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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Guidelines for Prescribing and Administering Digoxin in adults

Digoxin is a cardiac glycoside, its main therapeutic effect is to increase the force of myocardial contraction (positive inotrope) and reduce myocardial conductivity, particularly through the atrioventricular node. Digoxin is used as a second line agent to treat supraventricular arrhythmias mainly to control ventricular rate in atrial fibrillation and atrial flutter, when first line agents such as beta-blockers or calcium channel blockers aren't tolerated or are ineffective. Digoxin is also used to treat heart failure, in patients with systolic dysfunction, who remain symptomatic despite standard therapy.

When to use oral and intravenous digoxin

Oral Therapy

Oral digoxin, usually given as a single daily dose, is the preferred route of administration. Onset of action occurs within 2 hours and reaches a maximum effect after about 6 hours. If a rapid therapeutic effect is required (rapid digitalization) an oral loading dose should be given as digoxin has a large volume of distribution, followed by an appropriate daily maintenance dose. When used to treat heart failure, a loading dose is not necessary, and therapy should be initiated with a daily maintenance dose allowing digoxin to accumulate slowly. Steady state serum digoxin concentrations occur within 1 to 3 weeks, depending on renal function.

Intravenous Therapy

Intravenous (IV) digoxin therapy should only be used in the following situation:

- Rapid oral digitalization is not possible e.g. patient has persistent vomiting or is unable to take digoxin via the enteral route **AND**
- The patient's condition **requires a rapid response** e.g. ventricular rate control in fast atrial fibrillation and other first-line agents such as beta-blockers and calcium channel blockers have been considered and are contra-indicated.

If the patient has received any cardiac glycoside in the previous 2 weeks, IV digoxin should only be used if clinically indicated and with caution due to the risk of toxicity. Seek specialist advice from cardiology as a reduction in loading dose may be necessary.

IV digoxin produces an effect within 5 to 30 minutes (this will be longer if the loading dose is given as a slow infusion, refer to dosing section) and reaches a maximum effect within 1 to 5 hours. The patient should be switched to oral therapy as soon as possible. The use of IV digoxin for the treatment of heart failure is rarely indicated due to lack of clinical urgency.

Digoxin must not be given intramuscularly.

Contra-indications and cautions

Digoxin is contra-indicated in the following situations:

- Supraventricular arrhythmias associated with accessory pathways e.g. Wolff-Parkinson-White syndrome
- Intermittent complete heart block or second degree AV block

Use with caution in the following situations:

- Hypothyroidism - effects of digoxin may be enhanced.
- Hypertrophic obstructive cardiomyopathy – seek advice from cardiology
- Ventricular arrhythmias – in patients with a history of life threatening arrhythmias, seek advice from cardiology
- Severe respiratory disease: increased myocardial sensitivity to digoxin
- Direct current cardioversion: withdraw digoxin 1 to 2 days before procedure, if possible, due to risk of provoking arrhythmias

Electrolyte disturbances e.g. hypokalemia, hypomagnesaemia and hypercalcemia should be corrected before treatment otherwise the effects of digoxin may be enhanced.

Note: Digoxin toxicity is common and may precipitate arrhythmias. Always consider the possibility of digoxin toxicity in any patient taking digoxin presenting with arrhythmias.

Interactions with other medicines

Important interactions with digoxin include:

- Amiodarone or dronedarone: increase in plasma digoxin concentration. Reduction in digoxin dose by one third to a half is recommended.
- IV calcium: risk of arrhythmias, avoid IV calcium during use of IV digoxin.
- Any medication known to cause renal impairment e.g. ACE inhibitors and NSAIDs: risk of digoxin toxicity due to reduced renal excretion. Monitor plasma digoxin levels and reduce dose as appropriate.
- Diuretics: increased cardiac toxicity if hypokalaemia occurs.
- Beta blockers: increased risk of bradycardia and heart block.
- Calcium channel blockers (CCB): digoxin plasma concentrations increased by some CCBs e.g. verapamil and diltiazem. Monitor plasma levels and reduce dose as appropriate. Also, increased risk of bradycardia and heart block.
- Macrolide antibiotics can increase digoxin levels.

Refer to the BNF and the manufacturers SPC for full details, or contact medicines information for advice.

Dose and administration

The ePMA digoxin power plan should be used to prescribe loading and maintenance doses.

Digoxin has a narrow therapeutic index, the plasma concentration required for a therapeutic effect is between 1 and 2.6 nmol/litre (current biochemistry reference range). Plasma concentrations at the lower end are adequate for heart failure. Factors such as patients' cardiovascular status, renal function, thyroid status, age, lean body weight and concomitant medication can alter the pharmacokinetics and/or pharmacodynamics of digoxin. Dosage should be carefully adjusted to avoid toxicity.

Oral Therapy

ORAL LOADING:

A total loading dose of 750 to 1500 micrograms of digoxin may be given during the initial 24 hour period. The loading dose should only be given as a single dose if there is an absolute clinical urgency for rapid digitalization. More commonly the loading dose is given in divided doses to reduce the risk of toxicity.

A practical regimen is:
500 micrograms as a stat dose repeated 6 to 12 hours later.

Assess the patient's response after the first stat dose by checking the pulse before administering the second stat dose (do not give if heart rate less than 60 bpm). If the patient is elderly, has a low body weight or significant renal impairment, consider reducing the second stat dose to 250 micrograms.

ORAL MAINTENANCE DOSE:

Start oral maintenance therapy the day after the loading dose. **The usual maintenance dose is 62.5 to 250 micrograms daily.** The dosage must be adjusted to individual needs considering the following factors:

- Age
- Lean body mass
- Renal function
- Thyroid status
- Electrolyte balance

For the elderly, patients with renal impairment and those with a low body weight, maintenance doses should be lower e.g. 62.5 to 125 micrograms daily.

Note: Tablet and liquid formulations of digoxin are not equivalent. To aid administration 62.5 micrograms tablet = 50 micrograms liquid.

Intravenous Therapy

Consider seeking advice from Cardiology or Acute Medicine before using IV digoxin. IV digoxin should only be administered with heart rate, blood pressure and ECG monitoring – refer to the injectable monograph for further information on administration.

RAPID EMERGENCY IV LOADING:

Give a loading dose of 750 to 1000 micrograms as a slow infusion over 2 hours (unlicensed, BNF recommendation).

Alternatively the licensed IV loading dose of 500 to 1000 micrograms may be given in divided doses: administer half the total loading dose initially e.g. 250 to 500 micrograms and give further fractions of the remaining loading dose e.g. 250 micrograms at intervals of 4 to 8 hours depending on the patient's response. Give each IV loading dose as a short infusion over a minimum of 10 to 20 minutes. If the IV loading dose is given in divided doses it is preferable to switch to oral loading as soon as possible. Avoid rapid IV administration as this can cause vasoconstriction leading to hypertension and reduced coronary blood flow.

The elderly, patients with renal impairment and those with a low body weight should receive a loading dose at the lower end of the range to reduce the risk of toxicity.

Start oral maintenance therapy the next day.

IV MAINTENANCE THERAPY:

If digoxin cannot be given orally e.g. patient is vomiting or nil by mouth and it is clinically necessary to continue digoxin therapy, IV maintenance may be used. In this situation the usual oral dose is reduced by approximately one-third to convert to an equivalent IV dose to account for differences in bioavailability between preparations:

62.5 micrograms tablet ≡ 40 micrograms IV

However, it may be necessary to round the IV dose up or down to facilitate administration of the dose due to the strength of the IV preparation. Administer the IV daily maintenance dose as a slow infusion over at least 2 hours with appropriate monitoring.

Recommended monitoring

Monitoring digoxin plasma concentrations may be useful in the following situations:

- If poor compliance is suspected
- If poor or fluctuating clinical response
- Deteriorating renal function
- To monitor drug interactions
- To monitor clinical toxicity

Blood samples for digoxin should be taken at least 6 hours after a dose to allow for distribution of digoxin. Renal function and plasma potassium should also be measured to help interpretation of digoxin levels. Thyroid status and age should also be considered

when interpreting levels. Contact medicines Information for further advice.

If digoxin therapy is initiated as an in-patient, plasma monitoring, usually 1 week after initiation of therapy, should be undertaken especially in patients at increased risk of toxicity e.g. the elderly, patients with renal impairment, those with a low body weight and those on interacting medication e.g. amiodarone. If the patient is discharged before this time period, specific guidance should be given to the GP to monitor digoxin levels after discharge and review the maintenance dose as appropriate.

Adverse Effects

Adverse effects are common, early signs of digoxin toxicity include:

- Nausea, vomiting, anorexia and diarrhoea
- Headache, fatigue, weakness, dizziness, drowsiness, bad dreams, disorientation and confusion
- Blurred vision and changes in colour vision e.g. yellow tint to vision
- Heart failure, supraventricular or ventricular arrhythmias

References

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