## For Refractory HT, Consider Secondary Causes

BY ROBERT FINN

San Francisco Bureau

ATLANTA — Clinicians should consider secondary causes when a patient's hypertension does not respond to aggressive treatment, Dr. Angela L. Brown said at a meeting sponsored by the International Society on Hypertension in Blacks.

The first rule, though, is that one must be careful in defining when hypertension is truly refractory, said Dr. Brown of Washington University in St. Louis. Hypertension is considered refractory only if a blood pressure under 140/90 mm/Hg cannot be achieved despite the use of three antihypertensive medications at their maximal doses, one of which must be a diuretic.

Too often, she said, other physicians refer patients with "refractory hypertension" who are on only two antihypertensives or who are at only the starting doses.

There are many secondary causes of

hypertension. Renal hypertension and endocrine hypertension are probably the most common, but other causes include aortic coarctation, sleep apnea, and panic disorder.

In addition, there are many exogenous substances that can raise blood pressure. Ethanol and caffeine are probably the most prominent of these, but physicians should carefully question patients about other possible causes, including cocaine, nicotine, sympathomimetics, chlorpromazine, erythropoietin, oral contraceptives, cyclosporine, tricyclic antidepressants, MAO inhibitors, and certain herbal supplements, such as the Chinese stimulant ma huang (ephedrine).

NSAIDs, corticosteroids, and sodium chloride can also interfere with antihypertensive therapy.

Anabolic steroids can also cause hypertension. "Particularly when you see young men who are athletic or buff, ask them about anabolic steroids," Dr. Brown advised. But she warned that the physician may not get an honest answer unless the young athlete's parents are out of the

Dr. Brown suggested a number of screening tests that can uncover some of the secondary causes, particularly the endocrine ones. (See box.)

But she placed a special emphasis on renal function.

"I think it's really important that we know the patient's level of kidney dysfunction," she said. "We get the serum creatinines, and we often see a creatinine of 1.4 or 1.6 [mg/dL], and we think, 'Oh, that's not too bad.' But it's clear that once the GFR [glomerular filtration rate] diminishes, and particularly around 45% or so, your thiazide diuretic is not going to be as effective."

Two equations have been developed for estimating GFR based on a patient's serum creatinine, age, and weight, with correction factors for the patient's gender and race (black versus nonblack), and there are Web sites where one can perform the calculations easily (www.medcalc.com/gfr.html, for example).

"Some labs have actually started reporting the estimated GFR," Dr. Brown said. "You actually get a much clearer picture of where the kidney level is. ... I think this is one of the most common causes of what is deemed to be resistant hypertension in my patients, and it is inadequate diuretic therapy."

The meeting was cosponsored by the American Society of Hypertension.

**Narrow Down** 

roidism, test TSH, free T4.

ma metanephrines.

terone:renin ratio.

suppression test.

The Possibilities

► For hyperthyroidism or hypothy-

► For pheochromocytoma, test plas-

► For primary aldosteronism, test morning plasma potassium; aldos-

► For Cushing's syndrome, administer the overnight dexamethasone

► For hyperparathyroidism, admin-

ister a test for albumin-corrected

**TOPAMAX®** 

**TOPAMAX®** (topiramate capsules) Sprinkle Capsules

Brief Summary of Full Prescribing Information for Migraine, CLINICAL STUDIES FOR OTHER INDICATIONS WILL HAVE DIFFERING ADVERSE EVENTS AND SAFETY CONCERNS, PLEASE SEE FULL PI FOR THIS INFORMATION REGARDING TOPAMAX® FOR EPILEPSY.

TOPAMMA'S
(topiamate)

Topiamate (appules)

Sprinkle Capsules)

Sprinkle Capsules

Beid Sumany of self Prescribing Information to Highes (CLICL), STRIBLES FOR CORT BRICKTON (TOPERS IN LINE OF THE MONOTORY CONTROLLED TO TOPERS IN CORT BRICKTON (TOPERS IN CORT BRICKTON (TOPERS IN LINE OF THE MONOTORY CONTROLLED TO TOPERS IN CORT BRICKTON (TOPERS IN CORT BRICKTON (TOPERS

leeds. Sumatriptan: Multiple dosing of topicamate (100 mg every 12 hrs) in 24 healthy volunteers (14 M. 10 F) did not affect the pharmacolineitics of single dose in 12 healthy volunteers (6 M. 6 F) leceving 200 mg/day of topicamae. Therefore, patients receiving risperidone in combination with topicamate should be dosed in 12 healthy volunteers (6 M. 6 F) leceving 200 mg/day of topicamae. Dividence of the common of the

trials has shown no race or gender related effects.

ADVERSE REACTIONS: The data described in the following section were obtained using TOPAMAX® (topiramate) Tablets. Migraine: In the four multicenter, andomized, double-blind, placeby-controlled, parallel group migraine prophylaxis clinical trials, most of the adverse events with topiramate were mild or moderate in severity. Most adverse events occurred more frequently during the fitration period than during the maintenance period. Table 1 includes those adverse events reported for patients in the placebo-controlled trials where the incidence rate in any topiramate treatment group was at least 2 % and was greater than that for

adverse event. Patients may have reported more than one adverse event during the study and can be included in more than one adverse event category. "Blurred vision was the most common term considered as vision abnormal, a preferred term.

Of the 1,135 patients exposed to opiramate in the placebo-controlled studies, 25% discontinued due to adverse events, compared to 10% of the 445 placebo patients. The adverse events associated with discontinuing therapy in the topiramate-treated patients included paresthesia (7%), fatigue (4%), nausse (4%), difficulty with concentration/lattention (3%), insomnia (3%), anorexia (2%), and dizziness (2%). Patients treated with topiramate experienced mean percent reductions in body weight that were dose-dependent. This change was not seen in the placebo group, Mean changes of 0%, 2%, -3%, and -4% were seen for the placebo group, topiramate 50, 100, and 200 mg groups, respectively. Table 2 shows adverse events treated with topiramate experienced mean percent reductions in body weight that were dose-dependent. Diverside cliental nervous system adverse events, including some that represented cognitive dysfunction, were dose-related. The most common dose-related adverse events were paresthesia, fatigue, nausea, anorexia, dizziness, didfluidly with memory darthea, weight offecease, difficulty with concentration and somnotions.

Table 2 Incidence (%) of Dose-Related Adverse Events From Placebo-Controlled, Migraine Titals: \*Adverse Event Inflowed by Placebo (M-445) lists. ToPAMAX® Dosage (mg/day) 50 (M-235) second, 100 (M-236) thind. 200 (M-514) but mit Paresthesia 6, 35, 51, 48 Fatigue 11, 14, 15, 19; Naussa 8, 9, 31, 14, Anorexia 6, 9, 15, 44 (Dizziness 10, 8, 9, 12 (Weight decrease, 16, 9, 11; Difficulty with Memory NOS 2, 7, 71; Dizzhea 4, 9, 11, 11; Difficulty with Concentration/Altention 2, 3, 6, 105 (Somnolence 5, 8, 7, 10; Hyposesthesia 2, 6, 7, 8, Anxiety 3, 4, 5, 6; Depression 4, 3, 4, 6; Mood Problems 2, 3, 6, 5, Dy Mouth 2, 2, 3, 5; Contilated 10, 136, 7, 20; Fatients and 10,

OVERDOSACE

Overdoses of TOPMMAY® have been reported. Signs and symptoms included convolsions, drowsiness, speech disturbance, blurred vision, diplopia, mentation impaired, lethargy, abnormal coordination, stuppor, hypotension, abdominal pain, agitation, dizziness and depression. The clinical consequences were not severe in most cases, but deaths have been reported after poly-drug overdoses involving TOPMMAY.\*

Topinamale overdose has resulted in severe metabolic acidosis (see WARMINGS).

A patient who ingested a dose between 96 and 110 g topinamate was admitted to hospital with coma lasting 20-24 hours followed by full recovery after 3 to 4 days. In autat TOPMMAY overdose, if the ingestion is recent, the storands should be empired immediately by larage or by induction of emesis. Adviated charcosal has been shown to adsorb topinamate in vitro. Treatment should be appropriately supportive. Hemodialysis is an effective means of removing topinamate from the body.



ORTHO-McNEIL NEUROLOGICS, INC.

Revised June 2005

serum calcium; intact parathyroid hormone; serum chloride:phosphate

7517113MB

► For renal artery stenosis, use the renal artery duplex scan; captopril renogram.

Source: Dr. Brown