Digoxin Poisoning Management

Introduction

- Digoxin is a cardioactive glycoside indicated for atrial flutter, atrial fibrillation, and heart failure
- Acts as a sodium/potassium pump inhibitor for cardiac myocytes → toxicity arises with too much intracellular Na+ inhibiting the sodium/calcium pump from working properly (increasing intracellular calcium)
    - Increased inotropy within the cardiac myocytes → dysrhythmias
- EKG abnormalities: premature ventricular contractions, biphasic T wave, shortened QT interval, AV block
- Digoxin therapeutic levels range from 0.8-2.0 ng/ml (toxicity can begin >2 ng/ml)

Pharmacology	
	Digoxin Immune Fab (DigiFab or DigiBind)

Dose	• 1 vial = 40mg (binds to 0.5mg of digoxin)
	• **Unknown toxicity level: Initial → 10vials**
	• Vials = Total body load (mg) x 2
	• For chronic ingestion of unknown amount
	  ○ 3-6 vials can be given for adults
	  ○ 1-2 vials can be given for children

Administration	• IV infusion over 30 minutes • If cardiac arrest is imminent a bolus injection can be given
PK/PD	• **Onset: 20-90 minutes** • Duration of action: 15 – 20 hrs
Adverse Effects	• Orthostatic hypotension, ventricular tachycardia, hypokalemia
Mechanism of Action	• Immune antigen-binding fragments that rapidly bind with digoxin to decrease free digoxin levels within the body
Compatibility	• 0.9% NS Only
Comments	• Monitor **K+** closely as it shifts intracellularly potentially causing hypokalemia. • **Total concentration of digoxin may be falsely elevated after administration due to ↑ in free drug & bounded drug.** • Free digoxin concentrations are more clinically useful

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Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
Wei et al., 2021	Case reports (n=121)	**DigiBind** vs **DigiFab** adverse events reported to FAERS from 1986-2019	• **87.2% of DigiBind** reports were serious AEs vs. **62.8% of DigiFab** • Hypotension, cardiac arrest, and death were among the most serious AEs
Ward et al, 2000	Observational (n=16)	**DigiBind** vs **DigiFab in healthy volunteers**	• Both Fab products reduced free digoxin serum concentrations to **below assay detection** • Total digoxin serum concentrations increased approximately 10-fold (indicated fab product binding digoxin)
Renard et al., 1997	Observational (n=16)	Influence of **age & renal dysfunction** on digoxin-specific Fab pharmacokinetics •Doses 80-800mg infused over 0.25-2hr •Patients aged 35-90 with CrCl 10.6-122.1 ml/min	• **Linear decrease** of total body clearance is linked to renal function and age, but not Vd • Plasma half-lives ranged from **11-34.5hrs** • All patients recovered and no adverse effects were reported
Antman et al., 1990	Open-label trial (n=150)	Digoxin-specific Fab fragment dosed based on total ingested amount (mg) or digoxin serum concentration (ng/ml)	• **90%** of patient toxicity resolved or improved with **10%** showing no response • Median dose ~ 200mg (5 vials) • Highest dose ~ 1600mg (40 vials)

Conclusions

- Digoxin toxicity is a serious & life-threatening condition if not appropriately reversed by an available antidote
- For unknown amount of ingestion, administer 10 vials of digoxin Immune Fab to treat digoxin toxicity
- Age and renal function are proven not to be factors prohibiting digoxin toxicity treatment

References

1. Bismuth C, Gaultier M, Conso F, Efthymiou ML. Hyperkalemia in acute digitalis poisoning: prognostic significance and therapeutic implications. *Clin Toxicol*. 1973;6(2):153-162. doi:10.3109/15563657308990513
2. David MNV, Shetty M. Digoxin. [Updated 2022 Sep 5]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK556025/
3. Lexicomp Online, Lexi-Drugs Online. Waltham, MA: UpToDate, Inc.; January 2023. Accessed January 16, 2023. https://online.lexi.com.
4. Antman et al. Treatment of 150 cases of life-threatening digitalis intoxication with digoxin-specific Fab antibody fragments. Final report of a multicenter study. *Circulation*. 1990;81(6):1744-1752. doi:10.1161/01.cir.81.6.1744
5. Renard C, Grene-Lerouge N, Beau N, Baud F, Scherrmann JM. Pharmacokinetics of digoxin-specific Fab: effects of decreased renal function and age. *Br J Clin Pharmacol*. 1997;44(2):135-138. doi:10.1046/j.1365-2125.1997.00654.x
6. Roberts DM, Gallapatthy G, Dunuwille A, Chan BS. Pharmacological treatment of cardiac glycoside poisoning. *Br J Clin Pharmacol*. 2016;81(3):488-495. doi:10.1111/bcp.12814
7. Ujhelyi MR, Robert S. Pharmacokinetic aspects of digoxin-specific Fab therapy in the management of digitalis toxicity. Clin Pharmacokinet. 1995;28(6):483-493. doi:10.2165/00003088-199528060-00006
8. Wei, S., Niu, M.T. & Dores, G.M. Adverse Events Associated with Use of Digoxin Immune Fab Reported to the US Food and Drug Administration Adverse Event Reporting System, 1986–2019. *Drugs - Real World Outcomes* 8, 253–262 (2021). https://doi.org/10.1007/s40801-021-00242-x
9. Ward SB, Sjostrom L, Ujhelyi MR. Comparison of the pharmacokinetics and in vivo bioaffinity of DigiTAb versus Digibind. Ther Drug Monit. 2000 Oct;22(5):599-607. doi: 10.1097/00007691-200010000-00016. PMID: 11034267.