MONITORING OF DIGOXIN BLOOD LEVELS AND OTHER GRAVITY FACTORS IN CHILDREN

THESIS

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By

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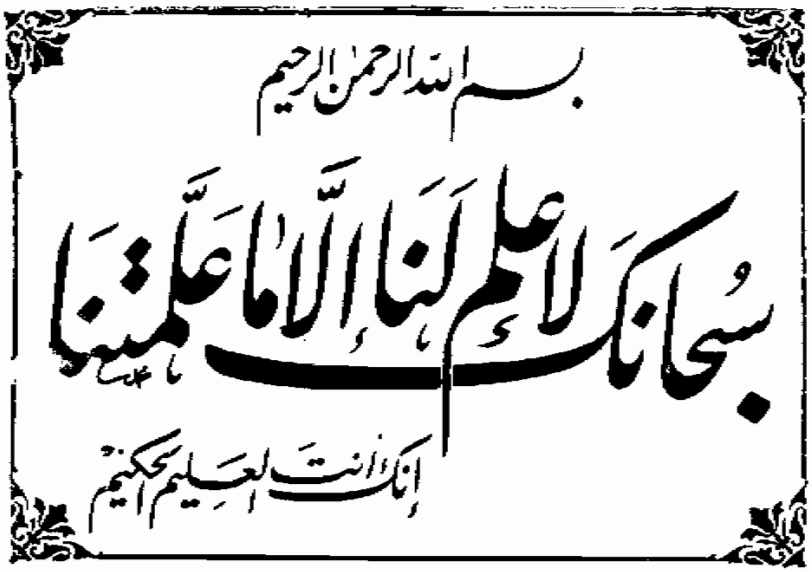

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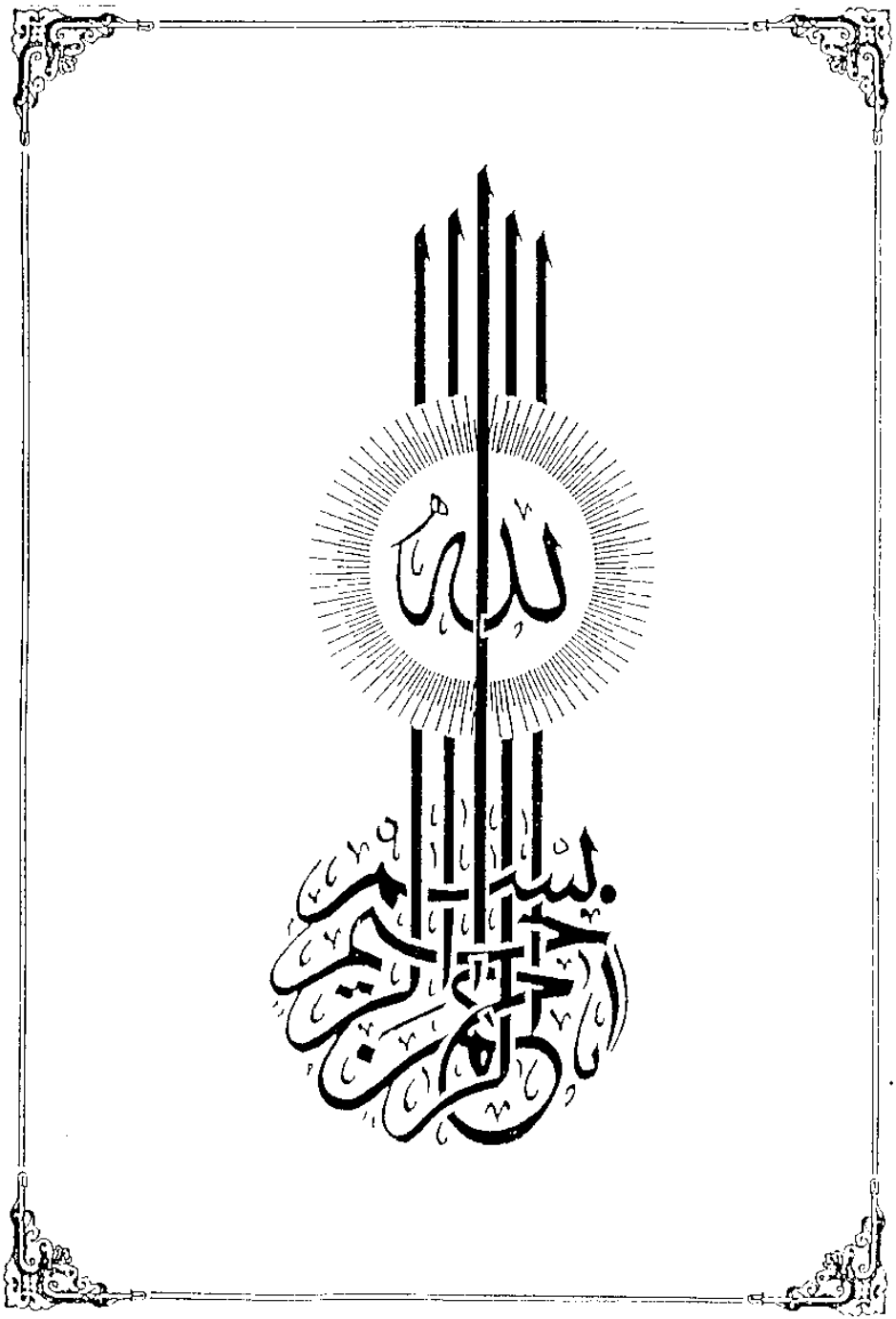

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In clinical practice digitalis toxicity is sometimes found despite giving the proper calculated dose. On the other hand the therapeutic dose is sometimes not as effective as should be. This is because digoxin as a drug is affected by many factors which interfere with its effectivity and metabolism. Unfortunately, digitalis has a narrow margin of safety, i.e. a narrow therapeutic range (Friedman & George, 1984).

Three major factors contribute to the high prevalence of digitalis intoxication:

1. The use of potent diuretics with attendant depletion of potassium and/or dehydration with impairment of renal function.

2. The use of above average doses of digitalis glycosides.

3. Failure to consider the effect of impaired renal

function on digitalis tolerance.

There are multiple determinants of digoxin therapeutic efficacy and of severity of intoxication, so it cannot be overemphasized that any dosage schedule of digitalis preparations is only a guide, since also there are individual differences among patients (Hoffman, 1980).

Therefore in acute intoxication, digoxin blood levels cannot be considered as the sole indicator, but other important parameters and investigational studies also yield useful information.

AIM OF THE WORK

This research aims to assess and compare the effect of other gravity factors in digoxin therapeutic practice as well as in the overdosed child.

REVIEW OF LITERATURE

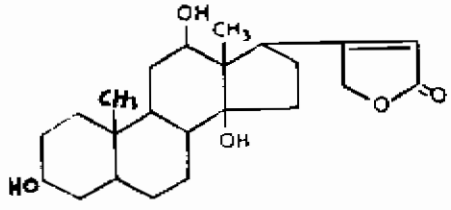
REVIEW OF LITERATURE

Digitalis glycosides:

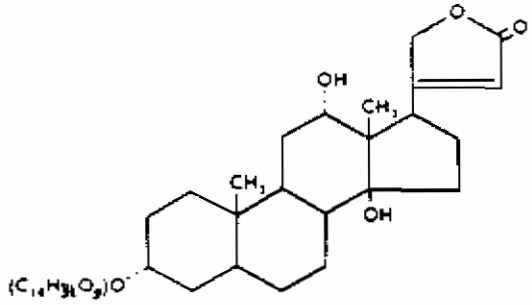
The term digitalis is used generally to refer to any of the cardioactive steroid glycoside compounds that have characteristic positive inotropic and electrophysiologic effects on the heart. These glycosides are derived from digitalis purpurea or digitalis lanata. Ouabain is an exception, which is derived from the seed of strophanthus gratus (Smith, 1976).

Chemical nature of cardiac glycosides: (Fig. 1)

The basic structure is the steroid (cyclopentaneperhydrophenanthrene) ring structure.To this ring structure, at carbon 17,is attached a five membered beta lactone ring. The combination of the steroid nucleus and the lactone ring is known as the genin or aglycone. Although there is some cardiotonic activity in the genin alone, it is only when one or more sugars are attached to carbon 3 that full cardiotonic activity is attained. The genin alone has a short action. For the specific long sustained action on the heart muscle, the attachment of the sugar moiety is



Digoxigenin



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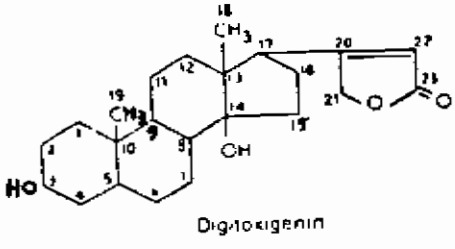
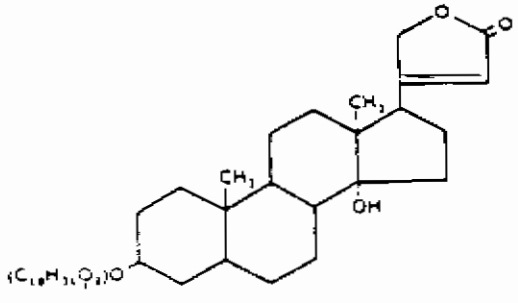


Digitoxigenin



Digitoxin

Fig. 1: The cardiac aglycones and cardiac glycosides. (Hoffman & Bigger, 1980).

essential. The total molecule, including the steroid nucleus, the lactone ring and the attached sugar is known as the cardiac glycoside DeGraff, 1985).

Two other requirements for cardiotonic activity are the following :

1. Spatial arrangement of the ring structure (which is not noted in other steroids).

2. A hydroxyl group in the beta position at carbon 14 also has been shown to be essential (Fullerton et al., 1979).

Pharmacodynamics:

The main pharmacodynamic property of digitalis is its ability to increase the force of myocardial contraction. The benificial effects of the drug in patients with heart failure are all explained on the basis of increased contractile force i.e. a positive inotropic action (Fig. 2).

These effects are : 1- increased cardiac output 2-

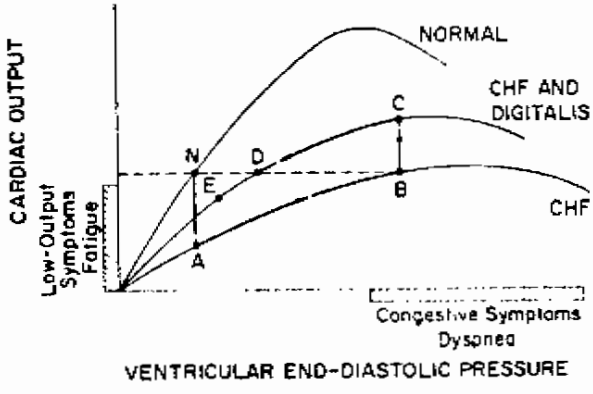


Fig. 2: Diagramatic represention of the mechanism of compensation and effect of digitalis in congestive heart failure.(Mason, 1982).

decreased heart size, venous pressure and blood volume 3- diuresis and relief of edema.

Another important action of digitalis is to slow the ventricular rate in atrial fibrillation. This effect is by increasing block at the atrioventricular node, so that fewer atrial beats will be followed by a ventricular beat (vagal action of digitalis).

Another vagal effect is an increase in carotid sinus sensitivity. A patient with a hypersenstive carotid sinus should not be given digitalis unless the heart is previously protected by the installation of an artificial pacemaker (DeGraff, 1985).

Digitalis also acts directly on the smooth muscles of the vascular system. In addition it exerts a number of effects on the neural tissues and thus indirectly influences the mechanical and electrical activity of the heart and modifies vascular resistance and capacity (Hoffman & Thomas, 1980).