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Antibiotic Prophylaxis Disputed for Infective Endocarditis

By Barbara A. Biedrzycki, RN, MSN, AOCN, CRNP

Summary*—Experts estimate that 4000 to 15,000 new cases of infective endocarditis* (see definitions, p. 10) *occur annually in the United States. Bacteremias result from many etiologies, including dental or surgical procedures. Prevention is critical to this relatively uncommon yet deadly disease, and it has been the rationale for antibiotic prophylaxis for four decades. Through the examination of epidemiological and outcomes measurement data, researchers conclude that the relatively low incidence of endocarditis and the lack of data supporting the efficacy of prophylactic antibiotic use call for reconsideration of existing policies recommending antibiotic prophylaxis.*[1] *Although prophylaxis was examined in dental patients, the implication applies to patients preparing for any type of surgery.*

INFECTIVE ENDOCARDITIS IS NOT A REPORTABLE DISEASE, AND THE incidence rate cannot be accurately determined; however, based on data from developed countries, it is estimated that 4000 to 15,000 new cases occur in the United States each year. Bacteremias may occur during dental and surgical procedures, and the current standard regimen for prophylactic antibiotics to prevent infective endocarditis in susceptible patients is amoxicillin 2 g orally one hour before the procedure.[2] A study reported in *Annals of Internal Medicine* suggests that clinicians and practitioners may want to take another look at practice standards and protocols.

Study subjects were recruited over a 27-month period from a population-based network of 54 hospitals in eight counties in the Philadelphia metropolitan statistical area and the county of New Castle, DE. Patients with the diagnosis of infective endocarditis were identified by hospital staff and invited to participate in a study to explore the dental and cardiac risks for infective endocarditis focusing on the indications for antibiotic prophylaxis.[1]

Risk of Infective Endocarditis

Individuals at greatest risk of infective endocarditis include:

- those with pre-existing heart disease, including the relatively high risk associated with prosthetic heart valves, previous infective endocarditis, cyanotic congenital heart disease, aortic valve

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disease, mitral regurgitation, mitral regurgitation and stenosis, patent ductus arteriosus, ventricular septal defect, and coarctation of the aorta;
- the elderly, possibly related to underlying degenerative or calcified valve lesions;
- intravenous drug users who might inject bacteria directly or have secondary infections from the skin flora or local infected injection sites. More than 50% of drug-related endocarditis is caused by a strain of *Staphylococcus aureus* from the drug users' skin or mucosal bacterial flora;
- post-cardiac surgery patients, especially those with valve replacements (while *S. epidermis* infections usually occur from inoculation during or immediately after surgery, streptococci may infect the prosthesis at any time, unrelated to surgery);
- and patients on hemodialysis who have an increased risk due to their arteriovenous shunts, which serve as a ready portal of entry for bacteremias. Two to 6% of patients receiving long-term hemodialysis develop endocarditis, and they have a high mortality rate of 53%.[2]

Study Methodology

After obtaining informed consents from both the case patient and the physician, the study proceeded by securing medical records to identify echocardiographic and microbiology reports. Three of the researchers reviewed this information to determine whether the data supported a case of infective endocarditis. Concurrence by at least two of the three researchers determined the inclusion of a case. There was agreement on 379 cases.[1]

Study controls were enrolled through the Wakesberg random-digit dialing method. Excluding those younger than 18, intravenous drug users, and those who developed endocarditis in the hospital, case and controls were matched for age, sex, and neighborhood of residence. Ninety-two cases were excluded: 65 for intravenous drug use and 27 for nosocomial infection. Ninety-five percent of the remaining 287 cases completed a structured telephone interview to elicit data, including:
- demographic characteristics;
- diagnostic and therapeutic medical and dental procedures in the year before the study date;
- potential host risk factors, including pre-existing cardiac lesions, pre-existing local infections, risk factors for oral and dental disease, diabetes mellitus, immune deficiencies, family history of endocarditis, alcoholism, malignant conditions, and autoimmune disease;
- previous antibiotic use;
- and other recent illnesses.

Medical and dental records were requested (1,381), and 92% (1,265) were reviewed to validate procedures and diagnoses. Major study variables included:
- dental flora infection—if organism was viridans streptococci, nutritionally variant streptococci,

Defining Endocarditis

- **Infective endocarditis (IE):** microbial infection of the endothelial lining of the heart.
- **Subacute bacterial endocarditis (SBE):** evolves over a period of weeks or months. Usually caused by low virulence organisms with limited ability to infect other tissues.
- **Acute bacterial endocarditis (ABE):** evolves over a period of a few days to a few weeks. Course is hectic. Complications occur quickly. Primary pathogen is *Staphylococcus aureus.*
- **Native valve endocarditis (NVE):** occurs on previously normal valves or those damaged by congenital or acquired disease.
- **Prosthetic valve endocarditis (PVE):** infection of artificially created valve. May be early PVE occurring within two months postoperatively, or late PVE, occurring after two months.

Source: Durack D. Infective Endocarditis. In: Alexander RW, Schlant RC, Fuster V, eds. *Hurst's The Heart.* New York City: McGraw-Hill; 1998:2205-2237.

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Actinobacillus species, *Cardiobacterium hominis*, anerobes, alpha-hemolytic streptococci (not group D), unspecified streptococci, or *Haemophilus, Eikenella, Kingella,* or *Neisseria* species;
- any valvular heart abnormality—mitral valve prolapse, congenital heart disease, history of rheumatic fever with heart involvement, prosthetic heart valve, previous episode of endocarditis, or other heart disease;
- and dental treatments—both invasive (dental hygiene, extractions, periodontal treatment, endodontic treatment, mouth or gingival surgery, treatment of tooth abscess) and noninvasive (simple restorations, prosthetic and restorative dentistry, fluoride treatments).[1]

Study Results

Case and control patients were similar in age, sex, ethnicity, education, occupation, and dental insurance status. No significant relationship was found in these demographic data variables. A significant relationship (P=0.001) did exist with case patients whose care was paid for by a government program in which:
- 272 (95%) had multiple positive blood cultures;
- and 12 of 15 cases with negative blood cultures received antibiotic prior to obtaining blood cultures.

Among case and control patients with cardiac valvular abnormalities, researchers found no statistically significant increased risk from dental procedures when infected with dental flora (P > 0.3) or effect from prophylaxis antibiotics (P > 0.2).

The only significant relationship identified among dental procedures and endocarditis was tooth extraction two months prior to hospital admission (P = 0.03). This variable could not be included in the full model study because there was an inadequate sample with only six case patients and no controls having a tooth extraction.[1] *(See table below.)*

Implications for Practice

While antibiotic prophylaxis for at-risk patients has been a widely accepted practice for more than four decades, this study challenges its premise. The researchers concluded "only a few cases of infective endocarditis could be prevented by antibiotic prophylaxis for dental procedures even if 100% efficiency was assumed."[1]

By this strong statement they recommend that policies for antibiotic prophylaxis be reviewed and updated based on this scientific evidence of low incidence and questionable efficacy. The logic of the principles that created the framework for the widely accepted guidelines for antibiotic prophylaxis for dental procedures is upturned by research documenting outcomes.

It is generally accepted that dental procedures have the potential to induce bacteremia. It is known that endocarditis has high morbidity and mortality rates and that prophylactic antibiotics prevent endocarditis in animal experiments. In addition, some express concern that malpractice claims may be propagated when there is a failure to give prophylactic antibiotics.[3]

Now there is scientific epidemiologic and outcomes measurement data on which to base future practice. The benefits of reducing overuse of prophylactic antibiotics are plentiful, including decreased risk for adverse reactions such as anaphylaxis, fewer side effects, lower cost, and less potential for drug-resistant organisms.[3]

Already researchers note viridans streptococci, the

Table

Top 4 Infective Organisms among 287 Study Patients		Patients with Valve Infections	
Organism	**Case Patients n = 287**	**Native valve n = 248**	**Prosthetic valve n = 39**
Viridans streptococci	95 (33.1%)	85 (34.3%)	10 (25.6%)
Staphylococcus aureus	66 (23%)	61 (24.6%)	5 (12.8%)
Nonenterococcal group D *streptococcus*	19 (6.6%)	13 (5.2%)	6 (15.4%)
Enterococcus species	19 (6.6%)	15 (6%)	4 (10.3%)

98 (94%) of 104 case patients and 11 (65%) of controls had pre-existing valvular heart disease.

Dental procedures	2 months before hospitalization		3 months before hospitalization	
	Case	*Control*	*Case*	*Control*
	16.8%	14.3%	23%	23%

Source: Strom BL, Abrutyn E, Berlin JA, et al. Dental and cardiac risk factors for infective endocarditis. *Ann Int Med* 1998;129:761-769.

most frequent bacterial organism inducing infective endocarditis, have become more resistant.[4] This research may stimulate questions about the scientific basis of other widely accepted guidelines and tenets of medical practice. Advanced practice nurses need to realize that guidelines are just that: principles by which to determine a course of action. Guidelines are not necessarily a standard of care, nor do they provide a substitute for clinical judgment.

Practitioners need to look beyond the words of the guidelines, to their scientific foundation, and then add intrinsic, holistic nursing framework to plan and provide the best possible care and treatment. ❖

References

1. Strom BL, Abrutyn E, Berlin JA. Dental and cardiac risk factors for infective endocarditis. *Ann Int Med* 1998;129:761-769.
2. Durack D. 1998. Infective Endocarditis. In: Alexander RW, Schlant RC, Fuster V, eds. *Hurst's The Heart.* New York City: McGraw-Hill; 1998:2205-2237.
3. Durack DT. Antibiotics for prevention of endocarditis during dentistry: Time to scale back? (editorial). *Ann Int Med* 1998;129:829-831.
4. Doern GV, Ferraro MJ, Brueggemann AB, et al. Emergence of high rates of antimicrobial resistance among viridans group streptococci in the United Sates. *Antimicrob Agents Chemother* 1996;40:891-894.

Tips on Managing Status Epilepticus

By Sally Beattie, MS, RN, CS, GNP

Summary*—Generalized convulsive status epilepticus (GCSE) threatens the lives of 65,000-150,000 U.S. citizens annually and is most common in children and adults over age 60. Clinicians must provide prompt and effective treatment to ensure the best outcome. Several intravenous drug protocols exist; however, experts are uncertain about the best initial drug treatment. Investigators conducted a five-year multicenter, double-blind randomized trial of four regimens to determine the most efficacious. Results highlight the need for better therapies because the protocol recommended by the investigators proved successful in only 55% of patients. Practitioners should prepare with an established treatment plan, the availability of appropriate drugs in the appropriate doses, and the skills to deal with potential side effects.*

GCSE IS A DANGEROUS LIFE-THREATENING EMERGENCY affecting 65,000-150,000 people in the United States each year.[1] About half of the cases occur in young children; however, adults over age 60 may be particularly susceptible. GCSE is defined as more than 30 minutes of continuous seizure activity or two or more sequential seizures without full recovery of consciousness between seizures. It may occur after an acute cerebral insult in persons with previously established epilepsy, especially if they have stopped taking their medications, or as a first unprovoked seizure. It also might be associated with an acute or progressive neurological insult or systemic metabolic dysfunction, or it might occur without identifiable cause.[2] Untreated or ineffectively treated, GCSE may result in potentially dire consequences including circulatory collapse, acidosis, renal failure from myoglobinuria, or epileptic encephalopathy.[3]

Although several drug treatment protocols exist for treating GCSE, the best initial treatment was unknown. Data from controlled trials was sparse and did not directly compare available regimens. The need to identify and document the most efficacious strategy was paramount. To address the issue, a five-year randomized, double-blind trial was conducted at 16 Veteran's Administration and six affiliated university hospitals.

Current Treatment Regimens

Investigators decided to compare four existing intravenous (IV) regimens:

1. diazepam (0.15mg/kg) followed by phenytoin (18mg/kg);
2. lorazepam (0.1mg/kg);
3. phenobarbitol (15mg/kg);
4. phenytoin (18mg/kg).

Researchers recruited 518 study subjects. Of these, 30% were nonveterans and 18% were female,[4] thus contributing to generalizable study results. An additional 52 patients were included in an intention-to-treat analysis. Eligible patients were classified as having:

- overt GSCE (easily visible), N=384;
- or subtle GSCE (indicated by coma and ictal discharges on an electroencephalogram, with or without visible convulsive movements such as rhythmic muscle twitches or tonic eye deviation), N=134.

In randomized blind fashion, one of the aforementioned treatments were administered to study subjects. Successful outcome was indicated by cessation of all motion and EEG seizure activity within 20 minutes after giving the initial drug infusion and without recurrence during the next 40 minutes. Patients were given a second blind drug infusion if needed to stop the seizure activity. The study/observation period lasted 12 hours.

Results: Better Methods Still Needed

The results revealed that the first treatment regimen was successful in just 55.5% of patients with verified overt GCSE but in only 14.9% of those with subtle GCSE. Among the overt GCSE group, lorazepam was significantly more effective than the phenytoin group, but no more so than the diazepam or phenobarbital groups. There were no differences in efficacy among treatments in the subtle GCSE group. Finally, there were no significant differences among the four treatments in either group regarding the frequency of the commonly reported drug-related side effects (hypoventilation, hypotension, and cardiac rhythm disturbance), recurrence during the 12-hour study period, or outcome at 30 days after the episode of GCSE.

In the intention-to-treat analysis, the differences among treatment groups with overt and subtle status epilepticus were not significant.

It is widely acknowledged that prompt administration of appropriate treatment is associated with favorable outcomes in treating GCSE. In this study, treatments that included phenytoin required the most time to administer. Lorazepam required the least time and was the easiest to use and the most effective drug in the paired comparisons. As a result, investigators recommend using lorazepam for initial IV treatment of GCSE until new therapies become available.

Data from much earlier studies[5,6,7] have reported better efficacy rates but included other classes of status epilepticus and less stringent definitions of treatment success. The investigators in this trial thought the use of a period >20 minutes in the definition of treatment success would expose patients to unnecessary risk including further neurological abnormalities and death.

Practice Implications

This study highlights the need for practitioners, regardless of practice setting, to be aware of the possible need to manage a patient experiencing an episode of generalized convulsive status epilepticus. Several universal aspects of treating this life-threatening emergency need to be in place:

- a clear plan of immediate treatment;
- prompt administration of effective drugs in adequate doses;
- and ability to deal with the possibility of apnea or hypoventilation.[2]

A neurologist should be consulted if treatment is unsuccessful and to help establish a long-term treatment plan pending the episode's etiology. Reinforcing the need for patients with established epilepsy or other seizure disorders to take their medication religiously is mandatory. Although the results of this study cannot be generalized to the pediatric population, the need for a plan, availability of appropriate medications, and the ability to deal with adverse side effects is no less indicated. ❖

References

1. Delorenzo RJ, Pellock JM, Towne AR, et al. Epidemiology of status epilepticus. *J Clin Neurophys* 1995;12:316-325.
2. Working Group on Status Epilepticus. Treatment of convulsive status epilepticus; recommendations of the Epilepsy Foundation of America's Working Group on Status Epilepticus. *JAMA* 1993;270:854-859.
3. Adams RD, Victor M, Ropper AH, et al. Epilepsy and disorders of consciousness. In: *Principles of Neurology*. 6th ed. McGraw-Hill; New York; 1997:339.
4. Treiman DM, Meyers PD, Walton NY, et al. A comparison of four treatments for generalized convulsive status epilepticus. *NEJM* 1998;339:792-798.
5. Waltregny A, Dargent J. Preliminary study of parenteral lorazepam in status epilepticus. *Acta Neurol Belg* 1975;75:219-229.
6. Sorel L, Mechler L, Harmant J. Comparative trial of intravenous lorazepam and clonazepam in status epilepticus. *Clin Ther* 1981;4:326-336.
7. Levy RJ, Krall RL. Treatment of status epilepticus with lorazepam. *Arch Neurol* 1984;41:605-611.

Salmeterol More Effective for Asthma than Albuterol

By Patricia McGinley, FNP, MSN

Summary*—An acute asthma attack can be frightening for patient and caretaker. The Centers for Disease Control and Prevention in Atlanta indicates 15 million U.S. citizens suffer from asthma, and the number is increasing. A specific definition of asthma eluded experts for decades, and available treatment was less than ideal for many patients. The recent report of a research study comparing the efficacy of albuterol, which must be administered frequently, and salmeterol, a longer-acting β_2-agonist, offers hope for today's asthmatics.*

The Centers for Disease Control and Prevention estimates that 15 million Americans suffer from some form of asthma, a common respiratory disorder in adults and children, with a noted increase in the incidence over the past five years.[1] Health care utilization by

asthmatics has increased steadily over the past 15 years. In 1995, 1.8 million emergency department (ED) visits were due to asthma. The rate was 48.8 per 10,000 among whites and 228.9 per 10,000 visits among African-Americans. Hospitalization rates have risen as well, with 10.9 per 10,000 among whites and 35.5 per 10,000 visits among African-Americans.[1]

Attempts to define asthma precisely have been difficult, and some experts call it a syndrome rather than a disease. With the inception of pulmonary function testing in the 1950s, identification of pathologic components of asthma in the 1970s, and research focusing on bronchoscopic evaluation identifying inflammation with eosinophils and mucosal sloughing in the 1980s, medical science advanced to the latest current definition: Asthma is an inflammatory disease of the airways with reversibility of airflow obstruction and bronchial hyperresponsiveness as key components.[2]

Three Diagnostic Criteria

The National Institutes of Health in Bethesda, MD, has developed diagnostic criteria for asthma, including:

- history or presence of episodic symptoms of airflow obstruction;
- airflow obstruction that is at least partially reversible;
- and exclusion of other alternative diagnoses.[3]

Clinical manifestations of asthma include wheezing, cough, shortness of breath, and chest tightness. Management often includes the use of inhaled β_2-adrenoceptor agonists such as albuterol, pirbuterol, and metaproterenol.

The New England Journal of Medicine recently reported a study comparing the use of a newer inhaled β_2-agonist (salmeterol), albuterol, and a placebo. Salmeterol is a derivative of albuterol but has a longer binding capacity to the β_2-adrenoreceptor protein, thus providing up to 12 hours of bronchodilation. It is dosed on a BID schedule instead of the QID schedule of shorter-acting albuterol.[4]

The multicenter randomized, placebo-controlled study compared the use of albuterol (180 µg four times daily) and salmeterol (42 µg twice daily) in the treatment of mild to moderate asthma. The 234 patients meeting criteria for inclusion in the study included 150 males and 84 females between ages 12 and 73. In addition to having a confirmed diagnosis of asthma, subjects had to be nonsmokers, at least 12 years old, and on a daily medication regimen to control the symptoms.

Study subjects received albuterol, salmeterol, or placebo once every 12 hours during the 12-week study period. Subjects were permitted to use albuterol supplementally for short-term relief of symptoms. Subjects using inhaled corticosteroids or cromolyn could enroll but had to maintain constant doses of these medications during the study. If asthma symptoms worsened between doses of the study medication, the subject's usual "rescue" medications were taken as needed.

At the beginning of the study, each subject's forced expiratory volume in one second (FEV1) was measured 30 minutes before and immediately after inhalation of the study drug and 12 hours later. These measurements were taken again four, eight, and 12 weeks into the study. Other measured variables included maintenance of a diary that recorded:

- the number of episodes of symptom exacerbations;
- use of rescue medications;
- and twice-a-day peak expiratory flow rate using a handheld peak flow meter.

Study Results

The study showed salmeterol to have advantages over albuterol and placebo in the management of asthma. A significant increase in the morning FEV1 was seen throughout the study period when salmeterol was compared with albuterol and placebo. When compared with pretreatment values, salmeterol resulted in a mean increase of 24 liters per minute, whereas albuterol showed a decrease of 6 liters per minute. Placebo resulted in an increase of 1 liter per minute.

In addition, there was a more sustained bronchodilation effect with salmeterol than with albuterol in which study subjects experienced less frequent and less severe breakthrough symptoms, thereby reducing the use of rescue medications. There was no evidence of a tolerance effect with the use of salmeterol over a long period of time.

The side effect profile for salmeterol was less than that of albuterol and placebo. Twelve percent of patients in the salmeterol group reported adverse effects, vs. 23% in the albuterol group and 20% in the placebo group. Reported side effects included headache, tremor, and tachycardia in the albuterol and salmeterol group; headache was most common in the placebo group.

Researchers concluded that salmeterol twice daily for the management of mild-to-moderate asthma is superior to albuterol given either as needed or four times daily.

Practice Implications

Once an individual is diagnosed with asthma, the key to better quality of life, less frequent utilization of health care resources such as ED visits and hospitalization, and less loss of time in work or school lies in the treatment regimen developed by the health care provider. The

mainstay of therapy for patients with chronic, persistent asthma in the outpatient setting includes:

- reduction of environmental triggers;
- behavior changes;
- home peak flow monitoring;
- and therapeutic drug agents such as corticosteroids, theophylline, β_2-agonists, leukotriene agonists, and cromalyn.

Management of asthma often includes the use of inhaled β_2-adrenoceptor agonists such as albuterol, pirbuterol, and metaproterenol. The β_2-agonists cause relaxation of the bronchial smooth muscle with duration of action between three and eight hours. These agents are used alone or in combination with corticosteroids or anti-inflammatory drugs. The selective β_2-agonists are preferred due to a better side effect profile. However, if used more than every four hours, the selectivity of β_2-receptor sites is diminished; therefore, β_1-agonist effects are exhibited. The β_2-agonists are prescribed on a QID schedule with instruction to increase utilization during periods of acute distress.

Intense patient and caregiver education on the nature of the disease, compliance with therapeutic regimens, and the need for follow-up care on a regular and emergency basis are crucial to successful management of the asthmatic patient. As with any chronic illness, the use of multiple drugs taken many times a day often leads to poor compliance and repeated exacerbations of symptoms.

This research study presents scientific evidence of a safe, effective medication that lasts longer than commonly used bronchodilators that have a QID dosing schedule. The use of salmeterol on a BID schedule is more convenient and has the potential for better compliance, thereby reducing the incidence of office and ED visits. Because the salmeterol study included adolescents, and the drug was proven safe, effective, and superior to albuterol, it offers a treatment modality more conducive to the busy lifestyle of this population. Clinicians may wish to consider salmeterol, especially for patients with compliance problems or those who don't obtain the desired response from current medications. ❖

References

1. Centers for Disease Control and Prevention. *Asthma Rates in the U.S. Increase.* Press Release, April 24, 1998. Web: http://www.cdc.gov/od/oc/media/pressrel/r980424.htm.
2. Barbee RA and Murphy S. The natural history of asthma. *J Clin Immunol* 1998;102(4), part 2:S65-66.
3. National Institute of Allergy and Infectious Diseases. *Practical Guide for the Diagnosis and Management of Asthma*. NIH Publication 97-4053, October 1997:4. Web: http://www.nhlbi.nih.gov/nhlbi/lung/asthma/prof/asthgdln.htm.
4. Pearlman D, Chervinsky P, Laforce C. A comparison of salmeterol with albuterol in the treatment of mild to moderate asthma. *NEJM* 1998;327:1420-1425.

Clinical Briefs

Simultaneous or Sequential Therapy for HIV-1?

By Joan Unger, RN, MS, ARNP-C

EXPERTS AGREE A COMBINATION OF ANTIRETROVIRAL drugs markedly suppresses human immunodeficiency virus (HIV) replication. The U.S. Department of Health and Human Services recommends a combination of two nucleoside analogue reverse transcriptase inhibitors and a potent protease inhibitor as preferred treatment for HIV infection. The durability of antiretroviral activity and duration of HIV suppression with the combination is unknown. Several reports in late 1997 indicated that 30-60% of patients on a combination regimen did not maintain viral suppression in clinical practice. This led scientists to ask if the problem could result from sequential rather than simultaneous administration of the drugs.

Study Included Three Regimens

This randomized, multicenter double-blind study compared the effects of a three-drug simultaneous regimen with a sequential regimen in patients with HIV.[1] Ninety-seven patients were treated with zidovudine for at least six months and had serum HIV RNA levels of at least 20,000 copies/mL and a CD4 cell count 0.05-0.40 x 10^9/L. Three regimens were initiated:

- indinavir 800 mg every eight hours;
- zidovudine 200 mg every eight hours and lamivudine 150 mg every 12 hours;
- or all three drugs.

After 24 weeks of blind therapy, all patients received open-label three-drug therapy.

At 100 weeks, simultaneous use of indinavir, zidovudine, and lamivudine suppressed HIV RNA to less than 500 copies/mL and increased the median CD4 count to 0.209 x 10^9/L above baseline in 78% of patients. When the drugs were initiated sequentially, only 30% of patients in the zidovudine-lamivudine group and 45% of

those in the indinavir group had a reduction in HIV RNA to < 500 copies/mL and increased median CD4 cell count to 0.101-0.163 x 10^9/L over baseline at 100 weeks.

The researchers concluded that a three-drug simultaneous regimen has durable antiretroviral activity for at least two years, whereas sequential administration was much less effective. ❖

Reference

1. Gulick R, Meliors J, Havlir D, et al. Simultaneous vs. sequential initiation of therapy with indinavir, zidovudine, and lamivudine for HIV-1 infections. *JAMA* 1998;280:35-41.

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After reading each issue of *RN Advanced Practice Alert,* the reader will be able to do the following:

- Identify current scientific research and thinking regarding prevention, diagnosis, and treatment of specific diseases and health care concerns. (See *Update on Infective Endocarditis* and *Tips on Managing Status Epilepticus* in this issue.)
- Identify research-based indications and opportunities to implement appropriate changes in day-to-day advanced nursing practice. (See *Salmeterol More Effective for Asthma than Albuterol* in this issue.)
- Identify strategies and opportunities to educate patients about diagnoses and current medical treatment options to assist them in making informed choices about health care.

To Treat or Not to Treat Suspected TB

ALTHOUGH TODAY'S READILY AVAILABLE AND RAPID laboratory cultures improve diagnosis of *Mycobacterium tuberculosis,* the bacteria causing tuberculosis (TB), it still takes 2-3 weeks to learn the outcome, and researchers say this delay in initiating treatment increases deaths.

A study supported by the Agency for Health Care Policy and Research found that treatment of HIV-infected patients who have negative acid-fast bacteria (AFB) smears decreased deaths by an average of 2%.[1] When community prevalence of multidrug-resistant TB (MDR-TB) exceeds 9.6%, starting drug-resistant therapy for AFB smear-positive patients (before results from culture and drug-resistant tests are available) minimizes costs and decreases risk of mortality at an additional cost of $8,000 per life saved. This figure is still lower than costs per life-year saved for health care interventions such as screening blood donors for HIV.

Treatment Can Reduce Risks

Investigators point out that the average patient's risk of death and health care costs while waiting 2-3 weeks for results of laboratory tests can be reduced by treating all TB-suspect patients who have a positive AFB sputum smear or are infected with human immunodeficiency virus (HIV). They recommend treating HIV-positive patients even if the AFB smear is negative, because such patients are at high risk for TB.

According to study authors, the potential for death from drug toxicity in treating numerous people without TB is slightly outweighed by the death potential of not treating those with smear-negative disease while waiting for culture results.

Researchers conclude that early treatment with drug-resistant therapy for AFB smear-positive patients rather than the usual four-drug regimen recommended (ethambutol, isonicotinic acid, pyrazinamide, and rifampin) minimizes both risk of mortality and costs. A quinolone drug is added to the above regimen for MDR-TB. ❖

Reference

1. Brewer S, Heymann J, Ettling M, et al. An effectiveness and cost analysis of presumptive treatment of *Mycobacterium tuberculosis. Am J Infect Control* 1998;26:232-238.

In Future Issues:

Treatment for depression in primary care

Anticonvulsive drug effective for post-herpetic neuralgia

Stop-smoking campaigns must target college-age community