Increases in P-Wave Duration and Dispersion After Hemodialysis Are Totally (or Partially) Due to the Procedure-Induced Alleviation of the Body Fluid Overload: A Hypothesis with Strong Experimental Support

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Increases in the P-wave duration (P-du) and P-wave dispersion (P-d) following hemodialysis (HD) are attributed to changes in the electrolytic milieu with HD, or are considered to be due to an unknown mechanism. Such changes are thought to be proarrhythmic, and thus have potential clinical implications. Increase in the amplitude of QRS complexes following HD has been amply documented in the literature. Also, recent work linking attenuation/augmentation of amplitude of QRS and P-wave complexes in patients with increase/subsequent decrease weights due to anasarca peripheral edema/and its alleviation, or before/after hemodialysis (HD) suggests that the increase in the P-du and P-d after HD may be totally (or partially) mediated by the alleviation of the fluid overload by the procedure. This is supported by the decrease/increase in the QRS duration noted with anasarca/and its alleviation. To further clarify this issue, and prove or refute the above hypothesis, it is recommended that correlations of changes in the P-du and P-d with the loss of weight or net fluid dialyzed are carried out, in addition to the traditional considerations of electrolytic alterations after HD.

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Increases of the P-wave duration (P-du) and P-wave dispersion (P-d) from standard ECGs or Holter ECG monitoring sessions with subsequent development of atrial fibrillation (AF) have been identified in patients with a wide range of cardiovascular pathology, and in patients undergoing aorto-coronary bypass grafting, or hemodialysis (HD).¹⁻⁷ Indeed, the last group is identified as one characterized by very high peri-HD incidence of arrhythmias, with excessive morbidity and mortality.⁸⁻¹⁰ These changes in the P-du (specifically maximum P-du) and P-d are viewed as expressions of disturbances in the intra- and inter-atrial conduction (delays and inhomogeneous propagation) auguring AF, and in patients undergoing HD have been attributed to changes in the electrolytic and metabolic milieu, resulting from the procedure.^{6,7} Although statistically significant

correlations between K^+ , Mg^{2+} , Ca^{2+} , phosphate, bicarbonate, blood urea nitrogen, serum creatinine, and maximum P-du or P-d were found after HD,⁶ or changes in these P-wave variables are seen in patients with enlarged left atrium,⁷ it does not follow that a cause and effect relationship is at play. In fact values of the electrolytes after HD are closer to normal than prior to it, and it is hard to believe that such improvement is associated with electrophysiological P-wave derangements. Also, alleviation of the fluid overload is expected if anything to decrease the atrial volumes, something that intuitively should impart decrease in the P-du or P-d, than increase, as reported.^{6,7} Thus, it is prudent to look for alternative mechanisms for the change in the P-du or P-d after HD, or at least entertain possible confounding factors.

HD #13: 36 year old hypertensive woman on chronic HD

Figure 1. Standard ECGs before and after one of the 26 hemodialysis (HD) sessions. Note the increase in the amplitude of QRS complexes and P waves. Standardization signal is shown on the right side of the ECG tracing.

A case in point is of a 36-year-old woman previously reported,¹¹ with hypertension and a rejected transplanted kidney, who had standard ECGs with fixed precordial recording sites immediately before and after 26 HD sessions. This patient reproducibly revealed augmentation of the amplitude of the QRS complexes¹¹ (Fig. 1), something amply noted in the literature,¹²⁻¹⁸ and of the amplitude of the P waves,¹⁹ a novel finding. In addition, it was obvious by merely glancing at her ECGs before and after HD, and for all 26 HD sessions, that the P-du had increased after the procedure. Unfortunately, the ECGs had not been processed routinely, and thus we were deprived of the automated ECG measurements,²⁰ which would have provided the P-du for all ECG leads, and the calculated P-d. Also, we felt uncertain about measuring the P-du using the manual approach,²¹ as we did for the QRS complexes, in ECG hard copies recorded at calibration of 1.0 cm = 1.0 mV, and paper speed of 25 mm/s. However, looking at the width of P waves (Figs. 1 and

2) in most of the ECG leads, it was clear that the P-du had increased after HD, commensurate with resultant loss of weight and fluid.

The above provide an opportunity for considering an alternative explanation to the one usually cited for the changes in the P-du and P-d resulting from HD. The sequence of arguments for the proposed hypothesis goes as follows:

1. Changes in the QRS complexes after HD had been noted for many years, and had been attributed to changes in heart volumes or the electrolytic milieu after the procedure,¹²⁻¹⁷ although the role of the body volume conductor (BVC) has also been rarely considered.¹⁸ However, evidence is gathering that such alterations are due to the alleviation of the fluid overload changing in turn the electrical impedance of the BVC.¹¹ In this respect, these changes in the QRS amplitude are the inverse of the ones seen in patients with anasarca peripheral edema (AN) of

Figure 2. Selected enlarged P-waves from the ECGs of Figure 1, before (A) and after (B) hemodialysis. Note the increased amplitude and duration of P-waves following the procedure.

- various etiologies.²² Moreover, increase in the QRS complexes following alleviation of the AN was noted,²² and it was interpreted to be extracardiac in nature, since the marked increase in the QRS amplitude in the standard ECGs was associated with stable intracardiac electrograms.²²
- These extracardiac changes of the QRS complexes in the surface ECGs were noted in patients with a wide range of pathology, or after HD, and thus they are not specific disease-dependent. Indeed even the pacemaker stimulation "spikes" were subjected to changes in their amplitude with alterations of the fluid status of patients with AN, and there was a correlation of the "spikes" changes, with the corresponding changes in the paced QRS complexes.²³
 - The above changes in the amplitude of QRS complexes were associated with changes in the QRS duration.²⁴ When the QRSs decreased in amplitude, the corresponding QRS duration was shortened, and when they increased in patients with AN who subsequently lost weight, the QRS duration was increased²⁵; also the amplitude changes correlated with changes in duration.^{22,24,25}
 - These changes in the amplitude and duration of QRS complexes in patients with AN correlated with corresponding changes in weights.^{22,24}
 - Since changing edematous states impart these alterations on the entire ECG curve, it is not surprising that they also affect the amplitude of P-waves, a finding just reported.¹⁹
 - By analogy of what has been noted in the QRS amplitudes²² and QRS duration,²⁴ one should also expect that changes in the P-wave amplitudes¹⁹ should be associated with changes in the P-du, as noted in the patient presented briefly herein throughout her 26 HD sessions (Figs. 1 and 2).
 - Increases in P-d attributed to HD may be an arithmetic consequence of increase in the maximum and minimum P-du. Thus if one considers using the mean values from a paper cited above,⁶ a case in which the maximum P-du prior to HD is 98 ms, the minimum P-du is 71 ms, and the calculated P-d is 27 ms, and assumes that a percentage increase (e.g., 27.6%, equal to the change in the mean maximum P-du from that paper⁶) will equally affect the maximum P-du and the minimum P-du values (the maximum

P-du will increase to 125 ms, and the minimum P-du to 90 ms, with an increased calculated P-d of 35 ms). Thus, the mere increase by the same proportion in the maximum and minimum values of P-d imparts an increase in the calculated P-d.

The mechanism leading to the above described changes in the measurements of QRS and P-wave amplitudes and durations in patients gaining or losing weight, in the context of fluid overload or its alleviation, is based on an alteration of the "composite impedance" of the BVC surrounding the heart.²⁶⁻²⁹ Thus, the organs and tissues composing the BVC with their varying electrical impedances exert a different "transfer impedance" on the electrical currents emanating from the heart, as they are registered at the body surface. When the water content of the BVC increases or decreases,²⁶⁻²⁹ and since the water's electrical resistivity is the lowest in the human body,³⁰ the fluid overload leads to decrease "composite" impedance (and decrease in the amplitudes and durations of the various ECG components), and alleviation of fluid overload leads to increase in the impedance (and increase in the amplitudes and durations of the various ECG components).

Accordingly, when investigators report increases in the P-du or P-d after HD, they should look at the relationship of the changes in these P-wave parameters and the weight and net fluid loss imparted by the procedure. However, correlations with the electrolytic or metabolic changes should not be neglected, and more work is needed to associate etiologically the imparted correction or improvement of the acid-base imbalances with the increases in P-du and P-d; nevertheless it is hard to associate intuitively improvements in Canon's "internal milieu" after HD with increases in the P-du and P-d, traditionally thought to be indicative of electrophysiological deterioration. Accordingly, it is prudent to consider such changes also as being "apparent" than "real." Another matter for consideration pertains to the possibility that the antihypertensive and other drugs, taken by patients on HD, exert some effect on the P-du or P-d, via their altered serum or tissue concentration or receptor density or sensitivity, issues which will require future scientific scrutiny. Indeed, the incorporation of measurements of the weight and fluid changes to the ones of cardiac volumes and all the other parameters which are being currently evaluated^{6,7}

(including the drug electrolyte and acid-base changes) in a multivariate statistical model will most probably elucidate the mechanism(s) leading to increases in P-du and P-d after HD.

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