Neurodevelopmental Outcomes of FICare & FICare Cases of Intubated Infants

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There is no Conflicts of Interests.
2015, in Hunan province:
• Total population is 633 million (urban population 50.89%)
• Birth rate is 13.58 ‰
• Mortality rate is 6.86 ‰
• Number of NICUs with bed No. > 40 is 20

- 2015 Government White Book of Economy & Social Development of Hunan
The capital city of Hunan: Changsha

2015:
• Birth rate: 10.09‰
• Mortality rate under 5 years old: 4.77‰
• Mortality rate under 1 years old: 2.88‰
• Neonatal mortality rate: 1.57‰

- 2015 Statistic Data from Department of Maternity & Child Health of Hunan
A Neurodevelopmental Study

FiCare Cases of Intubated Infants
A Neurodevelopmental Study
Title of Initial FICare study in China: Impact and Cost-effectiveness of the Family Integrated Care Model on the Outcomes of Stable Preterm newborns in Intensive Care Units (NICUs) in China: A Cluster Randomized Controlled Trial.

(Funds: CIHR CTP87518, CMB OC 13-162)
Inclusion Criteria

1. GA 28 weeks~35 weeks; and
2. Have been receiving enteral feeds for >24 hours; and
3. Have vital signs been stable for >24 hours.
Exclusion Criteria

1. Require either invasive or non-invasive ventilation support;
2. Require surgical intervention(s);
3. Are receiving palliative care;
4. Are likely to be discharged within 1wk;
5. Weigh less than 400 g at birth;
6. Parents have language barrier; and/or
7. Parents do not sign the consent form.
Both Moms and Babies are doing great!
Working hours (upper) and Limited visiting hours (lower) in most NICUs in China
Let parents stay in the NICU and integrate them into the team.
Fig 1. NBNA score @ CGA 37wk
Peri- FiCare studies and funds

- **CMB OC 13-162**
  - **USD 135,000**

- **CCNCRP (2014/2015/2016)**
  - **RMB 60,000**
    - To do Baylay at 18M of age.

- **CIHR CTR87518 (2014)**
  - **RMB 60,000**
    - To do aEEG study.
  - **CAD 20,000**
    - Infant-care Team.

- **RMB 100,000**
  - To expand centers from 6 to 10.

Adelaide, Mingyan Hei, China
Human neurodevelopment is closely related to the maturity of brain, which happens in the last 4~6 weeks of the gestation.

-- Kinney HC et al. Semin Perinatol, 2006, 30 (2): 81-88
The objective of this study was to understand the neurodevelopment of FICare infants at 18M of age.
Methods

• A prospective parallel case-control study.
• Study period: July 2015 ~ July 2016.
• Venue: Department of Child Healthcare in the Third Xiangya Hospital of Central South University.
• FICare group: preterm infants enrolled in previous FICare study with gestational age (GA) 28-35wks.

• Control group: preterm infants matched with gender, birth weight (BW), BW percentile and days of life (DOL) at follow-up (1:1 ratio) who did not enter FICare in NICU.
No. of FICare infants met inclusion criteria, n = 100

Excluded No. of infants, n= 33
- Parents refuse to sing on the consent, n = 14
- Died before 18M of age, n = 0
- Hospitalization within 2 weeks before 18M of age, n = 4
- Expected not to be discharged from hospital within 2 weeks at 18M of age, n = 2
- Lost of contact with the parents, n = 11
- Delayed BSID for more than 2 weeks d/t unknown reasons, n = 2

No. of FICare infants enrolled n = 67

Non FICare infants matched with gender, birth weight (BW), BW percentile and days of life (DOL) at follow-up (1:1 ratio)

Final sample size n=134
(n=67 in each of FICare and Control group)

Figure 1. Protocol of patient enrollment
• Parameters:
  • Demographic data: GA, BW, gender, wt@18M etc.
  • Family and parent background:
    • Maternal education year
    • Socioeconomic Status (SES), by Graffar method
    • Home Observation for Measurement of the Environment (HOME)
  • Mental Development Index (MDI) and Psychomotor Development Index (PDI) by Bayley Scales of Infant Development (BSID).
• Statistical Analysis
  • SPSS 20.0
  • chi-square test, $t$ test, Pearson coefficient test and Spearman coefficient
<table>
<thead>
<tr>
<th></th>
<th>FICare (n=67)</th>
<th>Control (n=67)</th>
<th>(X^2/t)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n(%)</td>
<td>35(52)</td>
<td>34(51)</td>
<td>0.030</td>
<td>0.863</td>
</tr>
<tr>
<td>GA, wk</td>
<td>32.4±1.7</td>
<td>32.2±1.6</td>
<td>0.744</td>
<td>0.458</td>
</tr>
<tr>
<td>BW, g</td>
<td>1690±415</td>
<td>1719±412</td>
<td>-0.390</td>
<td>0.697</td>
</tr>
<tr>
<td>SGA, n (%)</td>
<td>5(8)</td>
<td>6(9)</td>
<td>0.099</td>
<td>0.753</td>
</tr>
<tr>
<td>Apgar&lt;7@5min, n(%)</td>
<td>2 (3)</td>
<td>1 (2)</td>
<td>0.000</td>
<td>1.000</td>
</tr>
<tr>
<td>C/S born, n(%)</td>
<td>27(40)</td>
<td>29(43)</td>
<td>0.123</td>
<td>0.726</td>
</tr>
<tr>
<td>PPROM&gt; 18h, n(%)</td>
<td>28(42)</td>
<td>18(26)</td>
<td>3.310</td>
<td>0.069</td>
</tr>
<tr>
<td>RDS</td>
<td>38(57)</td>
<td>33(49)</td>
<td>0.749</td>
<td>0.387</td>
</tr>
<tr>
<td>Suspected/ Sepsis</td>
<td>34(51)</td>
<td>29(43)</td>
<td>0.749</td>
<td>0.387</td>
</tr>
<tr>
<td>Asphyxia</td>
<td>14(21)</td>
<td>11(16)</td>
<td>0.443</td>
<td>0.506</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>11(16)</td>
<td>13(19)</td>
<td>0.203</td>
<td>0.652</td>
</tr>
<tr>
<td>Intubated &gt;72h, n(%)</td>
<td>9(13)</td>
<td>8(12)</td>
<td>0.067</td>
<td>0.795</td>
</tr>
<tr>
<td>NCPAP&gt;1wk, n(%)</td>
<td>8(12)</td>
<td>9(13)</td>
<td>0.067</td>
<td>0.795</td>
</tr>
</tbody>
</table>

**Table 1. Demographic & Clinical Data**
<table>
<thead>
<tr>
<th>Maternal Dis</th>
<th>FICare (n=67)</th>
<th>Control (n=67)</th>
<th>$X^2/t$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>11(16)</td>
<td>12(18)</td>
<td>0.052</td>
<td>0.819</td>
</tr>
<tr>
<td>GDM</td>
<td>4(6)</td>
<td>7(10)</td>
<td>0.891</td>
<td>0.345</td>
</tr>
<tr>
<td>Thyroid Dis</td>
<td>2(3)</td>
<td>4(6)</td>
<td>0.174</td>
<td>0.676</td>
</tr>
<tr>
<td>Maternal Education Yr, yr</td>
<td>15±2</td>
<td>15±2</td>
<td>0.379</td>
<td>0.705</td>
</tr>
<tr>
<td>SES</td>
<td>42±6</td>
<td>41±6</td>
<td>1.567</td>
<td>0.119</td>
</tr>
<tr>
<td>HOME</td>
<td>31±5</td>
<td>32±5</td>
<td>-0.072</td>
<td>0.943</td>
</tr>
</tbody>
</table>

**Table 2. Maternal & Family Data**
<table>
<thead>
<tr>
<th></th>
<th>FICare (n=67)</th>
<th>Control (n=67)</th>
<th>$X^2/t$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOL @ BSID, d</td>
<td>545±5</td>
<td>545±5</td>
<td>0.306</td>
<td>0.760</td>
</tr>
<tr>
<td>Wt @ BSID, kg</td>
<td>10±1</td>
<td>10±1</td>
<td>0.798</td>
<td>0.426</td>
</tr>
<tr>
<td>MDI</td>
<td>95 ± 9</td>
<td>86 ± 9</td>
<td>5.506</td>
<td>0.000</td>
</tr>
<tr>
<td>PDI</td>
<td>87 ± 9</td>
<td>80 ± 8</td>
<td>4.502</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 3. MDI & PDI at 18M of age
<table>
<thead>
<tr>
<th>GA</th>
<th>n</th>
<th>MDI FICare</th>
<th>MDI Control</th>
<th>PDI FICare</th>
<th>PDI Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>28~29</td>
<td>14</td>
<td>85.4</td>
<td>81.9</td>
<td>81.3</td>
<td>76.1</td>
</tr>
<tr>
<td>~30</td>
<td>10</td>
<td>80.4</td>
<td>77.4</td>
<td>80.2</td>
<td>71.6</td>
</tr>
<tr>
<td>~31</td>
<td>12</td>
<td>87.7</td>
<td>76.5</td>
<td>83.8</td>
<td>71.3</td>
</tr>
<tr>
<td>~32</td>
<td>42</td>
<td>96.7</td>
<td>91.3</td>
<td>89.1</td>
<td>85.1</td>
</tr>
<tr>
<td>~33</td>
<td>28</td>
<td>99.0</td>
<td>86.3</td>
<td>88.4</td>
<td>80.8</td>
</tr>
<tr>
<td>~34</td>
<td>20</td>
<td>99.2</td>
<td>85.6</td>
<td>87.5</td>
<td>79.2</td>
</tr>
<tr>
<td>~35</td>
<td>8</td>
<td>100.0</td>
<td>92.3</td>
<td>90.8</td>
<td>87.3</td>
</tr>
</tbody>
</table>

Table 4 MDI & PDI difference between 2 groups

The MDI and PDI of all groups were positively related to GA ($r=0.398$, $P=0.000$, $r=0.272$, $P=0.001$), but the difference between 2 groups was not related to GA ($r=0.679$, $P=0.094$; $r=-0.393$, $P=0.383$).
Baby FuYi, GA 33wk6d, BW 1730g. Now 2yr5m old. Her Mom had hysterectomy d/t HPT.
Baby GeeGee, GA 30wk1d, BW 1010g. SGA. Now 2yr 4mon. Very naughty, active & talkative.

Baby TingTing, GA 29wk1d, BW 1100g. Had huge feeding problems + apnea + corpus callosum displasia. Now 2yr 4mon. Healthy and happy.
About BSID

• It fits for infants between 2~30M of age.
• Totally 244 items (81 items for MDI, 163 for PDI).
• The 1st choice for assessing the pre- and post-development of infants.

-- Bayley N. Child Dev., 1965, 36: 379-411
• Control infants were matched with FICare infants only by GA, BW, and BW-GA percentile. Not by disease. -- Variation issue. – To do hierarchy (subgrouping).

• The difference between 2 groups was not related to GA, indicating that we cannot say “The smaller the infants, the better effect the FICare”.
Why not cluster randomization

• Loss of follow-up!

<table>
<thead>
<tr>
<th>Site</th>
<th>FICare</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site 1</td>
<td>67.1%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Site 2</td>
<td>23.5%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Site 3</td>
<td>&lt;5%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Site 4</td>
<td>17.9%</td>
<td>21.6%</td>
</tr>
<tr>
<td>Site 5</td>
<td>&lt;5%</td>
<td>(late joined in)</td>
</tr>
<tr>
<td>Site 6</td>
<td>(late joined in)</td>
<td>/</td>
</tr>
</tbody>
</table>

Table 5. Followup rate in each center at 18M
Reasons for the lose of follow-up

• Parents did not agree to sign the consent.
• Infants were in hospitalization within 2 weeks peri-18M of age.
• Loss of contact with the parents.
• Parents considered it to be too troublesome to go to the hospital for follow-up (currently living in other cities).
• Parents consider their infants very good and just did not want to go for the follow-up.
<table>
<thead>
<tr>
<th>City</th>
<th>Age @ F/U</th>
<th>F/U Method</th>
<th>Rate of F/U</th>
<th>Ref &amp; year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shenzhen</td>
<td>18M &amp; 24M</td>
<td>Phone call</td>
<td>81.5% &amp; 49.2%</td>
<td>Wei Z et al. 2012</td>
</tr>
<tr>
<td>Beijing</td>
<td>18M</td>
<td>Community &amp; Home visit</td>
<td>66.7% &amp; 83.1%</td>
<td>Zhou WJ et al, 2013</td>
</tr>
<tr>
<td>Shanghai</td>
<td>18M</td>
<td>Home visit</td>
<td>75.2%</td>
<td>Ma JQ. 2015</td>
</tr>
</tbody>
</table>

-- Ma JQ. J Shanghai Community Univ., 2015
About the SES & HOME in this study

<table>
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• The family is at middle-upper level of Chinese society.
• HOME indicates generally stable and typical family structures in China.
About SES by Graffar method

• Total score: 45
• Parameters: No. of family members, parent marriage status, the highest education degree of parents, parents’ employment status, self-own house or rental house, house area, running water status, rental or self-own furniture, self-assessment of crowdness of the house.
• The average SES in China is ~32.

-- Shu M. City, 2008, 155(6): 46-50
About HOME score

• Total score: 65
• For assessing the influence of mood, social activity, behavior of parents to the infants.
• Parameters: 45 items in 5 regimens (parental responsibility, parents’ self-regulation, house tidiness and maintenance, family study atmosphere, diversity of parent’s knowledge.
• The HOME in China is 30~36.

Neurodevelopmental outcomes at 18M of age for FICare infants is quite positive!
FICare Cases of Intubated Infants
1. Venue: Preterm NCIU of Hunan Children’s Hospital (Director is Dr. Xirong Gao, Chief nurse is Ms Yue-E Xiong)

2. Total No. of FlCare cases: 141
   (1) Enrolled in the previous multicenter RCT trail: 47
   (2) Further excluded: 28 (21 with GA <28wk, and 7 with GA > 35wk)
   (3) Extension of FlCare: 21 intubated infants and 45 NCPAP infants.
Case 1

1. ID 484315, male, GA:27+1w, BW:900g
2. C/S born in a municipal hospital with Apgar 1’-8, 5’-9, and transferred on DOL06
3. Discharge Diagnosis:
   1. ELBW (GA27+1 wks)
   2. NRDS
   3. BPD
   4. ROP (stage II)
   5. Sepsis (clinical diagnosis)
   6. Anemia of Prematurity
Respiratory support (for 143 days):

- SIMV (65 days)
- HFOV (4 days)
- NIPPV (21 days)
- nCPAP (10 days)
- Nasal catheter oxygen (43 days)
• Started FICare on DOL60 (on SIMV) & total FICare 95d;
• Discharge wt 4660g & feeding @ 80ml q3h (137ml/lg/d)
Case 2

1. ID 482053, M, GA 24w3d, BW 1100g, Apgar 1’-3, 5’-6, 10 ’-7
2. Transferred on DOL 21d
3. Discharge Diagnosis :
   1. ELBW (GA 24+3 wks)
   2. Severe BPD
   3. Neonatal sepsis（Candida infection）
   4. ROP(stage III)
   5. Congenital heart disease（VSD,PFO）
   6. Anemia of Prematurity
Respiratory support (Totally for 131 days):

- SIMV (39 days)
- HFOV (22 days)
- NIPPV (12 days)
- nCPAP (30 days)
- NC O2 (28 days)
• Start FICare on DOL 66 (on NIPPV), & totally FICare for 110 days.

• Discharged on DOL 155 with Wt 4900g & feeding @ 83ml Q3h (TFI 135.5ml/kg/d)
Other Cases (1)
Other Cases (2)
Happy discharge home!
Take home messages...
• FICare in NICU is beneficial to the development of preterm infants at 18M of age.
• Further follow-up study should be continued as at 24M, 3yr, 6yr, and older age. But the loss of follow-up might be a big issue.
• Mechanisms of positive neuroprotective effect of FICare to preterm infants should be carried on.
• FICare for intubated infants is feasible, but more study should be further completed.
Acknowledgements

• Grants: Canada Institute of Health Research (CTP87518) & Chinese Medical Board (CMB OC 13-162)

• Policy support from the Third Xiangya Hospital of Central South University.

• Pediatricians and nurses in each joint NICU.

• Colleagues in MSH.
Doctors and nurses in the Preterm NICU of Hunan Children’s Hospital.

Doctors and nurses in the Third Xiangya Hospital of Central South University.
Welcome to Changsha, China
Thank you for your attention!