Benchmark Evidence Supporting Trials of Treatment in Pediatric Populations (BEST TRIP-Peds)

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Structure

- Phase III multi-center randomized clinical trial using a 2 group parallel design

Purpose

- To test the effect on outcomes of management of severe TBI in children ages 1-12 guided by information from ICP monitors vs. management using a protocol that uses imaging and clinical exams to guide treatment.
- To determine if management based on monitoring ICP reduces complications, decreases brain-specific treatments and decreases ICU length of stay.

Study Status

- NINDS U01 application to be submitted in February, 2018

Protocol
Inclusion /exclusion criteria

- **Inclusion Criteria**
  - Admission to study hospital within 24 hours of injury
  - Closed head trauma
  - Glasgow Coma Scale score (GCS) ≤ 8 on admission or within first 48 hours after injury (modified GCS for children under 2)
  - Age 1 to 12 years
  - Randomized:
    - within 24 hours of injury [for patients with GCS ≤ 8 on admission] or
    - within 24 hours of deterioration [patients deteriorating to GCS ≤ 8 within 48 hours of injury]
- **Exclusion Criteria**
  - GCS of 3 with bilateral fixed and dilated pupils
  - Injury intentionally inflicted by a family member or caregiver.
  - No consent

Protocol
ICP group management

- Based on BTF pediatric guidelines (revised to take newer results into account, e.g. ADAPT)

Protocol
Imaging and clinical exam management

- Based on adult protocol developed by a consensus method for the current observational study.
- Revised for children by Dr. Moya with input from others

Protocol
Finalization

- Meeting in the first few months of funding to revise the protocol for both arms.
- Consensus process similar to that used to develop the adult protocol currently being tested.
- Most of the participants, not all, will be from study sites

International aspects
Advantages

- Enthusiastic colleagues, happy to participate in an effort that may change practice, appreciative of respect shown for their expertise
- Dedicated, resourceful staff
- Excellent basic ICU care
- Willingness to randomize

International aspects
Advantages

- Data quality was good (with initial close oversight and frequent boosters)
- Sites without competing studies
- Capitated funding was acceptable

International aspects
Advantages

- Lower cost
- Funding for a NINDS-quality trial was easy to get through Fogarty International Center

International aspects
Disadvantages

- First participation in research for most site PIs
  - Had to get FWA for ethics committees, had to teach about informed consent, interrater reliability, exactly following instructions, …
- Need for much training and oversight
  - Monitoring/retraining visits every 2-3 patients initially; Spanish-speaking resident sent to every site to train on how the study wanted the monitors placed and used

International aspects
Disadvantages

- Language barrier
  - Misunderstandings
  - Translation both ways
    - Simultaneous translation for all-team meetings
    - Protocols, consent forms, letters of support
  - Indigenous languages

International aspects
Disadvantages

- Cultural issues
  - Importance of personal relationships
  - 'Si pero no'
  - Timeliness, speed
    - CTs broken for months
    - Running out of medications
    - Long turnaround from colleagues, sites
    - Timed neuropsych tests

International aspects
Disadvantages

- Cultural issues
  - Families pay for medication, CTs
  - Paying participants=coercion
  - Not everyone has a phone—or an address
  - Trails, not paved roads
  - Political unrest

International aspects
Disadvantages

- Fiscal Issues
  - Fogarty $500,000 annual max
    - NINDS 18-20% across-the-board cut
  - Paying sites
  - Wire transfers
    - Lost
    - Taking weeks
  - Argentina 20% tax on money leaving the country

International aspects
Disadvantages

- Government issues
  - No distribution network for catheters
  - Customs delays, fees
  - Changing health landscape
    - 4 Ministers of Health in 1 year
    - SOAT

Opportunities for InTBIR

- Companion trial in high income countries
- Replication of CER studies in different environment

Obstacles for InTBIR

- Unclear how regular reviewers/funders will view studies in middle income countries
- Steep learning curve

Thank you

- Questions?