History of Fluid Therapy in Newborn Medicine

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Relevant financial relationships
-Nothing to disclose

FDA
-Nothing to disclose
Objectives

• Describe fluid therapy in the past

• Discuss technical and conceptual advances that led to current state of the arts in fluid therapy

• List gaps of knowledge in implementing fluid therapy, particularly with reference to very low birth weight infants
Historical Notes

- In the 18th and 19th centuries, fluid therapy for sick newborns was virtually non-existent.

- Quality of care for the newborn was primitive, resulting in high infant mortality rate.

- Infant mortality rate was quoted as 290/1,000 live birth.
Historical Notes

• Priority was to improve survival and the focus was on thermo-regulation

• Notable individuals (French obstetricians):
  – Stephane Tarnier
  – Pierre Budin
  – Martin Couney
French Obstetricians Pioneers for Newborn Care

Stephane Tarnier
- Invented Incubator

Pierre Budin
- Incubator for premie
- Sent Couney to Berlin

Martin Couney,
- Incubator sideshow in Berlin world Fair
- Later came to U.S to continue the Show with live premature
Martin Couney

- He charged a quarter pp to see the exhibits – considerable controversy on the financial aspect

- Exhibited the incubators (with the babies) in 22 World Fairs (1901-1945) including Coney Island, NY, Buffalo, Philadelphia, Louisiana, San Francisco, Chicago

- The public display popularized the use of incubator for premature resulting in improved survival rates
U.S. Infant & Neonatal Mortality Rate

Per Thousand Live births

Incubator show started in 1901

Adapted from Wegman ME Pediatrics, 1985, 76:861
Advent of Fluid Therapy

- Improved survival of premature infants necessitated the use of parenteral fluid administration particularly for those who could not tolerate enteral feeding

- The approach was primitive for lack of physiological rationale and technical resource
Nasal spoon for feeding premature infants
Subcutaneous Fluid Administration

25 cc syringe with saline

Intrascapular injection
The Usher Needle
Percutaneous Intravascular Central Catheter
Physiologic Basis

• Technology is extremely important

• However, optimal fluid and electrolyte therapy needs evidence based physiologic concepts

• Many advances were achieved in the past several decades
The Pioneers in Pediatric

• In the 30’s-50’s, Dr. James L Gambles and several colleagues at Harvard, including Drs. William Wallace, Malcolm Holliday and Jack Metcoff

• Performed a series of investigations that set the foundation of fluid and electrolyte therapy in Pediatrics
Neonatal Pioneer

• Dr. Clement A Smith: One of the pioneers in Neonatology in the U.S

• His Textbook ‘Physiology of Newborns’ (1945) established many of the basic physiologic concepts of neonatal care

• On fluid balance, he stated that newborns have abundant of fluid content, thus, “minimal fluid intake should be given in the first day of life”
Issues in Neonatal Fluid Therapy

• Insensible water loss

• Transitional changes in body fluid compartments during the first week

• Lack of transition: its effects on clinical outcomes

• Conditions that present challenges to fluid therapy
Maintenance Fluid Requirement

- Insensible water loss
- Water for renal excretion
- Stool losses
- Allowance for growth
Insensible Water Loss

Increases

- Lower maturity
- Phototherapy and warmer
- Ambient temperature above neutral thermal zone
- Skin defect e.g. omphalocele

Decreases

- Increasing postnatal age
- Higher relative humidity
  - Use of Giraffe incubator
  - On ventilator with warmed humidified air (30% reduction, no respiratory IWL)
Transitional changes in body fluid

• Contraction of extracellular fluid compartment occurs universally during the first week

• Amount of reduction in ECF is inversely proportional to gestational age

• Mechanism is unknown

• Contraction of ECF is associated with
  – Diuresis
  – Negative sodium balance
  – Postnatal weight loss

• Degree of contraction is affected by fluid intake
High VS Low Fluid Intake in VLBW infants

• 170 infants 750-2000 g were randomized into high and low fluid intake groups to assess the effect on the incidence of symptomatic PDA

• High fluid (n=84) received an average of 165 cc/kg/day

• Low fluid (n=85) received an average of 120 cc/kg/day

• Primary outcome: Symptomatic PDA

• Secondary outcome: NEC

## Results

<table>
<thead>
<tr>
<th>Group</th>
<th>Gestation</th>
<th>Birth weight</th>
<th>PDA</th>
<th>NEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>High N=85</td>
<td>31.4 ± 2.4 wk</td>
<td>1422 ±340 g</td>
<td>35 (41%)</td>
<td>8 (9.4%)</td>
</tr>
<tr>
<td>Low N=85</td>
<td>31.5 ± 2.2 wk</td>
<td>1435 ±333 g</td>
<td>9 (10.6%)</td>
<td>1 (1.2%)</td>
</tr>
</tbody>
</table>

P value: n.s. n.s <0.001 0.03
Ancillary Study to Demonstrate Effect of High Fluid Intake on Transitional Changes in ECF

• In a subset of infants in the RCT

• Inulin space was determined using standard indicator dilution technique

• Measurements done on day 2 and repeated on day 8

Stonesstreet, BS  AJDC 137:215,1983
Changes in ECF (Inulin Space) and Effect of High Fluid Intake

Stonestreet, BS, AJDC, 137:215, 1983
Weight Loss from Birth

Stonestreet, BS AJDC 137:215, 1983

Fluid intake (ml/kg/day)
- 126
- 162

--P<.05--
Postnatal Diuresis in VLBW infants

(Bidiwala, Pediatrics, 1988)

Fetal maturation and renal function

**Fractional sodium excretion (%) filtered Na**

![Graph showing fractional sodium excretion over gestation weeks](image)

- $r = 0.755$
- $p < 0.001$

**Urinary sodium excretion (μEq/Kg/Hr)**

![Graph showing urinary sodium excretion over gestation weeks](image)
Summary of Transitional Changes during the first week in VLBW Infant

- Contraction of approximately 10-15% of ECF
- Removal of the isotonic ECF via kidney
- Accounting for diuresis with high urinary sodium excretion (natiuresis) and postnatal weight loss
- Fluid overload impairs transition with higher incidence of PDA and NEC
- What about the effect on the incidence of BPD
Fluid intake and BPD(O₂ dependent @ 28 days)-a Case Control Study

VAN MARTER, LJJ  PEDIATR 1990 116:942
Association of high fluid Intake Less Postnatal Wt Loss & BPD

• Secondary analysis of Neonatal Research Network Glutamine trial

• N=1378 ELBW infants

• BPD defined as oxygen dependence at 36 wk completed postmenstrual age

Oh, W et al J. Pediatr 2005147:786-90
Parenteral Fluid Intake and BPD

All differences $p < 0.05$

Oh, W. et al. J Pediatr 147:786, 2005
Weight loss and BPD

% of birth weight

P <0.05 on day 4-10
Postnatal Weight Loss and BPD

• Retrospective analysis of Neonatal Research Network data base

• To establish association between postnatal weight loss and BPD

• Logistic regression analysis to obtained adjusted odds ratio

Postnatal Weight Loss and BPD

Death or BPD

No postnatal Weight Loss
Birth weight
Outborn
Postnatal Steroid
Antenatal antibiotics
How about sodium Intake during the first days of life, Does it affect the fluid balance and incidence of BPD?
Effects of Sodium Intake and BPD

- RCT involving 46 infants between 25-28 weeks gestation

- Group 1 Na Supplemented on day 2 n=24

- Group 2 Na Supplemented when weight loss is > 6% Or on day 6 of life n=22

- Fluid intake was similar

HARTNOLL G. ET AL: ARCH DIS CHILD 82: F19,2000
Results

Maximum weight loss ( % )

Na Supplementation

--- P<0.05 ---
Results - 2

% of infants requiring oxygen

P < .02

Day 7

Day 28

36 WK

Early

Late
Lack of Physiologic Transition & BPD

• Data suggest an association of excessive fluid and sodium intake and BPD

• There is no single magic bullet for prevention of BPD; fluid and Na restriction may be one of several bullets

• An important practical approach is to monitor daily weight change using a standard weight chart
Other Challenging Issues

• Birth weight or current weight in fluid calculation

• Managing infants with acute renal failure

• Infants with third ‘spacing’
Birth Weight or Current Weight

• No data to support either choice

• Physiologic consideration suggests that we use current weight
  – Water requirement is metabolism dependent
  – Using birth weight in an infant who has postnatal weight loss may overestimate water requirement of up to 10-15% of what is needed
Infants with Acute Renal Failure

• Problem is particularly challenging in full term infant with perinatal asphyxia and acute tubular necrosis

• Lack of urine output reduces the maintenance fluid requirement

• Inability to provide adequate calories because of fluid limitation

• The good news:
  – Renal failure often transient
  – Full term infant has larger energy reserve
  – Using radiant warmer may help increase fluid intake because of higher IWL
Infants with Third ‘Spacing’

- Management is not evidence based
- Physiologically, third space fluid adds weight but not participating in metabolism
- Using actual weight would over estimate the fluid volume
- Use weight prior to onset of third spacing and aim at maintaining circulatory integrity
Gaps of Knowledge in Fluid Therapy: Opportunity for Research

• Mechanism of transitional changes in body fluid during the first week

• Confirmation of conservative fluid and sodium during the transitional period

• Basis for use of weight in fluid and electrolyte calculation (third spacing, current or birth weight etc.)
Summary

• We have come a long way in fluid therapy particularly with very low birth weight infant

• Availability of technological advances and physiological concepts along with expertise of staff, particularly nursing allow us to deliver appropriate fluid therapy

• There are still gaps of knowledge that need future research
THANK YOU