Neonatal Respiratory Distress Syndrome and the Prevention in Northwest regions of China

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NRDS

- Neonatal Respiratory Distress Syndrome (NRDS) caused by pulmonary surfactant (PS) insufficient and lung structure premature.
- It’s the main disease which take up an important part of newborn and child morbidity and mortality in China.
- Account for 30% of all neonatal death.
- 50% ~ 70% cause of premature death.
China is one of the 10 countries that 65% neonatal death occur around the world.
The highest mortality rates are in the northwest region, China.

U5MR in China
The death of neonatal diseases is the main part

Causes of Death in Children Under Five

The United Nations children's fund (UNICEF), 2014
The cause of death in different areas

No matter in the city or countryside, the most reason of death is ...

The original of the ministry of health
The northwest region is one of the seven geographic divisions in China. Because of inland and highland, the transportation was not developed well for a long time and some other long-term problems, the economic level is relatively backward, medical and health care also lag behind the domestic east and other advanced region of China.
Research of Northwest Region

• Due to different economic development, the hardware, treatment technology are also uneven in northwest region of China.

• There is no large sample research about incidence, mortality, risk factors, interventions of NRDS in northwest China.
Research of Northwest Region

• NRDS epidemiological and NICU resource allocation investigation are urgent in northwest.

• In order to promote the neonatal clinical work and scientific research in northwest region.

• We established the Northwest Neonatal Professional Collaboration Group (network) in 2012. The members come from the hospitals of Shaanxi, Kansu, Sinkiang, Qinghai and Ninxia. The leading hospital is the First Affiliated Hospital of Xi ‘an Jiaotong University.
Research

• This is the first time investigation of NRDS by comparing the different of diagnosis and treatment in China and in different regions of northwest.

• To find the correlation between China's northwest NRDS and the economy growth, as well as the main reasons.
Research methods

• Twenty neonatal wards of the Northwest Neonatal Professional Collaboration Group were retrospectively investigated from January 1, to December 31, 2011, all patients were diagnosed with NRDS.
• Hospitals Including 13 in Shaanxi, 4 in Kansu province, 3 in Xinjiang autonomous region, level 3 hospital 12, level 2 hospital 8.
• Descriptive epidemiological investigation method, collection of all the cases data.
Investigation of different level hospital, different gestational age, different NRDS characteristics, the basic, perinatal condition, prevention, clinical manifestations and treatment, complications and prognosis, and economic relations in the northwest region.
Research methods

NRDS diagnostic criteria:

1. The progressive dyspnea shortly after birth to 12 h, or/and even respiratory failure.

2. Chest X ray show NRDS characteristics: lung transparency decreased, diffuse reticular fine particles, air-filled bronchi, even white lung;

3. The lung maturity teat has immature performance;

4. Ruled out the cases of infection, meconium inhaled, wet lung, severe asphyxia and other system diseases which affect respiratory function.
Excluded standard:

- The cases of progressive ease of breathing difficult.
- The manifestation disappeared within 1 d.
- The general condition and responded was well,
- X-ray chest radiograph alveolar and pulmonary interstitial fluid.

Xiao-mei Shao, Ye Hong decided, small mound shanyou,. Practical neonatology [M Beijing: people's medical publishing house, 2011.

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Technical route

Established the Northwest Neonatal Professional Collaboration Group
Design questionnaires and related software

To unified training physician for fill in the questionnaire, in strict accordance with the inclusion criteria collecting cases

Summary, statistics, analysis, and published
Results and discussion

1. NRDS baby’s basic data

- 20 hospital treated 17406 cases of neonatal patients in 2011;
- 580 NRDS cases, 3.3% of the total number of newborns admitted;
- Male cases 379 (65.3%) more than female 201 (34.7%).
- The median hospital stay was 13.0 (6.0, 21.0) d,
- The median hospitalization cost was RMB 1.42 (0.68, 2.32) ten thousand.
### NRDS Infant Basic Data

<table>
<thead>
<tr>
<th>Region</th>
<th>Gender cases (male/female)</th>
<th>Birthweight (g)</th>
<th>Gestational age (w)</th>
<th>Hospital stay [d, M(Q₁, Q₃)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shaanxi</td>
<td>236/131</td>
<td>1935 ± 595</td>
<td>33.0 ± 2.9</td>
<td>14.0 (8.0, 22.75)</td>
</tr>
<tr>
<td>Sinkiang</td>
<td>43/23</td>
<td>1873 ± 592</td>
<td>32.9 ± 2.8</td>
<td>6.5 (1.0, 14.0)</td>
</tr>
<tr>
<td>Kansu</td>
<td>100/47</td>
<td>1935 ± 595</td>
<td>33.0 ± 2.9</td>
<td>11.0 (4.0, 21.0)</td>
</tr>
<tr>
<td>X²值</td>
<td>1.213</td>
<td>3.786</td>
<td>3.920</td>
<td>30.981</td>
</tr>
<tr>
<td>P值</td>
<td>0.545</td>
<td>0.151</td>
<td>0.020</td>
<td>0.000</td>
</tr>
</tbody>
</table>

- Male had high incidence of NRDS in northwest region
- According to the length of hospital stay in the order is Shaanxi, Kansu, Sinkiang.
- Average gestational age (32-34 w) and weight was bigger

Sinkiang Uygur Autonomous Region
NRDS gestational age composition

<table>
<thead>
<tr>
<th>gestational age</th>
<th>&lt;30W</th>
<th>30~34+6W</th>
<th>35~36+6W</th>
<th>≥37W</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDS composition</td>
<td>9.8%</td>
<td>44.7%</td>
<td>30.7%</td>
<td>14.8%</td>
</tr>
</tbody>
</table>

Gestational age composition

- ≥37周, 14.80%
- <30周, 9.80%
- 35~36+6周, 30.70%
- 30~34+6周, 44.70%

Because treatment level and economic condition
NRDS Birth Weight Composition

<table>
<thead>
<tr>
<th>Birth weight</th>
<th>&lt;999g</th>
<th>1000~1499g</th>
<th>1500~1999g</th>
<th>2000~2499g</th>
<th>≥2500g</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDS composition</td>
<td>2.1%</td>
<td>21.4%</td>
<td>34.1%</td>
<td>22.6%</td>
<td>19.8%</td>
</tr>
</tbody>
</table>

Because treatment level and economic condition
Maternal condition compared with 2004

Antenatal corticosteroid utility ratio was low, high rate of cesarean delivery

2004 study: among Chinese medical journal. 2009, 12 (2) : 121-126
Total mortality was 85 death cases (14.7%, 85/580); 20 cases of death after active treatment, but 65 cases death after give up treatment.
## Perinatal Conditions

<table>
<thead>
<tr>
<th>Region</th>
<th>Antenatal corticosteroid</th>
<th>Cesarean delivery</th>
<th>Multiplets</th>
<th>Fetal distress</th>
<th>Low Apgar score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shannxi</td>
<td>25/265 (9.4%)</td>
<td>223/367 (60.7%)</td>
<td>76/367 (20.7%)</td>
<td>37/367 (10.1%)</td>
<td>87/367 (23.7%)</td>
</tr>
<tr>
<td>Sinkiang</td>
<td>8/66 (12.1%)</td>
<td>32/66 (48.5%)</td>
<td>17/66 (25.7%)</td>
<td>7/66 (10.6%)</td>
<td>36/66 (54.5%)</td>
</tr>
<tr>
<td>Kansu</td>
<td>33/140 (23.6%)</td>
<td>69/147 (46.9%)</td>
<td>21/147 (14.3%)</td>
<td>44/147 (29.9%)</td>
<td>69/147 (46.9%)</td>
</tr>
</tbody>
</table>

\[ \chi^2 \]

- 119.886
- 12.709
- 3.933
- 46.305
- 40.052

| \( P \)  | 0.000 | 0.048 | 0.415 | 0.000 | 0.000 |

- The corticosteroid use, cesarean section, fetal distress rate, low Apgar score of birth are significant differences in different provence.
- The perinatal high-risk factors related to NRDS were as follows: low Apgar score, multiplets, gestational hypertension, premature rupture of membranes, placental abruption, gestational diabetes, gestational cholestasis.

**Antenatal corticosteroid utility ratio was lower than other region.**
Antenatal examination in different levels of hospital

- Regular antenatal examination in level 3 hospital was better than in level 2, no antenatal examination rate was high in level 2.
- No regular antenatal examination was still high in both level hospital.
Prenatal Corticosteroid Application Proportion in Different Level Hospital

The proportion in level 2 was significantly lower than Level 3 hospital (lower economic level and PS shortage)
Compare with the Midwest in 2004 and Vermont – Oxford net in 1990

The application proportion was lower than the midwest in 2004 and Vermont – Oxford net in 1990, especially level 2.

(lower economic level and PS shortage)
## Conditions of used PS

<table>
<thead>
<tr>
<th>Region (Provence)</th>
<th>PS Used (cases, %)</th>
<th>Time PS used 【h, M(Q₁, Q₃)】</th>
<th>PS Dosage (mg/kg, x±s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shannxi</td>
<td>226/367(61.5)</td>
<td>2.5(1.0,7.0)</td>
<td>80 ± 43</td>
</tr>
<tr>
<td>Xinjiang</td>
<td>18/66(27.2)</td>
<td>4.5(3.0,8.2)</td>
<td>170 ± 32</td>
</tr>
<tr>
<td>Gansu</td>
<td>54/147(36.7)</td>
<td>24.0(7.0,24.0)</td>
<td>99 ± 25</td>
</tr>
<tr>
<td>χ²</td>
<td>40.572</td>
<td>7.940</td>
<td>52.576</td>
</tr>
<tr>
<td>P</td>
<td>0.000</td>
<td>0.019</td>
<td>0.000</td>
</tr>
</tbody>
</table>

- PS used was the top rate, and the earliest time of the first used PS after birth in Shaanxi. Economy is the best in the northwest region.
- The median time of PS used in northwest was 24.0 h, all the time were too late.
Pulmonary Surfactant (PS)

PS replacement therapy is a key and effective measure, but it is the current most expensive self-pay neonatal medicines in China.

The PS guidelines:
• Use PS as soon as possible after diagnosis.
• Dosage is 100-200mg/kg.

PS used was non-standard in northwest region.
Different level hospital PS utility ratio

Almost all of the level 3 hospitals was higher than the level 2 hospital.

The patients had better economic conditions in higher level hospital.
NRDS Treatment in Level 2 and Level 3 Hospital

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Level 2</th>
<th>Level 3</th>
<th>$X^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS use proportion</td>
<td>39/130 (30%)</td>
<td>171/340 (50.3%)</td>
<td>15.670</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Economic difficulties</td>
<td>23/85 (27.1%)</td>
<td>46/164 (28%)</td>
<td>34.447</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unused</td>
<td>27/85 (31.8%)</td>
<td>47/164 (28.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parents refused</td>
<td>20/85 (23.5%)</td>
<td>7/164 (4.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cause</td>
<td>5/85 (5.9%)</td>
<td>24/164 (14.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS shortage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No indications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time use PS (h) $M(Q_{25}, Q_{75})$</td>
<td>7 (2,15)</td>
<td>4 (2,20)</td>
<td>(-0.583)</td>
<td>0.560</td>
</tr>
<tr>
<td>INSURE use proportion</td>
<td>16/73 (21.9%)</td>
<td>164/281 (58.4%)</td>
<td>30.996</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventilation use proportion</td>
<td>107/135 (79.3%)</td>
<td>381/410 (92.9%)</td>
<td>1.558</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventilation time (h) $M(Q_{25}, Q_{75})$</td>
<td>62 (18.75, 117.25)</td>
<td>60 (36, 86)</td>
<td>(-0.063)</td>
<td>0.949</td>
</tr>
</tbody>
</table>

The reason of unused PS: Economic difficulties was the first, PS shortages was second causes. The most of parents refused because of economic difficulties!
## Comparison of assisted ventilation

<table>
<thead>
<tr>
<th>Region (Provence)</th>
<th>INSUR E ventilation</th>
<th>CPAP</th>
<th>NIPPV</th>
<th>Conventional ventilation</th>
<th>High frequency ventilation</th>
<th>ventilation time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shannxi</td>
<td>142/248 (57.3)</td>
<td>336/367 (91.6)</td>
<td>294/336 (87.5)</td>
<td>16/336 (4.8)</td>
<td>23/336 (6.9)</td>
<td>3/336 (0.8)</td>
</tr>
<tr>
<td>Sinkiang</td>
<td>10/51 (19.6)</td>
<td>38/66 (57.5)</td>
<td>15/38 (39.5)</td>
<td>0/38 (0.0)</td>
<td>23/38 (60.5)</td>
<td>0/38 (0.0)</td>
</tr>
<tr>
<td>Kansu</td>
<td>28/55 (50.9)</td>
<td>139/147 (94.5)</td>
<td>113/139 (81.3)</td>
<td>1/139 (0.7)</td>
<td>25/139 (20.0)</td>
<td>0/139 (0.0)</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 23.992 \]
\[ P = 0.000 \]

- Shaanxi, main assisted ventilation was nCPAP and the longest time.
- Sinkiang, main assisted ventilation was CV and the shortest time.
At present, the use of the PS technology of the international guideline is “IN SU RE”
(sequence: intubation-surfactant-extubation)

\[ \text{nCPAP} (\text{Nasal Continuous Positive Airway Pressure}) \]

The INSURE method is effective in reducing the need for mechanical ventilation (MV), the duration of respiratory support, and the need for surfactant replacement in preterm infants with NRDS.
Different Level Hospital INSURE Technology Usage

INSURE used in all the level3 hospital, but not all level2
Level2 was lower than level3 hospital

Economic and new knowledge level
## NRDS complications and prognosis

<table>
<thead>
<tr>
<th>Region</th>
<th>PVL</th>
<th>PDA</th>
<th>air leak</th>
<th>BPD</th>
<th>NEC</th>
<th>ROP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shaanxi</td>
<td>11/321(3.4)</td>
<td>11/344(3.2)</td>
<td>3/332(0.9)</td>
<td>8/327(2.4)</td>
<td>6/291(2.1)</td>
<td>4/324(1.2)</td>
</tr>
<tr>
<td>Sinkiang</td>
<td>0/64(0.0)</td>
<td>1/39(2.6)</td>
<td>1/64/(1.6)</td>
<td>0/38(0.0)</td>
<td>0/41(0.0)</td>
<td>0/64(0.0)</td>
</tr>
<tr>
<td>Kansu</td>
<td>21/143(14.7)</td>
<td>36/139(25.9)</td>
<td>3/135(2.2)</td>
<td>9/137(6.6)</td>
<td>16/144(11.1)</td>
<td>1/144/(0.7)</td>
</tr>
</tbody>
</table>

\[ \chi^2 \]

<table>
<thead>
<tr>
<th></th>
<th>26.500</th>
<th>63.721</th>
<th>1.316</th>
<th>11.941</th>
<th>27.449</th>
<th>36.410</th>
</tr>
</thead>
<tbody>
<tr>
<td>( P )</td>
<td>0.000</td>
<td>0.000</td>
<td>0.518</td>
<td>0.063</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

- The occurrence of gas leakage, BPD differences had no statistical significance. The remainder differences were statistically significant.
- As a result of the examination of different backward levels, Diagnosis and treatment of complications had bigger difference.
## NRDS complications and prognosis

<table>
<thead>
<tr>
<th>Region</th>
<th>PVL</th>
<th>IVH</th>
<th>HIE</th>
<th>PPHN</th>
<th>mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shaanxi</td>
<td>6/281(2.1)</td>
<td>31/290(10.7)</td>
<td>70/306(22.9)</td>
<td>1/250(0.4)</td>
<td>30/367(8.2)</td>
</tr>
<tr>
<td>SinKiang</td>
<td>2/64(3.1)</td>
<td>28/64(43.8)</td>
<td>0/63(0.0)</td>
<td>0/66(0.0)</td>
<td>29/66(43.9)</td>
</tr>
<tr>
<td>Kansu</td>
<td>4/143(2.8)</td>
<td>12/144(8.3)</td>
<td>34/144(23.6)</td>
<td>14/123(11.4)</td>
<td>26/147(17.7)</td>
</tr>
</tbody>
</table>

| $\chi^2$   | 26.757   | 80.362   | 42.529   | 32.123   | 60.110    |
| $P$        | 0.000    | 0.000    | 0.000    | 0.000    | 0.000     |

Sinkiang’s abandon rate was significantly higher than Shaanxi and Kansu province. The mainly reason of give up is economic problem.
Conclusion

China's Northwest Region

- Cesarean delivery rate, especially full term selective cesarean delivery rate is higher than other region.

- The use of antenatal corticosteroids and INSURE method ratio was low. The use of PS was non-standard.

- The level of understanding and examination of neonatal complications was backward.
Conclusion

The economy and medical technology in northwestern region was backward.

• The price of PS is too expensive (belongs to self-paying, families have to undertake all expenses). The treatment cost of NRDS was difficult to bear. PS in county-level hospitals was shortages,

• The assisted ventilation of respiratory support was also expensive, both respirator and support technology were shortage,
Conclusion

• Assisted ventilation of nCPAP application is not enough, less NIPPV, high-frequency mechanical ventilation, NO inhaled and others, all the special treatment methods still have gap with the domestic developed regions and international level.

• So that the mortality of NRDS is very high especially in Sinkjiang, and many families give up treatment because no money.
Conclusion

• Our study supported the research worldwide: a small gestational age, low birth weight, male, perinatal asphyxia, selective cesarean section (<39W), multiple births and inadequate application of antenatal corticosteroid were high risk factors of NRDS.

• The treatment of China's northwest NRDS level is lower than the domestic middle and eastern region, level 2 hospitals is lower than level3 hospital. Antenatal examination, early diagnosis and control the risk factors which didn’t improved well.
**Suggestion**

- To improve the quality of obstetric and perinatal health care, detect mother’s risk factors and handle complications in time.
- To decrease the rate of cesarean section, especially selective cesarean section.
- The high-risk pregnant may cause premature, it should be treated with corticosteroid to promote lung mature.
Suggestion

- The premature infant with high risk factors should been treated with PS preventively and early.
- To full dose use PS as early as possible, and use INSURE technology as much as possible.
- To further improve the diagnosis and treatment of complications, reduce the complications such as HIE, PDA, ROP and so on, improve the management of NRDS.
Suggestion

• Government should enroll PS into medicare system, reduce the burden of family, and further reduced the give up in financial difficulties family.

• Government should increase medical investment in the northwestern region, especially in level 2 hospital and countryside, establish network for intrauterine or after birth transfer, to promote NRDS to get better treatment and reduce mortality
We hope everyone here to help us to promote the medical care development in northwest region of China!
Acknowledgement

• Maternal and Child Care Hospital of Kansu Province,
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• Burqin County people's hospital of Xinjiang,
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• Xidian Group Hospital, Jingyang county hospital of Shaanxi,
• Maternity and Child Health Care Hospital of Ankang,
• Maternity and Child Care Hospital of weinan,
• Baoji centers Maternal and child care Health Hospital,
• Maternal and Child Health Care Hospital of Tongchuan,
• Children's hospital of Yulin City……

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谢谢！

西北地区新生儿协作组(网)

（Northwest Neonatal professional Collaboration Group of Network, NNPCGN）