

Electrophysiologic Basis Of Digitalis Induced Arrhythmias

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More than 200 years have elapsed since the publication in 1785 of William Witherings classic account of Foxglove and its medical uses. With the clinical usage of digitalis came its toxicity and a gamut of troublesome arrhythmias. In the 1960s and early 1970s the reported incidence of digitalis toxicity was 25% with a mortality as high as 41%¹. So much was the extent of the problem that someone went on to say "Lanatoside has replaced homicide as the nation's number one killer". Recent data however suggest that the incidence is not so high; digitalis induced fatal arrhythmias have decreased to 1-5%². This is partly because the diagnosis of digitalis related arrhythmias is difficult and sometimes wrongly made. In order to understand the therapeutic and toxic effects of digitalis induced arrhythmias a clear understanding of the effect of the drug on the electrophysiological properties of the heart is mandatory.

Purkinje Fibres

The effect of increasing frequency of stimulation and concentration of the drug can be considered in three general categories.

- i) decreased resting potentials (RP) which slows the rate of phases 0 depolarization, as well as conduction velocity.
- ii) decreased action potential duration (APD) which results in decreased refractory period and increased responsiveness of fibres to electrical stimuli.
- iii) increase in rate of phase 4 depolarization.

iv) appearance of delayed after depolarizations.

The latter two mechanisms are responsible for increased automaticity.

Until relatively recently the favoured mechanism of digitalis induced arrhythmias was gradual depolarization secondary to inhibition of sodium potassium pump³. This increases with stretch and ischemia of the Purkinje fibre, ventricular rate and drug concentration.

Subsequent evidence suggests that digitalis promotes depolarizing after potentials often referred to as "transient depolarization", "Oscillatory after potentials", "delayed after depolarizations" or more popularly "delayed potentials". These may be related to transient decrease in membrane potential late in phase 3 or early phase 4 that reach threshold and depolarizes the ventricle. The likelihood that an after potential will reach threshold is enhanced by hypokalemia & hypercalcemia⁴.

SA Node

Most of the clinically important effects of digitalis on the rate of impulse formation are due to indirect effects that the drug exerts through enhanced parasympathetic and decreased adrenergic tone. Nevertheless, higher concentration of digitalis that cause severe toxicity has direct effect on the transmembrane potential of the SA node leading to sinus arrest or exit blocks.

AV Node

Digitalis prolongs the effective refractory period and delays conduction of the AV node due

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largely to increased vagal & decreased adrenergic activity. In toxic concentrations the drug acts directly on the AV node, reducing resting membrane potential, as well as the rate of rise and amplitude of the action potential. This increase in effective refractory period leads to advanced second or third degree blocks.

Blocks either at the SA & AV node or both, lead to escape rhythms nodal or ventricular. Indeed a combination of blocks, escapes, and increased automaticity be it due to increase in phase 4 depolarization or delayed after depolarization, is quite characteristic of digitalis induced arrhythmias.

Atrial and Ventricular Muscle Fibres

Changes in the duration of action potential in ventricular fibres, resembles the HPS though of lesser magnitude leading to decrease in QT interval. An increase in slope of phase 2 and a decrease in slope of phase 3 accounts for the ST-T changes. In higher, toxic concentrations there is an overall decrease in the resting membrane potential, amplitude of the action potential and the rate of depolarization of phase 0. This decrease conduction velocity and ultimately causes inexcitability. These dramatic effects are seldom seen in clinical settings. Digitalis may lead to delayed after potentials in atrial or ventricular fibres leading to increased automaticity.

Based on these electrophysiological factors we are now ready to look at the common arrhythmias induced by digitalis. And herein lies our problem.

The diagnosis of digitalis toxicity is never purely electrocardiographic for there is no electrocardiographically manifest arrhythmia that cannot be produced by digitalis toxicity.

"Digitalis is to the ECG what syphilis was to medicine the great imitator".

Although there are no arrhythmias that are pathognomonic of digitalis toxicity there are definite clues that can make us suspect digitalis as the culprit for the manifested arrhythmia.

Circumstances in which the electrocardiographer may suspect digitalis induced arrhythmia:

Any patient receiving digitalis who exhibits evidence of:

Both Increased Automaticity and Depressed Conduction:

- i) Supraventricular tachycardia with variable AV blocks (PAT with block) interspersed with extra systoles.
- ii) Simultaneous atrial and ventricular tachycardia with AV dissociation (double tachycardia).
- iii) Sinus bradycardia intermittent/established AV Block, with junctional or ventricular tachycardia.
- iv) Atrial fibrillation with some degree of AV Block and an accelerated junctional rhythm with resultant AV dissociation.
- v) The above combination with the junctional tachycardia showing Wenchebach periods.

Whenever such rare arrhythmias are encountered digitalis toxicity may be considered. When these arrhythmias are accompanied by multiform VPCs and ST-T changes in leads with predominantly positive QRS, digitalis toxicity becomes confirmed.

Excitants Effects

Ventricular extrasystoles are the most common manifestations of digitalis overdose but they are quite common in other disease states and also in healthy individuals. Clues to their being due to digitalis are:

- i) Ventricular bigeminy with alternating right and left axis deviation.
- ii) Repetitive multiform ventricular premature beats with varying or fixed coupling intervals specially in AF where rate was initially well controlled.

- iii) Concealed Bigeminy - Bigeminal runs may not be seen, but all interectopic intervals contain odd number of sinus beats.

Ectopic activity gives rise to tachycardia.

- iv) Automatic atrial tachycardia with variable shape and timing of P waves which are different from sinus: Multifocal atrial tachycardia.
- v) Accelerated idioventricular or idionodal tachycardia specially when associated with supra junctional blocks or AV dissociation.
- vi) Bidirectional tachycardia, when the ventricular rhythm is regular but QRS complexes alternate in morphology.
- vii) Fascicular tachycardias. Ventricular fibrillation also occurs due to digitalis toxicity but is rarely the first electrocardiographic manifestation. Atrial flutter and fibrillation have only occasionally been described as a manifestation of digitalis toxicity.

Supressant Effect

AV Blocks due to digitalis toxicity are generally type 1 - 2nd degree. Higher concentrations lead to complete AV Block, with escape rhythms.

In advanced intoxications, conduction in the ventricular expressways may be delayed. Digitalis typically cause SA exit blocks.

The dominant idea behind the understanding of the electrophysiological effects of digitalis is to apply this information towards early recognition and management of digitalis toxicity and related arrhythmias. A detailed discussion on these aspects is beyond the scope of this article. However, it must be emphasized that the clinician must remain alert to the extra cardiac symptoms as well as ECG findings suspicious of digitalis. One must watch for an increase in the frequency of multiform ventricular extra systoles, ST depression in leads that have a dominantly positive QRS, excessive slowing of ventricular response/regularization of ventricular rate in atrial fibrillation. These manifestations portend a more serious arrhythmia and are best treated with temporary drug withdrawal.

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