Aged Residential Care Digoxin Monitoring Guidelines

Version 2 2013
## Table of Contents

Summary ........................................ Page 3
Background ..................................... Page 4
Requirements for apical pulse monitoring .................................................. Page 5
Signs and Symptoms of digoxin toxicity .................................................... Page 6
Documentation for reporting signs and symptoms of digoxin toxicity .......... Page 7
Monitoring requirements digoxin therapy .................................................. Page 8
Actions on therapeutic level ................................................................. Page 9
Medication interactions with digoxin ...................................................... Page 10
Medical conditions which increase the risk of digoxin toxicity ................ Page 11

### Appendices:

Appendix 1. Aged Residential Care Digoxin Monitoring Wall Chart ........ Page 12
Appendix 2. Monitoring requirements during digoxin therapy wall chart .... Page 13
Appendix 4. Digoxin ISBAR ................................................................. Page 15
Appendix 5. Digoxin Monitoring Chart .................................................. Page 16
Summary
Routine therapeutic drug monitoring (TDM) during digoxin therapy is no longer required, including daily apical pulse assessment and digoxin serum levels. The patient’s heart rate should continue to be assessed as part of the patient’s routine monthly clinical assessment.

Indications for TDM during digoxin therapy include:
- Confirmation of toxicity (in the presence of symptoms of digoxin toxicity)
- Assessing the effect of factors that alter digoxin’s pharmacokinetics (e.g. renal impairment, drug interactions)
- Initiating therapy or dose changes (in patients with renal impairment)
- Therapeutic failure
- Medication adherence

Signs and symptoms of Toxicity
- Common
  - Nausea, vomiting, anorexia, fatigue, confusion
- Rare or dose dependant
  - Visual disturbances (blurred vision, green-yellow colour disturbances)
  - Cardiac arrhythmias

Therapeutic Range
- Heart failure
  - 0.6nmol/L – 1.2nmol/L,
  - Toxicity more likely >2.5nmol/L,
  - Small increase in mortality with concentrations >1.5nmol/L.
- Atrial Fibrillation (AF)
  - 0.6 – 2nmol/L,
  - Toxicity more likely >2.5nmol/L
  - Serum digoxin levels correlate poorly with ventricular rate.
  - In patients who are symptomatic, a low digoxin level may indicate the patient could benefit from a dose increase.

Samples for digoxin TDM should be taken at least six to eight hours after the last dose, or ideally immediately before the next dose.

Rate Control in AF
Recent guidance from the European Society of Cardiology, indicates lenient rate control (<110bpm) may be effective in patients who are asymptomatic.

Bradycardia (heart rate <60bpm) is poorly correlated with digoxin toxicity. Patients with heart failure presenting with bradycardia (<60bpm) who are asymptomatic can be safely given digoxin. If symptomatic bradycardia is present, or the patient displays signs and symptoms of digoxin toxicity, the prescriber should be contacted.
Background

Digoxin is a cardiac glycoside indicated in the treatment of atrial fibrillation (AF) and heart failure (HF). Digoxin’s mechanism of action is thought to be mediated through inotropic effects and neurohormonal effects.\(^1\) Positive inotropic effects from digoxin arise from the inhibition of Na\(^+\)-K\(^+\)-ATPase and secondary activation of the Na\(^+\)-Ca\(^{2+}\) membrane exchange pump resulting in increased force of cardiac contraction.\(^2\) Neurohormonal effects mediate increased vagal tone, decreased sympathetic tone, leading to prolonged refractory period and slowing of conduction through the atrioventricular node, thereby slowing ventricular rate.\(^3\) Neurohormonal effects are present at lower digoxin serum levels and are considered to be the primarily responsible for the therapeutic actions in both heart failure and atrial fibrillation.\(^4\) Inotropic effects are present at higher digoxin serum levels and are now considered less important in the therapeutic effects of digoxin.\(^5\)

Heart Failure

The national heart foundation and NZGG guidelines consider digoxin the drug of choice in patients with AF and heart failure.\(^6\) In patients with heart failure and sinus rhythm digoxin is considered for patients who remain symptomatic despite treatment with ACE-Inhibitor, β-blocker, diuretics and spironolactone.\(^7\)

Atrial Fibrillation

Digoxin slows resting ventricular heart rate in patients with chronic atrial fibrillation. Digoxin is less effective at controlling exercise or stress induced atrial fibrillation, and can be successfully used in combination with β-blockers, verapamil and diltiazem for the management of chronic atrial fibrillation.\(^8\)

---

\(^4\) Barclay M, Begg E. The practice of digoxin therapeutic drug monitoring. NZMJ. 2003;116(1187)
\(^5\) Barclay M, Begg E. The practice of digoxin therapeutic drug monitoring. NZMJ. 2003;116(1187)
\(^6\) National Heart Foundation of New Zealand. New Zealand Guideline for the Management of Chronic Heart Failure: 2009 Update. The National Heart Foundation of NZ. Auckland, New Zealand. 2010
\(^7\) National Heart Foundation of New Zealand. New Zealand Guideline for the Management of Chronic Heart Failure: 2009 Update. The National Heart Foundation of NZ. Auckland, New Zealand. 2010
\(^8\) Campbell T, MacDonald P. New Drugs, Old Drugs: Digoxin in heart failure and cardiac arrhythmias. MJA. 2003; 179: 98-102
**Requirements for Apical Pulse Monitoring**

Conflicting information exists in the literature as to whether apical pulse (see Appendix 3 for further information on apical pulse) monitoring is required before the administration of digoxin. Current NZGG atrial fibrillation\(^9\) and congestive heart failure\(^10\) guidelines do not require apical pulse monitoring, nor does the data sheet for Lanoxin\(^\circ\) brand of digoxin.\(^11\)

The BNF\(^12\) and MICROMEDEX\(^13\) suggest apical pulse assessment prior to the administration of digoxin, with each giving an apical pulse < 60 beats-per-minute (bpm) as a point in which the either patient or caregiver should contact the prescriber before administering digoxin.

The basis to this advice is that the presence of bradycardia may indicate digoxin toxicity or heart block.\(^14\) An early study correlating heart rate and digoxin toxicity found that sinus bradycardia or slow ventricular rate was poorly correlated with digoxin toxicity (6 out of 57 patients).\(^15\) A later study found that digoxin was inappropriately withheld in 81% of patients with a heart rate of < 60bpm.\(^16\)

The incidence of digoxin toxicity is considerably lower than that observed in early studies. Studies from the 1970s indicated 25% of patients on digoxin experienced toxicity, reducing to 4% with the DIG trial during 2000s.\(^17\) The advent of therapeutic drug monitoring standardised digoxin formulations and reduced target therapeutic ranges has reduced the rate of toxicity. Renal impairment is one the most important risk factors, with moderate renal impairment being present in 66% of toxicity cases.\(^17\)

Patients with AF have a rhythm which is defined as “irregularly irregular”. In overdose and severe digoxin toxicity heart block can develop, leading to sinus (regular rhythm) bradycardia of between 45 – 60bpm. Heart block can also occur with the combination of other AV node blocking agents e.g. \(\beta\)-blockers and calcium channel blockers. Other arrhythmias likely in digoxin toxicity include premature ventricular complexes and sustained ventricular tachycardia.\(^18\)

Patients with bradycardia should be assessed for other clinical signs and symptoms. It is unlikely that a patient will be symptomatic of bradycardia if their apical pulse is >50bpm. Patients presenting with hypotension, syncope, chest pain, and shortness of breath along with bradycardia should be assessed by their doctor.\(^19\)

**Recommendations:**

Assess blood pressure and apical pulse as part of the patient’s routine monthly clinical assessment.

---


\(^10\) National Heart Foundation of New Zealand. New Zealand Guideline for the Management of Chronic Heart Failure: 2009 Update. The National Heart Foundation of NZ. Auckland, New Zealand. 2010


See Appendix 1: Aged Residential Care digoxin monitoring wall chart
**Signs and Symptom of toxicity**

Digoxin toxicity can present as gastrointestinal symptoms, cardiac symptoms and neurological symptoms.

**Gastrointestinal** (most likely)

- Nausea
- Vomiting
- Anorexia

**Neurological**

- Weakness
- Fatigue (most likely)
- Confusion
- Visual disturbance
  - Blurred vision, flashing lights or halo’s
  - Green-yellow colour disturbances

**Cardiac**

- Supra ventricular arrhythmias
- Ventricular arrhythmias
- First, second or third degree heart block
  - Sinus Bradycardia
- Tachyarrhythmias are more common in patients with heart disease

---


© Hawke’s Bay District Health Board
Documentation for reporting signs and symptoms of toxicity

Many of the symptoms of digoxin toxicity (nausea, confusion, arrhythmias, and abdominal pain) are non-specific and are frequently present in acutely ill patients in general.

Suspected digoxin toxicity should be documented in the patient’s progress/medical notes, and the following information sent to the patient’s GP using the facility or digoxin ISABR (see Appendix 4):

- **Observations**
  - Blood pressure
  - Heart rate
  - Alterations in food intake
  - Neurological status

- **Signs of toxicity**
  - Gastrointestinal
  - Visual
  - Neurological
Monitoring Requirements Digoxin Therapy

Therapeutic range:
- HF 0.6 – 1.2 nmol/L
- AF 0.6 – 2 nmol/L (see notes below)

Digoxin therapy for HF symptoms has been shown to be effective at lower concentrations (0.6 to 1.2 nmol/L). Therapy in lower concentrations was associated with a small but significant reduction in all-cause mortality, worsening heart failure, all-cause hospitalisation and hospitalisation due to heart failure compared with placebo. Higher concentrations (>1.5 nmol/L) were associated with a small but significant increase in all-cause mortality, cardiovascular mortality and hospitalisation for digoxin-related toxicity. Mid-range was not significantly different from placebo for toxicity.

Studies evaluating the relationship of serum digoxin concentrations with pharmacodynamic effects in AF have in general, shown a poor correlation between digoxin levels and ventricular rate. This is understandable, considering the many other factors that affect conduction through the AV node. The ventricular rate, although a clinically important and easily monitored parameter in AF, may not always be a good measure of digoxin effect. In some patients, signs and symptoms of toxicity may develop before the desired decrease in heart rate. The serum digoxin level may provide, information that cannot be obtained solely from the clinical picture, but is of great relevance to therapeutic decision making.

The indications for digoxin TDM are relatively few and include confirmation of clinically suspected toxicity, assessing the reasons for therapeutic failure, assessing medication adherence, and assessing the effects of factors that alter the pharmacokinetics of digoxin (predominantly renal dysfunction and drug interactions). The clinical suspicion of toxicity correlates poorly with high digoxin concentrations. In those requests in which the indication for TDM was confirmation of toxicity, only 19% were associated with a high digoxin concentration.

Samples for digoxin TDM are required to be taken at least eight hours after the last dose or ideally immediately before the next dose. This allows for the redistribution of digoxin from plasma into the tissues. It is ideal that digoxin levels are taken when concentrations are at steady-state. The relatively long half-life of digoxin (30 hours in patients with normal renal function) means that following initiation or dose alterations, it takes at least 7 days for steady-state concentrations to be achieved. In the elderly with impaired renal function the half life can be extended to 3.5-5 days, meaning 14-20 days may be required before steady state is achieved.

Recommendations:
See Appendix 2: Monitoring requirements for digoxin wall chart
Appendix 4 is a suggested format for recording monthly blood pressure and apical, along with routine assessments of eGFR and potassium.

---

23 Barclay M, Begg E. The practice of digoxin therapeutic drug monitoring. NZMJ. 2003;116(1187)
26 Campbell T, MacDonald P. New Drugs, Old Drugs: Digoxin in heart failure and cardiac arrhythmias. MJA. 2003; 179: 98-102
29 Campbell T, MacDonald P. New Drugs, Old Drugs: Digoxin in heart failure and cardiac arrhythmias. MJA. 2003; 179: 98-102
Actions on Therapeutic Level
Serum digoxin levels should be interpreted within the clinical context. If the level is above the therapeutic range, the dose should be reduced even if toxicity is not observed. This is based on the observation that the patient is at risk of arrhythmia, and no further clinical benefit is likely with higher concentrations. Toxicity is observed when digoxin levels are within the normal range, due to other factors which alter tissue sensitivity to digoxin e.g.:

- Hypokalaemia (low potassium)
- Hypercalcaemia (high calcium)
- Hypothyroidism (thyroid disease resulting in reduced thyroid function)
- Hypoxia / acidosis (low blood oxygen, arterial blood pH <7.35)

Digoxin TDM may be useful to detect the patients who have a low digoxin concentration and who may benefit from an increase in digoxin dose, as opposed to those with higher concentrations who are likely to develop toxicity symptoms only from an increase in dose.

Recommendations:
See Appendix 2: Monitoring requirements for digoxin wall chart

---

33 Barclay M, Begg E. The practice of digoxin therapeutic drug monitoring. NZMJ. 2003;116(1187)
Medication Interactions

Digoxin is rapidly absorbed with a bioavailability of 70-80% from oral tablets. Digoxin is eliminated primarily by renal excretion, via P-glycoprotein (P-gp). Interactions with digoxin are mediated through the inhibition or induction of P-gp in the GI tract and renally. Inhibition of renally located P-gp results in increased serum digoxin levels. Induction of P-gp in the gut reduces digoxin absorption, resulting in lower levels.\(^{35}\)

**Medications which increase the risk of toxicity:**\(^{36}\)
- Reduce the dose of digoxin prior to initiating therapy:
  - Amiodarone (50% dose reduction when initiating amiodarone)
  - Verapamil (50% dose reduction when initiating verapamil)
- Monitor digoxin level (7 days-21 days depending on renal function after introducing the interacting medicine)
  - Clarithromycin / erythromycin / roxithromycin
  - Spironolactone
  - Cyclosporin
  - Itraconazole
  - Diltiazem
  - Quinine
  - Atorvastatin (high doses only 80mg daily)
  - Trimethoprim (courses >7 days)
- Monitor renal function and potassium level (every 3-6 months or after vomiting, diarrhoea or dehydration)
  - Diuretics (risk of hypokalaemia)
  - ACE-Inhibitors (reduction in renal function – monitor 7 days after starting then 3-6 monthly)

**Medications which decrease digoxin levels**\(^{37}\)
- Decreased absorption (Monitor Levels 7-21 days after introducing the interacting medicine)
  - Rifampicin
  - St John’s Wort
- Decreased absorption (separate administration by 2 hours)
  - Antacids (aluminium and magnesium, not calcium based)

**Recommendations:**
See Appendix 2: Monitoring requirements for digoxin wall chart


Medical conditions increasing the risk of toxicity

In the elderly reduced renal function and a reduction in muscle mass (20% between 20 and 70 years), increases serum digoxin levels and reduces elimination of digoxin. The following changes in medical conditions can increase the risk of digoxin toxicity either due to increased digoxin concentrations or sensitivity to digoxin.

- Dehydration – nausea and vomiting
- Renal impairment
- Unstable heart failure
- Hypokalaemia – diuresis
- Hypothyroidism
- MI
- Hypercalcaemia

If signs or symptoms of digoxin toxicity present, TDM is indicated.

---

Appendix 1. Residential Care Digoxin Monitoring Wall Chart
Clinical Signs of Digoxin Toxicity?
(nausea, vomiting, anorexia, fatigue, confusion, visual disturbances)

Yes

Refer to GP

No

Routine monthly assessment
(Blood Pressure, Apical Pulse)

Is Heart Rate <60bpm?

Yes

Clinical Signs of Bradycardia?
Hypotension (Systolic <100mmHg) Dizziness Shortness of breath)

Yes

Refer to GP

No

Continue monthly assessment &
3 or 6 or 12 monthly assessment
(renal function & electrolytes)

Decline in renal function OR hypokalemia

Yes

Refer to GP

No

Continue with monthly assessments
Appendix 2. Monitoring requirements during digoxin therapy wall chart

Monitoring of renal function and electrolytes

3 monthly
ACE-I (or ARB) + spironolactone + Diuretic

Change in CKD Stage
NB: Avoid Doses >125mcg with eGFR <60ml/min

Check digoxin level

Add potassium for 7 days then review
NB: Caution with Spironolactone

K+ <3.5mmol/L
Add potassium for 7 days then review
NB: Caution with Spironolactone
Reduce diuretic

6 monthly
ACE-I (or ARB) + diuretic or furosemide alone

K+ >5.2mmol/L
Reduce ACE-I, ARB or spironolactone

12 monthly
Routine Baseline ACE-I or ARB or low dose thiazide

Dyspnoea, oedema increase diuretic (not spironolactone)

Adding an interacting medicine

Alteration in digoxin level

Diuretics (hypokalaemia), ACE-I, AR2A (renal function)

Increased levels
Amiodarone
Verapamil
Macrolides
Cyclosporin
Spironolactone

Decreased levels
St Johns Wort
Rifampicin

Increased toxicity risk

Check potassium and renal function in 7 days

Check Digoxin Level 7-21 days

© Hawke’s Bay District Health Board

April 2013
Appendix 3. Guideline for Residential Care: Taking an apical (apex) beat

Definition
The Apical (Apex) is the heart beat of the heart. The heart beats with two distinct sounds (lub-dub). Each set of sounds (lub-dub) is one heartbeat. The Apical (Apex) Pulse is counted for a full minute denoting rate, rhythm and volume.

Good Practice: Any resident who is prescribed Digoxin is to have a monthly Apical (Apex) Pulse recorded and documented.

To assess
1. Provide resident privacy
2. Assist the resident to sit up or assume a semi-sitting position
3. Expose the resident’s chest
4. Examine the chest to find the anatomical landmarks for proper stethoscope placement.
5. First locate the first intercostal space (the space between the first and second rib) on the left side of the chest.
6. Count down to the fifth intercostal space (between the fifth and sixth rib).
7. Draw a straight line from the left nipple to the fifth intercostal space (or landmark by drawing a line from mid clavicular) to identify the area of the apical pulse.
8. Use your hand to warm the stethoscope diaphragm, (the flat disk) side of the stethoscope.
9. Listen and count for the heart beat for 60 seconds.
10. The heart beat consists of two distinct sounds, lub-dub.
11. Each lub-dub counts as one heartbeat.
12. Please report (refer to ISBAR communication tool to GP) if you denote the following:
   - The heart beat is not regular/missing a beat
   - Nausea (length of time)
   - Anorexia (length of time)
   - Chest pain (describe)
   - Dizziness (rule out postural drop)
   - The heart beat is weak or bounding
   - Vomiting (length of time)
   - Fatigue (describe)
   - Confusion (new/old)
   - Shortness of breath (new/length of time)
13. Don’t forget to document your findings.
Appendix 4: Digoxin ISBAR

COMMUNICATION TOOL

TO GENERAL PRACTITIONER FROM AGED RESIDENTIAL CARE

I

To Dr: …………………………………………………From: (Facility) …………………………………………………………

(Fax number of Facility)…………………………………………………………………………

Resident’s Name: …………………………………..Residents NHI: ……………..Residents DOB: …………………

Staff member: (Name and role) ……………………………………………………………………………………………

I am calling because I perceive there are concerns relating to the patients prescribed medication and
side effects – Medication = Digoxin

S

I believe this resident is (tick indicates concerns)

□ Stable but I have concerns

□ Unstable with rapid/slow deterioration

B

Has been described Digoxin (tick indicates concerns)

□ Long-term medication (months to year)

□ Recently prescribed by yourself

□ Recently discharged from a Hospital discharge

□ I am unsure of

A

I have taken the residents Apical Pulse and it is <60 beats per minute, along with symptoms of
bradycardia (hypotension, chest pain, syncope, and SOB) – this is new from last taken

The resident is complaining/displaying:

□ Nausea (length of time)

□ Vomiting (length of time)

□ Anorexia (length of time)

□ Fatigue (describe)

□ Chest pain (describe)

□ Confusion (new/old)

□ Dizziness (rule out postural drop)

□ Shortness of breath (new/length of time)

If you have ticked any of the boxes above the RN to please document your findings:

……………………………………………………………………………………………………………………………………………………………………

……………………………………………………………………………………………………………………………………………………………………

Apical Pulse (Reg/quality): ……………………………………(this is different from last assessment on

…/…./……)

Other Vital signs completed:

Temp:…………… BP (L & S):……………………………………………………………………………-Resps:………Oxygen Sats:….

Any changes

Skin colour Y/N  Pain Y/N  Urine output Y/N  Bowel changes Y/N

R

Please confirm advice on further management:

……………………………………………………………………………………………………………………………………………………………………
# Appendix 5. Digoxin Monitoring Chart

<table>
<thead>
<tr>
<th>Patient Details: Attach Sticker</th>
<th>Monitoring Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>BP and Apical Pulse:</td>
</tr>
<tr>
<td>NHI:</td>
<td>eGFR:</td>
</tr>
<tr>
<td>Doctor:</td>
<td>Potassium:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Apical Pulse</th>
<th>BP</th>
<th>eGFR</th>
<th>Potassium (K+)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Please refer to Digoxin Administration Monitoring Wall Charts and Guideline for further information