Losartan-Ramipril Combination Treatment

Sir,

For any follow-up on the important LORD trial, we advocate added steps. Hypertension among patients with type-2 diabetes mellitus carries an increased risk of atherosclerosis resulting in greater end-organ damage. Hence any added independent risks should be detected, particularly in patients with diabetes and hypertension. An abnormally low (deficient) heart rate variability (DHRV) and an abnormally high blood pressure variability (BPV), i.e., circadian hyper-amplitude-tension (CHAT), along with an elevated pulse pressure (EPP) all enhance the risk of myocardial infarction, stroke and stroke death. They can change an acceptable risk of less than 5% to a very high one of 80% or more. These conditions, silent to conventional medicine as well as to the patient, could be studied easily by collaboration with the Halberg Chronobiology Centre at the University of Minnesota in Minneapolis, USA (corne001@umn.edu), and the Division of Neurocardiology at Tokyo Women’s Medical University, Japan, centres helping with cost-effective ambulatory monitor acquisition and support at nominal cost to pharmaceutical companies and free of cost to individuals anywhere. Effects of the Losartan-Ramipril combination and/or other treatment on the 24-hour pattern of blood pressure in the pathogenesis of angiopathy, from the viewpoint of DHRV, CHAT, and/or EPP, could be thus studied in follow-ups of the important LORD trial.

In the Framingham Study, ambulatory electrocardiography on 1919 subjects sought any association of HRV with blood glucose concentrations, after previous findings of a reduced HRV in type-2 diabetes. In this population-based survey, HRV endpoints included SDNN, “high” frequency (HF; around 3.6 s) and “low” frequency (LF; around 10.5 s) power and their ratio. Plasma glucose concentrations related inversely to the LF/HF power ratio (at frequencies that are all very high by comparison with circadians, not to mention also demonstrated cycles covering decades). SDNN as well as LF and HF spectral powers were reduced in overt diabetes and already in subjects with glucose intolerance (among whom CHAT is more likely to occur, as compared with subjects having acceptable glucose concentrations, and in whom HRV is associated with increased sympathetic and low parasympathetic activity, indicating brain-heart dysfunction involving the neuroendocrines. The renin-angiotensin-aldosterone system (RAAS) is characterized, among others, by prominent circadian variations, as a determinant of alterations in blood pressure variability found by around the clock monitoring. Since ACE-inhibitors and angiotensin receptor blockers can influence the RAAS, a beneficial influence of a Losartan-Ramipril combination treatment might be mediated in part via effects on DHRV and BPV.

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REFERENCES


In-vitro Activity of Linezolid Against Clinical Isolates of Gram-positive Cocci in a Tertiary Care Hospital

Sir,

In vitro activity of a new oxazolidinone, linezolid was tested against 96 clinical isolates of Gram-positive cocci. The bacteria tested were 40 S. aureus (22 methicillin susceptible S. aureus; 18 MRSA), 40 coagulase - negative staphylococci (22 methicillin susceptible S. epidermidis; 18 methicillin resistant S. epidermidis) and 16 E. faecalis. Linezolid was active against all the isolates (100% sensitive) and has the potential to become a major therapeutic option for infections caused by these pathogens.

The incidence of infection with resistant Gram-positive cocci especially Staphylococcus and Enterococcus species has increased worldwide. The emergence of methicillin resistant Staphylococcus aureus (MRSA) and vancomycin resistant enterococci (VRE) pose problem in selecting out appropriate drugs for management. Linezolid is the first of a new group of agents, the oxazolidinones, which are synthetic antibacterial compounds unrelated to other known antimicrobial agents that are active against Gram-positive bacteria. The oxazolidinones have a unique mechanism of action that inhibits bacterial protein synthesis by selectively binding to the 50S ribosomal sub-unit and do not exhibit
cross-resistance with existing agents. Previous studies have shown linezolid to have promising laboratory and clinical activity. To document this, a study was conducted to know the in-vitro efficacy of linezolid against the Gram-positive clinical isolates.

A total of 96 non-duplicate clinical isolates obtained recently (2001) in our microbiology laboratory from pus, blood, urine samples and lower respiratory tract secretions derived from in-patients were tested against linezolid susceptibility by Kirby-Bauer disc diffusion method. The 96 Gram-positive cocci used consisted of the following: 40 S. aureus isolates, 22 methicillin susceptible S. aureus (MSSA) and 18 MRSA. The 40 coagulase - negative staphylococci consisted of 22 methicillin susceptible S. epidermidis (MSSE) isolates and 18 methicillin resistant S. epidermidis (MRSE). Enterococcus faecalis were 16 isolates.

The quantitative cut-off measurements (zone diameter in mm) to define sensitivity for Staphylococcus species and Enterococcus species was ≤ 21 mm and 23 mm respectively. Resistant zone for Enterococcus species was ≤ 20 mm. No resistant zone was defined for Staphylococcus species. Staphylococcus aureus ATCC 25923 was used as control strain (zone of inhibition 27-31 mm).

Linezolid was active against all the bacteria tested (100% sensitive) that correlates well with the other studies. The 96 MRSA isolation in our hospital was 42.5% in 1999 and no resistance to vancomycin has been encountered. All the MRSA and MRSE in the present study were also sensitive to linezolid and no linezolid resistance against Staphylococcus species including MRSA, MRSE and vancomycin intermediate resistant S. aureus (VISA) have been so far reported. Vancomycin is almost universally accepted as the drug of choice for the treatment of MRSA infections. However vancomycin used alone kills staphylococci slowly resulting in delayed recovery of patients with life-threatening infections. In addition, with emerging strains of vancomycin-glycopeptide intermediate resistant S. aureus (GISA), linezolid would seem to be an ideal alternative drug for methicillin resistant staphylococcus.

No resistance either to vancomycin or linezolid among E. faecalis was noted in the present study. However, five patients with infection due to linezolid-resistant vancomycin resistant E. faecium (resistance developed during treatment) has been reported from Chicago that warns cautious usage and to measure susceptibility of all the isolates at the start of therapy with linezolid.

Considering its advantage of no resistance, unique mechanism of action with no cross resistance and additional availability for switch over therapy (available both orally and parenterally) linezolid seems to be a promising drug against these resistant pathogens.

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