Procainamide Pharmacokinetics and Diuretic and Fluid Administration

The article by Kessler et al. (1) on procainamide pharmacokinetics is of interest. Although the volume of distribution is not a real volume, its calculation can be significantly affected by changes in extracellular volume, which may in turn be brought about by changes in diuretic dose or the quantity of fluids administered. As the authors state, volume of distribution is inversely related to serum drug concentration, a measurement that could be readily changed by changes in extracellular volume. Is it known that diuretic dose and fluid administration were held constant for all patients throughout the study? This would have to be the case before we could have confidence in the group means.

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Reference

 Kessler KM, Kayden DS, Estes DM, et al. Procainamide pharmacokinetics in patients with acute myocardial infarction or congestive heart failure. J Am Coll Cardiol 1986;7:1131–9.

Reply

Each patient was studied during a stable period wherein diuretic and fluid administration were kept constant for each individual. Moreover, with a calculated volume of distribution of procainamide averaging almost 2 liters/kg we would expect tissue perfusion/concentration factors to be the major determinant of drug volume of distribution (at steady state). For instance a 5 liter (11 pound) delta in extracellular volume would represent less than a 3% change in the volume of distribution (even if these were directly related, which they are probably not). We hope this explanation clarifies the issue.

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Atrial Sensing After Dual Chamber Pulse Generator Implantation

Klementowicz and Furman (1) observed the evolution of atrial sensing after dual chamber pulse generator implantation. Of 54 patients, sensing deteriorated in 26% (mean follow-up 58 weeks) and fluctuated in 20%, without associated increase in pacing threshold. The authors did not mention any clinical problem: the sensitivity setting was readjusted and all pacemakers remained in the DDD mode. We observed two patients in whom such atrial sensing deterioration was associated with clinical problems. Both received a dual chamber generator (Telectronics, Autima II), with a unipolar atrial J electrode (Telectronics, 030-403). Atrial sensitivity (two settings: 0.5 and 1 mV) was initially set at 1 mV. Radiologic follow-up did not show any atrial lead dislodgment. Increase in pacing threshold was not noticed. Drugs were not changed, and new cardiac problems (such as ischemia) did not occur. The first patient (an 81 year old woman with symptomatic sick sinus syndrome, without known tachyarrhythmias; atrial signal during implantation: 2 mV) had two symptomatic episodes of atrial fibrillation 3 weeks after implantation. The second episode occurred during Holter monitoring. It showed the clear atrial undersensing (in the hours before atrial fibrillation) probably responsible for it, by pacing during the atrial vulnerable period (2). Further evolution was uneventful (follow-up 8 months), the atrial sensitivity setting was not changed and atrial undersensing and atrial fibrillation did not recur.

The second patient (a 79 year old man with symptomatic mixed carotid sinus hypersensitivity; atrial signal during implantation: 3.7 mV) remained free of syncope and of any problem with his pacemaker during 14 months. He was then readmitted for syncope with epilepsy, attributed to an ischemic stroke. Atrial undersensing was present and intermittent (sometimes from beat to beat). Atrial fibrillation was never found. Resetting atrial sensitivity to 0.5 mV did not change the undersensing. No influence of breathing or position, and no abnormal motion of atrial lead were found. DDD mode was abandoned (although we did not think that the undersensing was responsible for the syncope).

In conclusion, we agree that atrial sensing must be continually monitored (1), because atrial undersensing may generate clinical problems, such as atrial fibrillation or a need to change the pacing mode.

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References

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- Furman S, Cooper J. Atrial fibrillation during A-V sequential pacing. Pace 1982;5:133-5.