Implementing a Standardized Approach to Neonatal Herpes Simplex Virus

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Background

- Neonatal herpes simplex virus (HSV) infections are associated with high mortality and long-term morbidity
- Testing can lead to higher costs and longer length of hospital stay
- Acyclovir has risk of toxicity

Background

- Appropriate identification of who to test and empirically treat is challenging
  - Low incidence
  - Neonates can present with few to no symptoms
Hospital medicine and Emergency medicine: When do you test?

Skin vesicles
Seizure
Maternal history of genital herpes
Ill appearance
< 21 days
Hypothermia
Family history of herpes labialis
Rash
Scalp monitor used
Vaginal delivery
Respiratory distress

Table 1: Survey results to identify factors that prompt testing for herpes simplex virus in infants undergoing evaluation for serious infection

Hospital medicine and Emergency medicine: How do you test?

HSV CSF PCR
Liver enzymes levels
HSV surface swabs for PCR
DFA or PCR of vesicle scraping
HSV serum PCR
Serologic testing

Table 2: Survey results that identify typical laboratory evaluation for neonatal HSV
Abbreviations: Herpes simplex virus (HSV); Cerebrospinal fluid (CSF); Polymerase chain reaction (PCR); Direct fluorescent antibody (DFA)
Background

- Multidisciplinary team collaborated to develop an evidence-based care pathway regarding HSV
  - Hospital medicine
  - Emergency medicine
  - Infectious disease
  - Neonatology
  - Pharmacy

Care pathway
High risk factors: History and physical exam

- Maternal HSV symptoms within 7 days of delivery
- Household contacts with oral/cutaneous HSV present at any time since the infant's birth
- Apnea in a former term infant
- Hypothermia in a former term infant
- Poor perfusion
- Seizure, altered mental status, abnormal neurologic exam
- Vesicular or petechial rash
- Poorly healing scalp electrode site
- Excessive bleeding
Care pathway

Start: ≤28 days of age and undergoing evaluation for serious bacterial infection

High risk factors:
- Cerebrospinal fluid >19 white blood cells/high power field
- Cell count
- Differential <50% neutrophils
- Gram stain No organisms
- No acyclovir

Non-high risk

>28 days at low risk of perinatally-acquired HSV

Workup
- ≤21 days CSF PCR
- 22-≤28 days Hold CSF

CSF risk factors?
- Yes
- No acyclovir
- No

Workup
- ≥28 days
- Acyclovir 20mg/kg q8hours

High risk factors:
Cerebrospinal fluid
Care pathway

**High risk**
- Polymerase chain reaction (PCR) testing
  - CSF, serum, surface, lesion
  - Hepatic panel
  - Creatinine
  - Acyclovir

**Non-high risk**
- $\leq 21$ days: CSF PCR
- 22-28 days: Hold CSF
- No acyclovir

**SMART AIM**
- To increase the percentage of patients, 0-60 days, undergoing evaluation for serious infection, who are tested and treated for neonatal HSV in accordance with local guideline recommendations from 40% to 80%.
Secondary measures

• High risk:
  – % treated with acyclovir
  – % undergoing complete PCR evaluation
  – Length of stay

• Non-high risk
  – % treated with acyclovir
  – PCR test per 100 patients
  – Length of stay

• Delayed diagnosis of HSV

Key Drivers

- Increase the percentage of patients, 0-60 days, undergoing evaluation for serious infection, who are tested and treated in accordance with local guideline recommendations from 40% to 80% within 6 months
- Clear, evidence-based guidelines for HSV evaluation
- Guideline availability at point-of-care
- Accurate identification of patients at risk
- Provider buy-in for practice standardization
Percentage of patients receiving guideline-adherent management

1) Guideline development
2) Automated system to identify patients
• Real-time identification of eligible patients
  – <60 days with collected blood culture or CSF culture

Vigilanz™

Percentage of patients receiving guideline-adherent management

1) Education about guideline to frontline providers
2) Guideline available in workrooms
Percentage of patients receiving guideline-adherent management

Visible on screens in the ED

Neonatal HSV:
Who should be tested?
Who should be treated with acyclovir?

- HIGH RISK – TEST and BEGIN ACYCLOVIR
  - High risk on history/PE:
    - Meningitis (symptoms 3 days before or after delivery and/or household contact) with oral febrile illness present at any time since the infant’s birth
    - Apgar or hyperbilirubinemia (JCAHO) in infant at birth
    - Poor perfusion
    - Seizures, altered mental status, abnormal neurologic exams
    - Vascular or potential cutaneous, newly healing scalp/membranes site, excessive bleeding

- High risk based on CSF:
  - CSF WBC >5000/mm³ with negative Gram stain and <10% neutrophils
Percentage of patients receiving guideline-adherent management

1) Guideline development
2) Automated system to identify patients

Visual reminders of key points of guideline

1) Education about guideline to frontline providers
2) Guideline available in workrooms

Orderset modifications in EMR
2) Electronic guideline in ED

Data Range for Each Group of 10 Patients
- % Guideline Adherence per 10 patients
- Median
- Goal (6.0)

ED Orderset: SBI Evaluation

Patients 0-28 Days AND High Risk for HSV
- Patients 0-28 Days AND High Risk for HSV
  - Note: High risk factors from history/exam: Presence of maternal HSV symptoms 7 days before or after delivery, known household contact with oral/genital HSV, syrinx in term infant, poor nutrition, hypothermia in term infant, sepsis, abnormal mental status, abnormal neuromuscular examination, vulvar or perianal rash, purulent fluid or scalp erythema, exudative blepharitis
  - Viral culture: positive HSV culture on swab plus increased Tzanck prep

Patients 0-28 Days AND NOT High Risk for HSV
- Patients 0-28 Days AND NOT High Risk for HSV
  - Note: No high risk factors from history/exam

Medications (Patients Less than 28 Days AND High Risk for HSV)
- Nursing and Labs (Patients Less than 28 Days AND High Risk for HSV)
- Patients Greater than or Equal to 20 Days
  - Patients Greater than or Equal to 20 Days
ED Orderset: SBI Evaluation

Per CCHMC Guidelines, acyclovir should be empirically started for patients under 28 days who are high risk for HSV along with antibiotics.

- Sodium chloride (NS) 0.9% IV bolus infusion
- Acetaminophen (TYLENOL) 160mg/5mL suspension
- Ampicillin (OMNIPEN) intermittent infusion (age <= 7 days)
- Ampicillin (OMNIPEN) intermittent infusion (age > 7 days, meningitis)
- Gentamycin (GARAMYCIN) intermittent infusion (age < 30 days)
- Acyclovir (ZOVIRAX) intermittent infusion
- Cefazolin (CLARITIN) intermittent infusion
- Vancomycin (VANCOCIN) intermittent infusion

ED Orderset: SBI Evaluation

Per CCHMC Guidelines, acyclovir should NOT be empirically started for patients 0-28 days who are non-high risk for HSV.
ED Electronic Availability

1. Guideline development
2. Automated system to identify patients

1. Education about guideline to frontline providers
2. Guideline available in workrooms

Visual reminders of key points of guideline

1. Orderset modifications in EMR
2. Electronic guideline in ED

Start of new academic year: New providers
Percentage of patients receiving guideline-adherent management

1) Guideline development
2) Automated system to identify patients

1) Education about guideline to frontline providers
2) Guideline available in workrooms
3) Visual reminders of key points of guideline

1) Orderset modifications in EMR
2) Electronic guideline in ED

1) Resident re-education: new providers
2) ED re-education

Percentage of patients receiving guideline-adherent management

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1) Resident re-education: new providers
2) ED re-education

Introduction to ED nursing staff
Swab Guidelines

For all swabs: Can use red or green-topped Stuart culturette swabs

- For lesions/vesicles:
  - Unroof vesicle (if present) with sterile needle
  - Swab deepest portion of unroofed vesicle or lesion
  - Swab specimens should be submitted in a sterile culturette
  - Swab specimens should be labeled as to the specific site of the collection and the patient label

- For Surface swabs:
  - Swab conjunctiva (along lower lid), nares (can be one or both), mouth and rectum
  - Can use 1 swab (done in above order) or multiple swabs
  - Rotate or rub swab on mucosal surface
  - Swab specimens should be submitted in a sterile culturette
  - Swab specimens should be labeled as to the specific site of the collection and the patient label

Percentage of patients receiving guideline-adherent management

- % of patients receiving guideline-adherent management
- % Guideline Adherence per 10 patients
- Median
- Goal (60%)
- Date Range for Each Group of 10 Patients
- Resident Data
- ED Nursing Staff
Secondary outcomes

Conclusions

• We increased the percentage infants undergoing evaluation for serious infection who are tested and treated for neonatal HSV in accordance with local guideline recommendations from 40% to 80% within 8 months

• Increased complete evaluations

• Optimized acyclovir usage
Limitations

• Single center
  – Small number of HSV cases

• Person-dependent process

Next Steps

• Continue sustainability work with EMR changes on the inpatient side
• Continue to follow the performance of the care pathway
• Thank you to the members of the team
• Providers in the ED and inpatient setting

• Questions?