CHRONOPHARMACOLOGY OF VALSARTAN AND AMLODIPINE

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INTRODUCTION

Hypertension is a worldwide health problem which if inappropriately managed is a predominant risk factor for cardiovascular events. The application of chronopharmacology principles in hypertension management aids clinical decision making on the best dosing times of antihypertensive drugs to achieve optimum circadian blood pressure (BP) control.[1]

AIMS

To test the effect on 24 hour BP profile of valsartan and amlodipine and to compare the effects of morning versus evening dosing on circadian BP.

METHOD

- Patients suffering from essential hypertension who were prescribed once daily valsartan (11 males and 10 females; mean age 55 years) or once daily amlodipine (5 males and 3 females; mean age 59 years) participated in the study.
- The patients were recruited from the Cardiac laboratory, the Medical Out Patients (MOP) at Mater Dei Hospital and from community pharmacies.
- Patients were initially asked to take their antihypertensive drug in the morning (8.00 am) or in the evening (8.00 pm) for 7 days. Their 24-hour systolic and diastolic BP (SBP and DBP) was then measured using an ambulatory BP monitor (ABPM).
- For the following 7 days, the patients were asked to administer their drug at the time opposite to that at which it was administered during the first week. Their ambulatory SBP and DBP was then measured for the second time.
- Statistical analysis was undertaken using SPSS version 22 and the Kolmogorov-Smirnov and the Mann–Whitney tests were performed.
- The study was approved by the University of Malta Research Ethics Committee.

RESULTS

Whole day BP means after morning and evening dosing were 124/78mmHg and 121/76mmHg respectively for valsartan and 126/77mmHg and 129/79mmHg respectively for amlodipine. When compared to morning dosing, evening valsartan dosing resulted in almost significantly lower DBP (p=0.079) during the early morning and significantly lower BP (p<0.05) during the night and whole day periods (Figures 1 and 2). When compared to evening dosing, morning amlodipine dosing resulted in non-significantly lower BP (p>0.05) during day time, almost significantly lower BP during night time (p=0.065) and non-significantly (p>0.05) higher BP during the early morning (Figures 3 and 4).

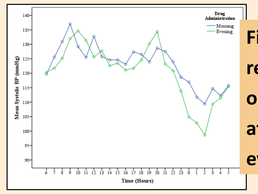

Figure 1: 24h SBP readings of patients on valsartan (n=21) after morning or evening dosing.

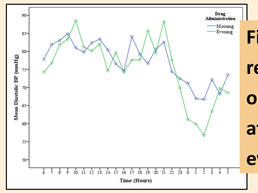

Figure 2: 24h DBP readings of patients on valsartan (n=21) after morning or evening dosing.

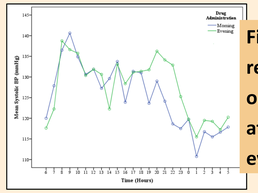

Figure 3: 24h SBP readings of patients on amlodipine (n=8) after morning or evening dosing.

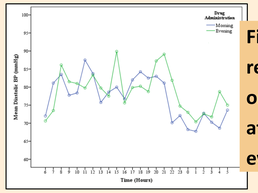

Figure 4: 24h DBP readings of patients on amlodipine (n=8) after morning or evening dosing.

CONCLUSION

This study underlines the importance of tailoring and individualising the treatment of hypertension according to the specific circadian blood pressure pattern of each patient. Valsartan and amlodipine were effective for 24 hour BP control irrespective of their dosing time. Evening valsartan dosing resulted in better control of 24 hour and night time BP and almost better control of early morning BP, implying that it is the ideal regimen for non- dippers. In dippers evening dosing could result in nocturnal hypotension, hence the morning regimen is preferred. Morning amlodipine dosing resulted in almost better control of BP during the night time period, suggesting that it could be the ideal regimen for non- dippers. Further studies are necessary to sustain the results obtained.

REFERENCE

Lemmer B. The importance of biological rhythms in drug treatment of hypertension and sex- dependent modifications. ChronoPhysiology and Therapy. 2012;2: 9-18.