Some Foot Neuropathy Responds to Nerve Surgery

BY SHARON WORCESTER

Southeast Bureau

TAMPA — About a third of diabetic patients with foot neuropathy have pain and loss of sensation resulting from nerve compression, and these patients probably will benefit substantially from nerve decompression surgery, Dr. A. Lee Dellon said at the annual meeting of the Wound Healing Society.

Data are increasingly demonstrating the

benefits of this surgery—which is much like the surgery used to treat carpal tunnel syndrome—in select patients with foot neuropathy, said Dr. Dellon, of the division of plastic surgery at Johns Hopkins University, Baltimore.

In a series of 765 patients, the ulceration rate following successful tissue reinnervation in patients with neuropathy but no prior ulceration was 0.5%, compared with an expected rate of 15% in nonsurgery patients. The rate in those with a previous ulcer that healed was 5%, compared with an expected rate of 50%. No amputations were required in the reinnervated patients.

Results for Dr. Dellon's first series of patients treated with nerve decompression for foot neuropathy were published in 1992. The site of compression was identified in the patients by a Tinel's sign, which in a more recent study was shown to have a positive predictive value of 92% for nerve compression, he noted.

In the 1992 series, outcomes in individ-

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS

Hyperpyrexia Oedema NOS Pyrexia

INFECTIONS AND INFESTATIONS

ual nerves were good to excellent in 80% of patients at an average follow-up of 2.5 years. In one recent study, restoration of sensation in patients who underwent nerve decompression for foot neuropathy was associated with a 3% ulceration recurrence rate, 80% improvement in pain, and 80% recovery of sensibility, with no new ulcers or amputations.

Patients who undergo nerve decompression surgery often have immediate results. One such patient told Dr. Dellon that her surgery, which had occurred just 24 hours prior, had already improved her pain by 50% and restored sensation to her toes.

When nerve fibers haven't totally died, they can have a reversible ischemic block. When the nerve is decompressed and blood flows into the nerve, the nerve can conduct a transmitted impulse again," he explained, adding that about half of patients will "actually wake up with this reaction."

It takes about a year, however, for the nerve to regenerate out to the toes, Dr. Dellon noted. Ideal nerve decompression candidates are those who have neuropathy symptoms and documented neuropathy, tight glycemic control, failure to respond to neuropathic pain medications, good circulation, no edema, and a positive Tinel's sign, he said at the meeting, which was held in conjunction with a symposium on advanced wound care.

Candidal Infection NOS Oral Candidiasis Sepsis NOS Urinary Tract Infection NOS INVESTIGATIONS Liver Function Tests NOS Abnormal 3 (1.7) 6 (3.3) METABOLISM AND NUTRITION DISORDERS Huid Overload Hyperglycaemia NOS Hyperkalaemia Hypermatraemia Hypocalcaemia Hypoglycaemia NOS Hypokalaemia Hypoglycaemia NOS Hypokalaemia Hypomagnesaemia Hypomatraemia Hyponatraemia PSYCHIATRIC DISORDERS Agitation 16 (8.8) 6 (3.4) RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS Acute Respiratory Distress Syndrome Nosocomial Pneumonia Pneumothorax NOS Respiratory Failure SKIN AND SUBCUTANEOUS TISSUE DISORDERS VASCULAR DISORDERS

included in this table.

Additional adverse experiences occurring in < 1% of patients or subjects in domestic and/or international trials conducted with omeprazole, or occurring since the drug was marketed, are shown below within each body system. In many instances, the relationship to omeprazole was unclear.

Bady 4s a Wibol.

Allergic reactions, including, rarely, anaphylaxis (see also Skin below), fever, pain, tatgue, malase, abdominal swelling.

Carriovasoular

Chest pain or angina, tachycardia, bradycardia, palpitation, elevated blood pressure, and peripheral edema.

the underlying utinuous, when is a some the Hepatic Hepatic Mild and, rarely, marked elevations of liver function tests [ALT (SGPT), AST (SGOT), "g-fularmly transpeptidase, alkaline phosphatase, and bilirubin (jaundice)]. In rare instances overt liver disease has occurred, including hepatocellular, cholestatic, or mixed hepatitis, liver necrosis (some fatal), hepatic failure (some fatal), and hepatic encephalopathy. Metabolic/Nutritional https://doi.org/10.1007/10.1

Hyponaterman, phogolycema, and weight gain.

Musculoskeletal

Muscle cramps, myaliqia, muscle weakness, joint pain, and leg pain.

Nervous System/Psychiatric

Psychic disturbances including depression, agitation, aggression, hallucinations, confusion, insomaina, nervousness, tremors, apathy, somnolence, anxiety, dream abnormalities, vertigo; paresthesia; and hemifacial dysesthesia.

Ocular
Blurred vision, ocular irritation, dry eye syndrome, optic atrophy, anterior ischemic optic neuropathy, optic neuritis and double vision.

Hematologic

Rare instances of pancytoperia, agranulocytosis (some fatal), thrombocytoperia, neutroperia,
leukoperia, ameria, leucocytosis, and hemolytic anemia have been reported.

The incidence of clinical adverse experiences in patients greater than 65 years of age was similar to that in patients 65 years of age or less.

Additional adverse reactions that could be caused by sodium bicarbonate, include metabolic alkalosis, sezures, and tetany.

MURRIDIAGRE

creased depth of respiration.
addition, a sodium bicarbonate overdose may cause hypocalcemia, hypokalemia,
mernatemia, and seizures

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Zegerid° omeorazole/sodium bicarbonate Brief Summary of Presc

INDICATIONS ARU USAGE
Duodenal Ulcer
TEGERID is indicated for short-term treatment of active duodenal ulcer. Most patients heal
within four weeks. Some patients may require an additional four weeks of therapy.

Gastric Ulcer
ZEGERID is indicated for short-term treatment 4-8 weeks) of active benign gastric ulcer.

(See CLINICAL PHARMACOLOGY, Clinical Studies, Gastric Ulcer.)

Treatment of Gastroesophageal Reflux Disease (GERD)

Symptomatic GERD ZEGERID is indicated for the treatment of heartburn and other symptoms associated

tenance of Healing of Erosive Esophagitis RID is indicated to maintain healing of erosive esophagitis. Controlled studies do

ZEGERID is indicated to maintain healing of erosive esophagitis. Controlled studies do not extend beyond 12 months.

Reduction of Risk of Upper Gastrointestinal Bleeding in Critically III Patients ZEGERID Powder for Oral Suspension 40 mg/1680 mg is indicated for the reduction of risk of upper 01 bleeding in critically iil patients.

CONTRAINDICATIONS

CERTIFIC is contraindicated in patients with known hypersensitivity to any components of the formulation.

PRECAUTIONS

General

Symptomatic response to therapy with omeprazole does not preclude the presence of gastric maligrancy.

INDICATIONS AND USAGE

nalignancy, gastritis has been noted occasionally in gastric corpus biopsies from patients ong-term with omeprazole.

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for Oral Suspension: Empty packet contents into a small cup containing 1-2 ones of water. Do NOT USE OTHER LIQUIDS OR FOODS. Stir well and drink tely, Refill cup with water and drink.

Powder for Oral Suspension: Empty packet contents into a small cup containing 1-2 statespoons of water. On NOT USE OTHER LIQUIDS OR FOODS. Str well and drink immediately. Refill cup with water and drink.

Drug Interaction: Commentation of discepam, warfarin and phenyloin, drugs that are metabolized by oxidation in the liver. There have been reports of increased INR and proformoth time in patients receiving proton pump limbitors, including omeyazoic, and warfarin concomitantly, increases in NRI and proformoth immediately. Refill cup with proton pump inhibitors and variatin concomitantly, the research in the patients receiving proton pump limbitors and variatin may need to be mornitured for increases in NRI and proformoth time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and variatin may need to be mornitured for increases in NRI and proformoth time. Patients freated subjects to interaction with helporylline or proparatiol was found, there have been clinical reports of interaction with helporylline or programation was found, there have been clinical reports of interaction with other increases should be mornitured to determine it is necessary to adjust the offices of the programation with the programation of the programation with the programation of the programatic determinant of their bioanalishibity (ep. Achaonazade, amportant determinant of their bioanalishibity (ep. Achaonazade ambientation of omerprazule and acaroniums may increase the serum levels of tacroniums.

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**Co-administration of omerprazule and distransivir has been reported to the control of the programatic expensivity of the programatic expensivity of the programatic expensivity of the programatic expensivity o

pregnancy are unlikely to pose a substantial teratogenic risk (the quantity and quality of data were assessed as fair).

Three epidemiological studies compared the frequency of congenital abnormalities among infrants born to women who used omeprazole during pregnancy to the frequency of abnormalities among infrants of women exposed to H2-receptor antagonists or other controls. A population-based prospective cohort epidemiological study from the Swedish Medical Brith Registry, overing approximately 99% of pregnancies, eported on 955 timester, and 131 exposed during the first trimester with 39 of these exposed beyond first trimester, and 131 exposed after the first trimester.

ventricular septal defects and the number of stillborn infants was slightly higher in the omegrazole exposed infants than the expected number in the normal population. The author concluded that both effects may be random.

A retrospective cohort study reported on 689 pregnant women exposed to either H2-blockers or orneprazole in the first trimester (134 exposed to onesprazole). The overall mail dimension rate as 4.4% (89% Cl 3.6-5.3) and the malformation rate for first trimester exposure to omegrazole was 3.6% (89% Cl 1.5-8.1). The retaitive risk of malformations associated with first trimester exposure to omegrazole was 3.6% (89% Cl 1.5-8.1). The retaitive risk of pradformations associated with first trimester exposure to omegrazole comprated with nonexposed women was 0.9 (89% Cl 0.3-2.2). The study could effectively rule out a relative risk greater than 2.5 for all malformations. Aleas of preterm delivery or growth retardation did not differ between the groups. A controlled prospective observational study followed 113 women exposed to omegrazole during preprainty (89% first trimiseter exposures). The reported rates of major competial malformations was 4% for the omegrazole group, 2% for controls exposed to nonteratiopers, and 2.8% in disease-period controls (background incidence of major malformations 1-5%). Rates of sportaneous and elective abortions, preterm deliveries, gostational age at delivery, and mean brith weight did not differ between the groups. The sample size in this study has 80% power to delect a 5-fold increase in the rate of major malformation.

Several studies have reported in apparent adverse short term effects on the infant when single dose and or intravenous omegrazole was administered to over 200 pregnant women as premedication for esserian section under general anesthesia.

Teratology studies conducted in pregnant rates at doses up to 13 mg/kg/day (about 2.8 to 28 times the human dose of 40 mg/day, based on body surface areal) and in gregnant ratabilist at doses up to 69 mg/kg/day (abou

patients. There are no adequate and well-controlled studies in peuseurs patients and **Certation Use**Undergraphe was administrated to over 2000 elderly individuals (c. 65 years of age) in clinical tribia in the U.S. and Europe. There were no difference in safety and reference between the elderly and younger subjects. Other reported clinical experience has not identified difference in regionase between the elderly and younger subjects, but greater sensitivity of some older individuals cannot be ruled out. Plarmacokinetic studies with buffered omergrapic here shown the elimination rate was somewhat decreased in the elderly and biosvaliability was increased. The plasma clearance of mergrapic was 50 ml mlm in chort half that of young subjects. The plasma helf-lie everaged one hour, about the same as that in noneliderly, healthy subjects to the control consideration of the control of the control of the control of control of the control of the control of control of

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ADVERSE REACTIONS

Omeprazed was generally well tolerated during domestic and international cumular in 3096 patients.

In 3096 patients.

In the U.S. clinical trial population of 465 patients, the adverse experiences summarized in Table 11 were reported to occur in 15 or more of patients on therapy with omeprazole. Numbers in paretineses indicate percentages of the adverse experiences considered by investigators as possibly, probably or definitely related to the drug.

Table 11: Adverse Experiences Occurring in 1% or More of Patients on Omeprazole Therapy

Omegrazole Placebo Ranifidine (n = 195)

17	170 of More of Fatients of Officeprazole Therapy				
	Omeprazole (n = 465)	Placebo (n = 64)	Ranitidine (n = 195)		
Headache	6.9 (2.4)	6.3	7.7 (2.6)	_	
Diarrhea	3.0 (1.9)	3.1 (1.6)	2.1 (0.5)		
Abdominal Pain	2.4 (0.4)	3.1	2.1		
Nausea	2.2 (0.9)	3.1	4.1 (0.5)		
URI	1.9	1.6	2.6		
Dizziness	1.5 (0.6)	0.0	2.6 (1.0)		
Vomiting	1.5 (0.4)	4.7	1.5 (0.5)		
Rash	1.5 (1.1)	0.0	0.0		
Constipation	1.1 (0.9)	0.0	0.0		
Cough	1.1	0.0	1.5		
Asthenia	1.1 (0.2)	1.6 (1.6)	1.5 (1.0)		
Back Pain	1.1	0.0	0.5		

Causal Relationship not Assessed			
	Omeprazole (n = 2631)	Placebo (n = 120)	
Body as a Whole, site unspecified			
Abdominal pain	5.2	3.3	
Asthenia .	1.3	0.8	
Digestive System			
Constipation	1.5	0.8	
Diarrhea	3.7	2.5	
Flatulence	2.7	5.8	
Nausea	4.0	6.7	
Vomiting	3.2	10.0	
Acid regurgitation	1.9	3.3	
Nervous System/Psychiatric			
Headache	2.9	2.5	
A consented attatact solution and cased to	050	t	

	ZEGERID® (N=178)	Cimetidine (N=181)
MedDRA		
Body System	All AEs	All AEs
Preferred Term	n (%)	n (%)
BLOOD AND LYMPHATIC SYSTEM DISORDI	ERS	
Anaemia NOS	14 (7.9)	14 (7.7)
Anaemia NOS Aggravated	4 (2.2)	7 (3.9)
Thrombocytopenia	18 (10.1)	11 (6.1)
CARDIAC DISORDERS		
Atrial Fibrillation	11 (6.2)	7 (3.9)
Bradycardia NOS	7 (3.9)	5 (2.8)
Supraventricular Tachycardia	6 (3.4)	2 (1.1)
Tachycardia NOS	6 (3.4)	6 (3.3)
Ventricular Tachycardia	8 (4.5)	6 (3.3)
GASTROINTESTINAL DISORDERS*		
Constipation	8 (4.5)	8 (4.4)
Diarrhoea NOS	7 (3.9)	15 (8.3)

Sitagliptin Add-On Helps Lower HbA_{1c}

SEATTLE — Sitagliptin can be safely added to other oral diabetes medications, producing a drop in hemoglobin A_{1c} levels that averages about 0.7%, according to a report at the annual meeting of the American Association of Clinical Endocrinologists.

In one trial, when 100 mg/day sitagliptin (Januvia) was added to metformin treatment (1,500 mg or greater per day) for 24 weeks, patients with type 2 diabetes had a mean reduction in HbA_{1c} of 0.65% from a baseline mean of 8.0%.

In another trial, when sitagliptin was added to pioglitazone treatment, at a dose of 30 mg or greater per day, patients had a mean reduction in HbA_{1c} of 0.7%, from a baseline HbA_{1c} of 8.1%, Dr. Peter Stein senior director in clinical research at Merck Research Laboratories, Rahway, N.J., said in the poster presentation.

Placebo controls in the studies had no decline in mean HbA_{1c} in the group that was also on metformin, and a decline of about 0.1% in the group that was also on pioglitazone.

Of the patients in the study who were also on metformin, 18% of the patients who took sitagliptin achieved an HbA_{1c} level below 6.5%, as did 25% of those also on pioglitazone.

In the controls, only about 5% achieved an HbA_{1c} that low. The studies were funded by Merck & Co.

—Timothy F. Kirn