CHARACTERIZING IRRITABILITY IN KRABBE DISEASE: IMPLICATIONS FOR EARLY DIAGNOSIS AND TREATMENT DECISIONS

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KrabbeConnect CONNECTING PATIENTS & RESEARCH

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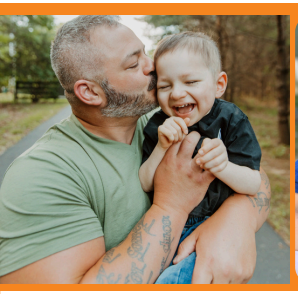
Introduction

- ***Krabbedisease*** is a rare and devastating condition; outcomes depend heavily on timing of stem cell transplant.
- Pre-symptomatic transplants typically result in better quality of life compared to late or no transplant.
- As partofthe grant *Caregiver-Reported Disease Burden in Infantile and Late Infantile Krabbe Disease: A Comparison of Quality-of-Life Outcomes in Transplant and Non- or Late-Transplant Patients* –a non-interventional, IRB-approved ObsRO*study–we collected:
  1. Caregiver-reported data on treatments, daily challenges, and quality-of-life impacts
  2. Specific insights on irritability, aiming to distinguish this symptom from common infant issues such as colic

*ObsRO Study – An Observer-Reported Outcomes study collects information from caregivers or others who observe the patient, especially when the patient is too young or unable to report.



Objectives

1. Characterizetheunique irritability seen in infants with IKD and determine whether it can be distinguished from common causes such as colic.
2. To explore whether distinguishing features can be identified, that are characteristics of KD using information from parents on the timing, severity, duration, alleviating/exacerbating factors, and behaviors associated with episodes of irritability in IKD infants.

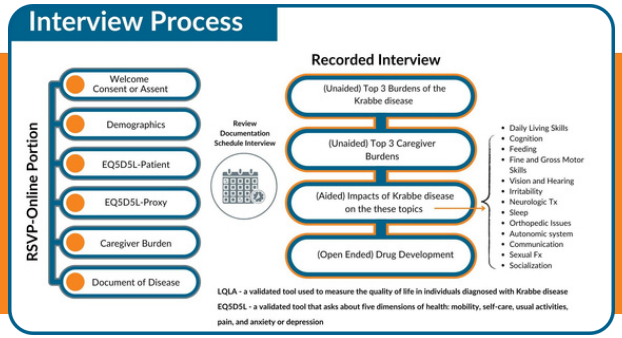
Methodology

01 Weconducted a non-interventional, IRB-approved ObsRO* study in collaboration with families impacted by Krabbe disease.

02 Engage Health developed the methodology, conducted interviews, managed and analyzed data, and delivered de-identified findings. A literature review of colic descriptions was also conducted and compared with caregiver-reported observations.

03 KrabbeConnect, United Leukodystrophy Foundation, and Partners for Krabbe Research promoted the study and assisted with recruitment

Interview Process



Comparison of Colic vs. Irritability

	Colic-ROME III Criteria (1)	Colic-ROME IV Criteria (1)	Roberts et al, 2003 (3)	PRO Burden in Infantile and LIKD; a Comparison of QOL in Transplant and Non-or-Late Transplant Patients
Age of Onset	Birth to 4 months	Birth to 5 months	Around 2 months	Varied, some at birth
Descriptor	Paroxysms of irritability, fussing or crying that stops and starts without obvious cuase	Recurrent and prolonged periods of fussing/crying/irritability which cannot be prevented or resolved by caregiver	Excessive crying, irritability or fussiness with "rule of 3" paroxysmal	Constant, inconsolable (48%) crying
Duration	3 or more hours per day	3 or more hour per day	More than 3 hours per day	Non-stop; 16 (64%) noted duration of hours to 10 hours or "constant"
Frequency	At least 3 days/week for at least 1 week	At least 3 days/week for at least 1 week	More than 3 days per week for more than 3 weeks	Constant until medicated; 16 (64%) noted more than 3 time per day, everyday
Other Associated Behaviors	-------	-------	Flushed face, furrowed brow, clenched fists, legs pulled up	Stiff muscle tone, shaking, seizure like
Description of Cry	-------	-------	Piercing, high pitched scream	40% noted as "screaming", distinct "neuro-cry"
Presence of Other Conditions	No FTT	No FTT, fever or illness	-------	Muscle tone issues
Resolution	First 6 months of life (2)	First 6 months of life (2)	By 4 months of age (3)	Unresolved until medicated
Overall Prevalence	10.4%	14.9%	5-25%	25 of 40 (62.5%) in our Krabbe disease patients, higher in non transplanted

Results

Prevelance

Patient Irritability Prevalence in Study Population- n=40

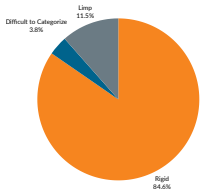
Age of Onset

IKD
Median: 3 months of age
Range: Birth to 10 months old

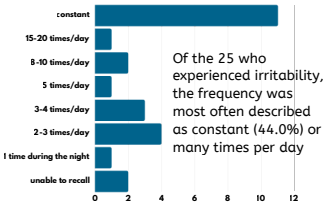
LIKD
Median: 2 years and 9 months
Range: 14 - 30 months

Tone Description

- "He would stiffen up and shake"
- "Very spasmatic, worked with him every day so his joints would work, 4-5 hours every day we'd do about an hour at a time and I would run with his legs and arms to get the movement, worked to make sure the comfortability was there"
- "Normal - except when he pushed his legs out but they wouldn't stay like that, at 5-6 months he would hold his arms in tighter and clench his fists"



Frequency



Of the 25 who experienced irritability, the frequency was most often described as constant (44.0%) or many times per day

Top Mentioned Medications

- Ativan (2 mentions)
- Baclofen (8 mentions)
- Gabapentin (10 mentions)
- Gripewater (2 mentions)
- G-tube (2 mentions)

Conclusion

- Irritability in early Krabbe disease can mimic colic, but red flags include a constant, high-pitched cry often paired with muscle stiffening.
- Collaboration with experts (Lawford, University of Queensland; Laguna) and AI tools to analyze cries may help detect distinctive patterns
- These patterns could serve as an early biomarker, supporting faster diagnosis
- This approach is especially valuable in regions without newborn screening for Krabbe disease

Challenges:

- Collecting cry recordings from families can be emotionally difficult
- Limited usefulness once patients are already diagnosed and treated
- There are irritability changes based on age and progression

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