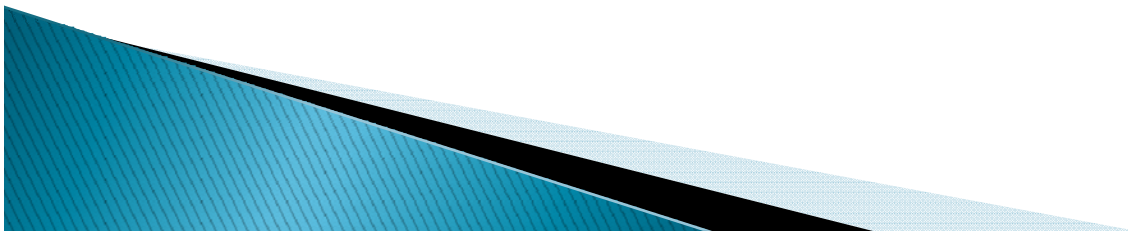


Is There Enough Evidence? Interventions Used to Manage Vaso-Occlusive Crises in Youth.

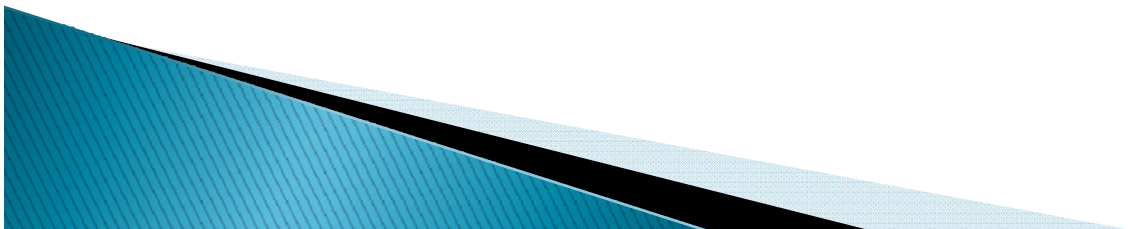
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May 29, 2009



Purpose of Study

To critically appraise research evidence on the effectiveness of pharmacological and non-pharmacological interventions to manage painful vaso-occlusive crises (VOC) in youth with sickle cell disease.



Presentation Overview

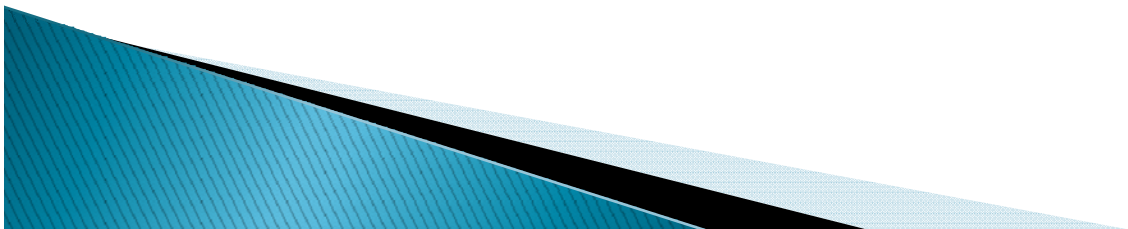
- ▶ Purpose
- ▶ Methods
- ▶ Results
- ▶ Discussion
- ▶ Future Directions
- ▶ Conclusions



Methods

Study Selection

- ▶ Peer-reviewed journal (1950–2009)
- ▶ Published in either English, Spanish or Portuguese
- ▶ RCTs
- ▶ School aged children (6–12 years) and/or adolescents (13–18 years) with sickle cell disease.



Methods

Review Process

- ▶ Two reviewers independently selected articles for review and assessed reporting quality.

Electronic searches

- ▶ EBM Reviews (Cochrane Central Register of Controlled Trials), Medline, EMBASE, CINAHL and PsychINFO.



Methods

Study Selection

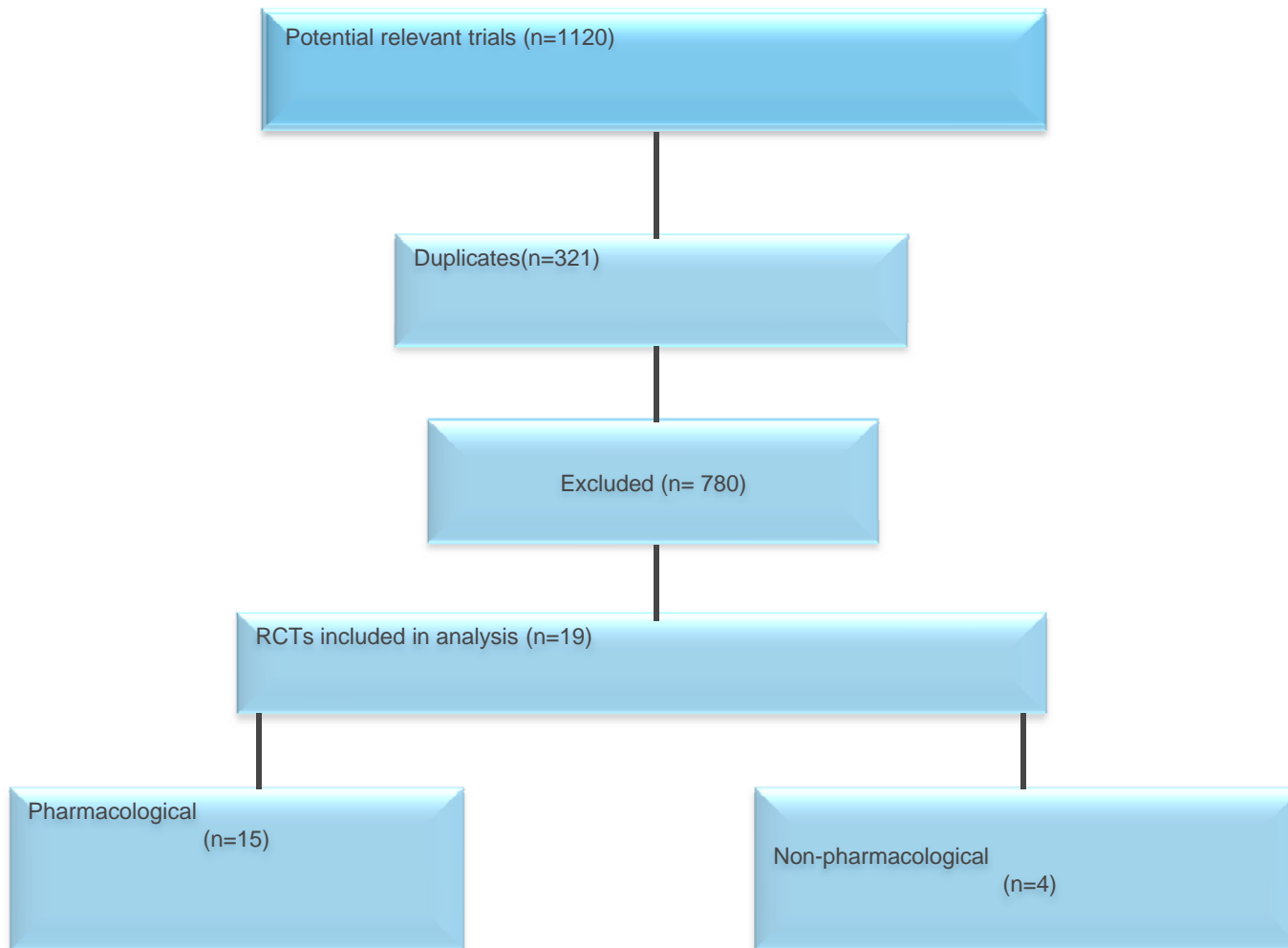
- ▶ Primary outcome → Pain due to VOC
- ▶ Pharmacological or non-pharmacological interventions.

Assessment of Quality

- ▶ CONSORT (Consolidated Standards of Reporting Trials)
 - Pharmacological RCTs → 22-items
 - Non-pharmacological RCTs → 23-items



Methods



Results

1. Quality of Reporting

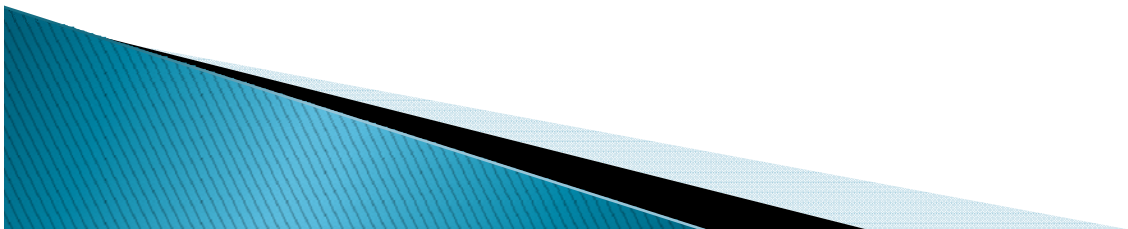
Pharmacological Studies

- ▶ Range → 9 to 19 items (14.9 ± 3.16)

Non-pharmacological Studies

- ▶ Range → 4 to 12 items (6.42 ± 3.58)

Overall pharmacological studies were scored from fair to adequate and non-pharmacological studies were scored from poor to fair.



Results

2. Pharmacological Interventions

Participants → 724 youth

Mean age → 11.10 ± 7.6 years

Gender → 47.3% males 52.7% females

(10 studies reported)

Pharmacologic interventions were divided:

a) To treat VOCs

b) To reduce the incidence of VOCs.



Pharmacological Interventions

Morphine

- ▶ Jacobson et al, 1997
 - Controlled release PO morphine versus continuous IV morphine.
 - IV Morphine (0.15 mg/kg) was given to the patients before randomization.
 - No significant difference in pain intensity, rate of analgesia, pain duration and discharge rate.

- ▶ Adawy et al, 2005
 - PCA Morphine + Ketorolac
 - PCA Morphine + Methylprednisolone
 - PCA Morphine + Saline solution
 - Pain scores and morphine requirements were significantly reduced in K and M groups compared with SS



Morphine

- ▶ Hardwick et al, 1999
 - Morphine + Ketorolac
 - Morphine + Placebo
 - No significant difference in pain severity and morphine requirements

Ketorolac


- ▶ Grisham et al, 1996
 - Ketorolac + standard analgesics
 - Meperidine + standard analgesics
 - Ketorolac provided significantly more pain relief than meperidine



Methylprednisolone

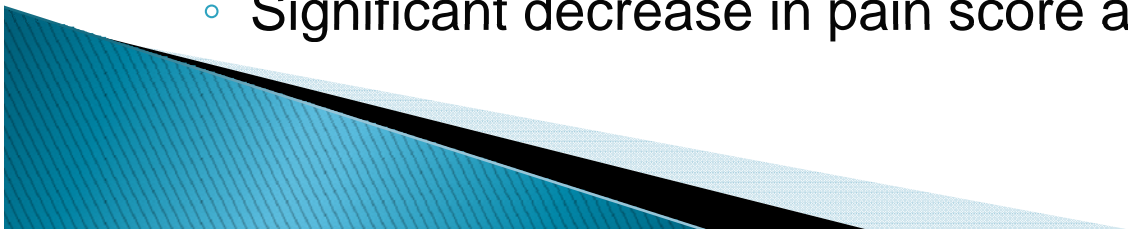
- ▶ Griffin et al, 1994
 - Methylprednisolone versus Saline placebo
 - No significant difference in CIV morphine and morphine injections
 - Significant difference in the duration of analgesic therapy
 - Methylprednisolone group → had recurrent episodes after discontinuing treatment

Poloxamer 188

- ▶ Orringer et al, 2001
 - Poloxamer 188 + IV or PO analgesics
 - Saline solution + IV or PO analgesics
 - There was significant effect in crisis resolution and duration of pain episodes in the P group
- 

Nitrogen and Oxygen

- ▶ Robieux et al, 1992
 - 50% oxygen + Morphine
 - Room air + Morphine
 - No significant difference in the duration of severe pain
- ▶ Zipurky et al, 1992
 - 50% oxygen-gas mixture + standard analgesics
 - Room air + standard analgesics
 - No significant difference between air and 50% oxygen in the duration of pain, opioid administration and hospitalization
- ▶ Weiner et al, 2003
 - Inhaled nitric oxide + Morphine
 - Room air + Morphine
 - Significant decrease in pain score and morphine consumption



Preventive Treatments

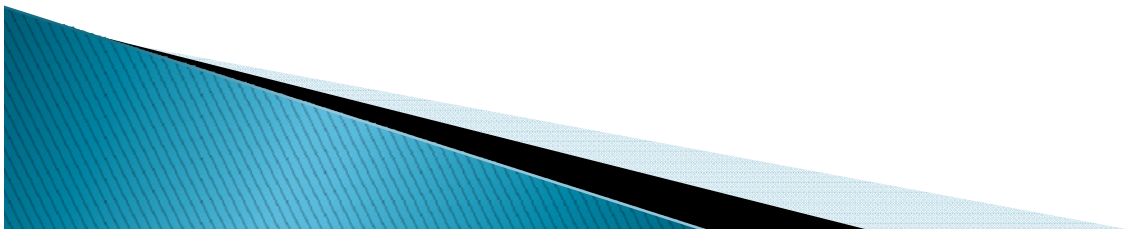
- ▶ Greenberg, et al, 1983
 - Aspirin versus placebo
 - There was no significant difference in frequency and severity of VOCs
- ▶ Ferster, et al, 1996
 - Hydroxyurea versus placebo
 - Significant decrease in the number of hospitalizations and the number of days in the hospital
- ▶ Miller, et al, 2001
 - Chronic transfusions versus standard care
 - There as a significant reduction in frequency of pain.



Piracetam

- ▶ Alvin et al, 2005
 - PO Piracetam versus placebo
 - No significant difference between groups
 - Not effective in preventing pain crises, pain intensity and days of hospitalization

- ▶ El-Hazmi, 1998
 - IV Piracetam (hospitalization) + PO Piracetam (home)
 - IV Placebo (hospitalization) + PO Placebo (home)
 - Clinical severity, number of pain crisis and days of hospitalization decrease significantly



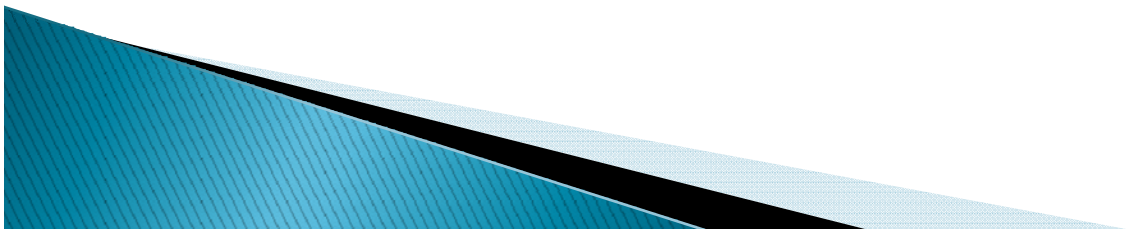
Results

3. Non-pharmacological Interventions

Participants → 281 youth

Mean age → 10.8 ± 6.9 years


Gender → 51% males 49% females



Cajanus cajan – Ciklavit

- ▶ Akinsulie et al, 2005
 - Ciklavit versus placebo
 - Significant reduction in the number of painful crisis in the C group.

Coping strategies

- ▶ Broome et al, 2001
 - Cognitive-behavioural techniques or Art Therapy versus Attention-control (fun activities)
 - Significant decrease in ER, clinic visits and hospitalizations over the time.
- 

Coping strategies

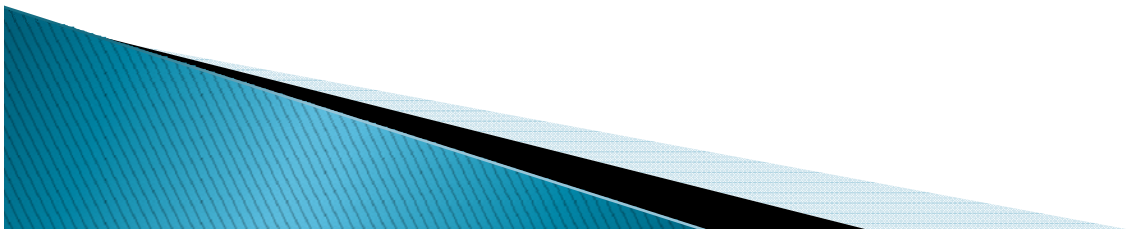
- ▶ Gil et al, 1997¹
 - Cognitive coping skills versus Routine medical care

- ▶ Gil et al, 2001²
 - 1 month follow-up of the intervention
 - Coping skills training increase coping attempts and decrease negative thinking
 - There was no significant difference in:
 - Pain sensitivity^{1,2}
 - Number of painful crises^{1,2}
 - Pain duration^{1,2}
 - Pain intensity^{1,2}
 - Health care use^{1,2}
 - Depression^{1,2}
 - Anxiety^{1,2}



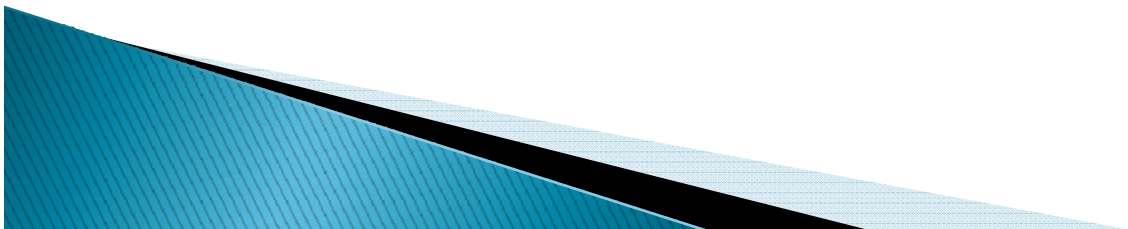
Discussion

- ▶ **Lack of reliable evidence** for the effectiveness of pharmacological and non-pharmacological interventions, confirmed by the small number of high quality studies retrieved for this review.
- ▶ **Morphine sulfate** is the most common treatment of VOCs and may be administered by several routes yet **few studies** in this review evaluated the use of morphine.



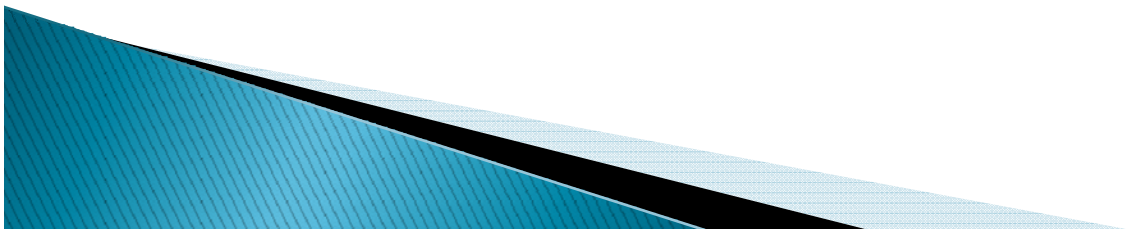
Discussion

- ▶ **Meperidine is no longer recommended** in the treatment of VOCs, the **potential toxicity** does not compensate the clinical benefit.
- ▶ A number of studies have evaluated the analgesic effect of **ketorolac** and its use is increasing in the ED. However, due to **lack of documented benefit** and **known toxicity**, the use of ketorolac in the treatment of SCD pain needs further evaluation.



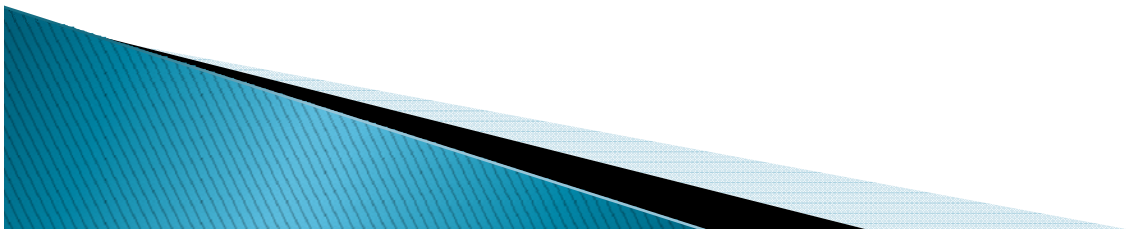
Discussion

- ▶ The effectiveness of inhalation **50% oxygen is not supported by the literature**; and the two RCTs included in this review failed to show any beneficial effect on the severity or duration of pain.
- ▶ **Hydroxyurea** has been shown **to be effective in preventing painful episodes**; more studies specifically in children and youth are needed.



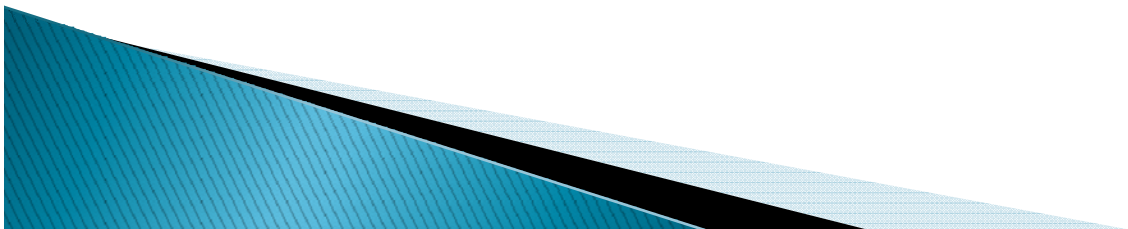
Discussion

- ▶ Guidelines **support the recommendation of a multimodal approach** to treatment involving individualized, evidence-based pharmacotherapy and self-management. **However**, the studies included in this review were **not sufficiently rigorous to provide evidence of the efficacy of psychological interventions** for sickle cell disease and pain.



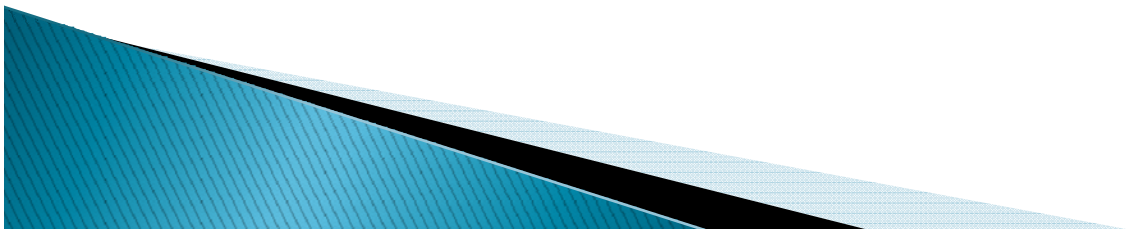
Future Directions

- I. High quality RCTs.
- II. Larger samples or multi-centered.
- III. Standardized outcome measures.
- IV. Research is needed approaching non-pharmacological interventions.



Conclusions

Limited evidence was found supporting the effectiveness of pharmacological and non-pharmacological interventions for painful VOCs in a paediatric population.



Acknowledgments

Sick Kids Hospital

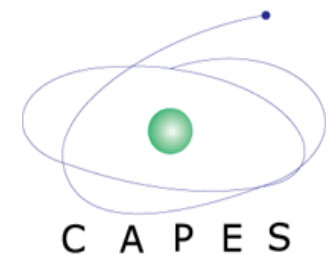
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THANK YOU !

