have looked at ARBs than ACE inhibitors in nephropathy from type 2 diabetes, ARBs have not been shown to be as good as ACE inhibitors at reducing all-cause mortality, the most important patient-oriented outcome.

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DRUG BRAND NAMES

Amlodipine • Norvasc
 Amoxicillin • Amoxil, Biomox, Polymox, Trimox, Wymox
 Azithromycin • Zithromax
 Cefaclor • Ceclor
 Cephalexin • Biocef, Keflex
 Clarithromycin • Biaxin
 Clindamycin • Cleocin, Dalacin
 Irbesartan • Avapro
 Losartan • Cozaar
 Ramipril • Altace
 Vancomycin • Vancocin
 Warfarin • Coumadin
 Xylometazoline • Otrivin