Scratch That Itch!

A retrospective audit on naltrexone for cholestatic pruritus in children

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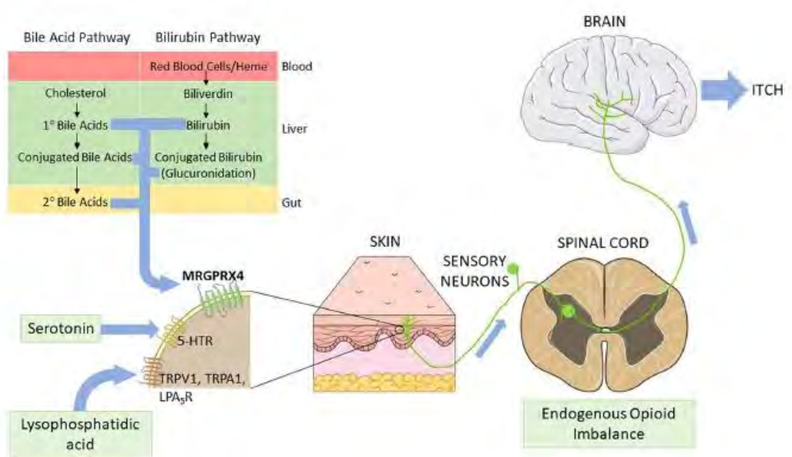
Background

- Cholestatic pruritus (CP) is caused by a reduction in bile flow.
- It is a debilitating condition that impacts children's quality of life by affecting their sleep, growth and function.[1,2]
- Current paediatric treatment options include ursodeoxycholic acid, rifampicin and cholestyramine. Their use is limited by unknown aetiology, adverse effects, non-specific action and conflicting efficacy. [2,4]
- Naltrexone may be proposed as an alternative treatment, considering its diverse use in adults and favourable safety and tolerability profile. [3,4]
- It is a competitive antagonist at the μ opioid receptor, which can decrease central opioidergic tone that is often raised in CP. [1,3]

Figure 1. Proposed itch pathways in cholestasis[4]



Aim

To conduct a retrospective audit of the efficacy, safety and dosing regimen of naltrexone for CP treatment at a tertiary paediatric hospital.

Method

An ethics application was submitted to Sydney Children's Hospital Network Human Research Ethics Committee (2023/ETH01529).

A comprehensive literature review on the use of naltrexone for CP in children was completed.

A retrospective review of medical records over 5 years (January 2018 to December 2022) for patients who used naltrexone for CP, was conducted.

Indication, dose, duration of treatment, adverse events and clinician notes were recorded.

Data was analysed and interpreted in consultation with gastroenterologist and clinical nurse consultants.

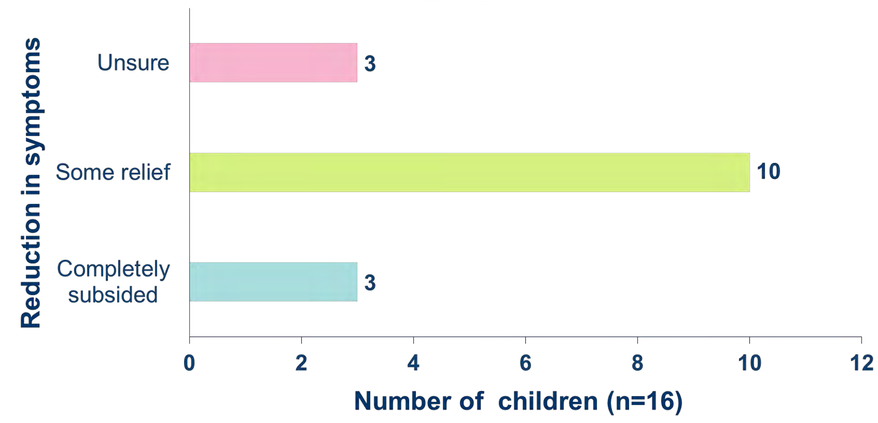
Results

Table 1. Indications for use of naltrexone

Indication for use	Number of patients (n=16)
Biliary atresia	8
Alagille syndrome	2
Progressive familial intrahepatic cholestasis type 3	2
Acute liver failure	1
Benign recurrent intrahepatic cholestasis	1
Jouberts syndrome	1
Liver transplant rejection	1

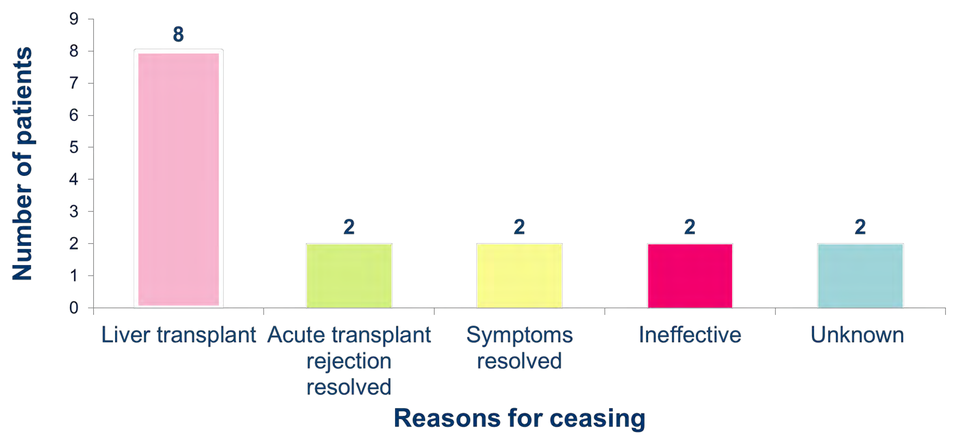
- 16 patients (n=10 female) were included in this study.
- Average age 5.3 years (range 0.4 to 15.5 years).
- All patients (n=16) had previously tried other medications:
  - Rifampicin (n=15)
  - Ursodeoxycholic acid (n=14)
  - Cholestyramine (n=2)
- The doses administered range: 0.25-1.95 mg/kg/DAY (12.5 mg to 50 mg/DAY).
- Naltrexone was shown to offer some relief in most patients (Figure 2).

Figure 2. Pruritus relief provided by naltrexone for CP



- Naltrexone was well tolerated: drowsiness (n=1).
- Treatment duration: median of 54 days (range 7 to 1234 days).
- No patients currently remain on naltrexone (Figure 3).

Figure 3. Reasons for ceasing naltrexone



- Medications trialled after naltrexone for CP relief include:
  - Cholestyramine (n=1)
  - Mirtazapine (n=1)
  - Odevixabat (n=1)
  - Ursodeoxycholic acid (n=1)

Conclusion

- Naltrexone was shown to be safe and effective to treat CP in children at a dose range of 0.25-2mg/kg/DAY, maximum 50 mg/DAY.
- Future studies should investigate long term safety and efficacy, particularly comparing naltrexone to newer treatments such as odevixabat.

References

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4. Vander Does, A., Levy, C., & Yosipovitch, G. (2022). Cholestatic Itch: Our Current Understanding of Pathophysiology and Treatments. American Journal of Clinical Dermatology, *23*(5), 647–659.

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