The Sinclair Method: A Structured Naltrexone Protocol to Reduce Alcohol Use

Overview



What is the Sinclair Method?

- The Sinclair Method is a structured, off-label approach to treating alcohol use disorder (AUD) that involves taking naltrexone, an opioid receptor antagonist FDA-approved for AUD, before consuming alcohol.
- Unlike traditional daily naltrexone use, which may be started after a period of alcohol abstinence or detoxification, the Sinclair Method can be used when individuals are still drinking alcohol with the goal to help control or cut down on their alcohol use.



How Does it Work?

- Naltrexone is taken on days the patient plans to drink, which could be every day.
- Naltrexone blocks opioid receptors, dampening the brain's release of endogenous opioids (i.e., endorphins), which causes the rewarding response to alcohol use.
- This process, known as *pharmacologic extinction*, diminishes alcohol's reinforcing properties and can lead to reduced drinking over time.

Patient Selection: Benefits and Considerations



Patient Selection

- Diagnosed with alcohol use disorder
- Interested in reducing alcohol use but not necessarily ready for immediate abstinence
- Not currently using opioids (contraindication with naltrexone)
- Able to self-manage medication timing and adherence



Advantages

- Supports risk mitigation and non-abstinence-based goals
- Offers an alternative for patients not interested in traditional daily dosing
- Empowers patient autonomy
- Allows for increased flexibility and individualized dosing



Limitations and Considerations

- Requires consistent adherence to the protocol to be effective
- Patients must be able to anticipate and plan for drinking occasions
- The risk of acute alcohol withdrawal still exists; mild withdrawal may be managed in the outpatient setting, but patients at risk for severe withdrawal may not be appropriate candidates

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Comparing The Sinclair Method to Traditional Naltrexone Use and Targeted Naltrexone Dosing

	Traditional Naltrexone Use	The Sinclair Method	Targeted Naltrexone Dosing
Treatment Goal	Typically abstinence	Gradual reduction in alcohol consumption over time	Reduce cravings or heavy drinking in high-risk situations
Timing of Dose	Daily (oral) or monthly (ER IM), regardless of use	Depends on alcohol use patterns, could be daily if patients are drinking daily	Before anticipated high-risk situations where alcohol craving is anticipated (e.g., party)
Mechanism Emphasized	Blocks reward pathways to reduce cravings and prevent return to use	*Pharmacologic extinction* - pairing alcohol use with naltrexone weakens alcohol-reward association	Blocks reward pathways during high-risk periods to reduce cravings or prevent use
Flexibility	Fixed daily dosing schedule	Allows flexibility and customization, taken only on days the patient has consumed alcohol	Allows flexibility and customization of dosing, only taken 1-3 days before high-risk situations

Protocol

- **Initial Assessment:** Assess current alcohol use and withdrawal risk. Patients at moderate/severe risk may not be suitable.
- **Customization:** Develop a personalized plan based on drinking habits and goals.
- **Dosing:** Start with naltrexone 50 mg PO on drinking days. Consider 25 mg for the first week to minimize side effects. Increase to 100 mg if response is inadequate.
- **Monitoring:** Regularly monitor for side effects and withdrawal symptoms. Consider outpatient management if mild withdrawal occurs (withdrawal infographic link). Refer to a higher level of care for more severe withdrawal. Modify protocol as needed based on response and patient goals.

Example Protocol (Day-by-Day Guide)

Day	Alcohol Use Goal	Naltrexone Use	Monitoring
0	Assess baseline alcohol volume	None	Evaluate for alcohol withdrawal risk
1-7	Reduce by 1 drink each drinking day	50 mg PO on drinking days	Monitor for alcohol withdrawal, side effects
8-14	Reduce by 2–3 drinks each drinking day	50 mg PO on drinking days	Monitor for alcohol withdrawal, side effects
15-21	Reduce by 3–5 drinks each drinking day	50 mg PO on drinking days	Assess response, modify regimen as needed
22-28	Consider further reduction or abstinence based on the patient's goal	50 mg PO on drinking days; consider increasing to 100 mg if inadequate response	Assess response, modify regimen as needed

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Efficacy and Research Findings

- High-quality evidence on the Sinclair Method is limited, **with no large randomized controlled trials to date.**
- Daily naltrexone has strong evidence from trials like the COMBINE study, a 16-week study of 952 participants with alcohol use disorder, which showed that daily naltrexone led to a higher percentage of abstinent days and a reduced risk of heavy alcohol use compared to placebo or medical management alone.

The Sinclair Method Summary

What?

The Sinclair Method is a structured, off-label protocol that uses naltrexone to support gradual alcohol reduction over time.

Who?

It may be beneficial for motivated, self-directed patients who want to reduce their alcohol use over time but may not be ready for full abstinence immediately.

How?

Naltrexone is taken only on drinking days (which could be daily), blocking the brain's reward response to alcohol and weakening alcohol's reinforcing effects over time.

Evidence

While the available evidence is limited, it suggests that the Sinclair Method may lead to meaningful reductions in alcohol consumption in select patients.

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