MANAGEMENT OF TETANUS IN ICU: A LOCAL EXPERIENCE.

Medical Intensive Care Unit
PIMs

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INTRODUCTION

- A nervous system disorder characterized by painful muscle spasms.
- Caused by Clostridium tetani obligate intracellular spore forming anaerobe.
- Spores found in soil, house dust, animal intestine.
- Enter normal tissues and persist for several months.
- Germinate under anaerobic conditions and produce toxin.
TETANOSPASMIN

- Inhibits release of neurotransmitters (GABA, Glycine).
- Reaches nerve end plates through blood and lymphatic.
- Centripetal spread to neurons.
- Increased muscle tone and reflex spasms.
- Once fixed cannot be removed.
- Recovery depends on sprouting of new nerve terminals.

- Annual incidence world wide one million cases.
- Developed countries 0.16-0.2 cases/million population.
- 300,000 infant death.
- Mortality rate 45%.
CLINICAL FEATURES

- Incubation period: 1-3 days to several months.

- Signs and symptoms progress for 2 weeks after onset.
  - Trismus or lockjaw
  - Tonic muscle contraction.
  - Painful tetanic contractions or spasms.
  - Apnea
  - Dysphagia
  - Autonomic over activity

- No impairment of consciousness.
CLINICAL CLASSIFICATION (EXTENT)

- **Local**: Tonic spasms in one extremity or body region
- **Cephalic**: seen with head injuries. Initial involvement of cranial nerves.
- **Neonatal**: Infants within 14 days of birth. Due to poor immunization of mother and infection of umbilical stump.
- **Generalized**: involvement of entire body musculature
CLASSIFICATION (SEVERITY)

- **Grade 1 (Mild):** Mild trismus, gen spasticity. No resp. embarrassment or dysphagia.

- **Grade 2 (Moderate):** Well marked rigidity, moderate trismus short lasting spasms.

- **Grade 3 (Severe):** Gen. spasticity, severe trismus, reflex or spontaneous prolonged spasms, resp. distress apnea, dysphagia.

- **Grade 4 (Very Severe):** Grade 3 plus violent autonomic disturbances, labile blood pressure, heart rate, profuse sweating.
GOALS OF TREATMENT

- Halting toxin production.
- Neutralization of unbound toxin.
- Active Immunization.
- Control of muscle spasms.
- Management of autonomic dysfunction.
- Supportive Care.
MANAGEMENT OF TETANUS IN ICU: A LOCAL EXPERIENCE

- **Objective:** To evaluate the clinical features, management, complications and outcome of patients with tetanus.
- **Design:** Prospective observational study.
- **Setting:** A nine bedded medical ICU in a 930 bedded tertiary care hospital.
- **Patients & Methods:**
  - Consecutive adult patients admitted to Medical ICU from October 2005 to December 2006.
  - Demographic data, history of injury, previous immunization status were noted.
  - Severity of the disease graded from 1 to 4.
  - Patients with moderate to severe disease were intubated electively.
  - Tracheostomy in first week for prolonged vent support.
STANDARD OF CARE

- Rapid sequence intubation to prevent reflex laryngospasm.
- Tetanus toxoid in ER.
- Human Tetanus immunoglobulin I/M (2000 to 6000 IU)
- Surgical wound debridement
- B. Penicillin 24 million units/d for 14 days.
- Sedation Diazepam, Morphine sulphate, Pancuronium.
- Hydration 3-4 L fluids (KCl 40 m eq + magnesium sulphate 2g/litre).
STANDARD OF CARE

- Enteral nutrition 1500 Cal/day
- Thromboembolism prophylaxis
- Isolation with minimal sensory stimuli
- Prevention of pressure sores
- Hemodynamic & clinic monitoring
RESULTS

- Total no of patients  20.
- 6 after Oct earthquake 2005
- Male to female ratio  13:7
- None was previously immunized.
- History of injury  15(75%)
- All required mechanical ventilation.
- Mean ICU stay 30 days
AGE WISE DISTRIBUTION

MEAN Age: 36 Yrs

Percent

age of the pts

16-25y

26-35y

36-45y

46-55y

>55y

0 10 20 30 40
INCUBATION PERIOD

Period between exposure to the Micro organism and manifestation of disease

<table>
<thead>
<tr>
<th>INC.PERIOD</th>
<th>NO.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;21 DAYS</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>8-14 DAYS</td>
<td>11</td>
<td>55</td>
</tr>
<tr>
<td>1-7 DAYS</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>GRADE</td>
<td>NO</td>
<td>%</td>
</tr>
<tr>
<td>-------</td>
<td>-----</td>
<td>----</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>30</td>
</tr>
</tbody>
</table>

**Grades of Tetanus**

![Graph showing grades of tetanus](image)
## Duration of Ventilation

<table>
<thead>
<tr>
<th>DURATION</th>
<th>NO.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 wk</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>1-2 wks</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>3-4 wks</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>5-6 wks</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>&gt;6 wks</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

![Bar chart showing duration of ventilation]
## TYPE OF SEDATION GIVEN

<table>
<thead>
<tr>
<th>Sedation</th>
<th>NO.</th>
<th>% age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Diazepam + morphine</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Diazepam + morphine + pavulon</td>
<td>17</td>
<td>85</td>
</tr>
</tbody>
</table>

![Bar chart showing the percentage of each type of sedation given]
Mortality rate 25%
## COMPLICATIONS

<table>
<thead>
<tr>
<th>COMPLICATION</th>
<th>NUMBER</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Arrest</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>HAP/Sepsis</td>
<td>16</td>
<td>80</td>
</tr>
<tr>
<td>PE/DVT</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Tracheostomy wound Infection</td>
<td>9</td>
<td>45</td>
</tr>
<tr>
<td>Bed Sores</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>Contractures</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>RefractoryShock</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>
## ANALYSIS OF MORTALITY

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Grade</th>
<th>Incubation</th>
<th>Injury</th>
<th>Cause of Death</th>
<th>Stay</th>
<th>Dose of TIG</th>
<th>Ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>F</td>
<td>4</td>
<td>10</td>
<td>Penetrating injury foot</td>
<td>Refractory shock</td>
<td>4</td>
<td>2500</td>
<td>Y</td>
</tr>
<tr>
<td>55</td>
<td>F</td>
<td>3</td>
<td>10</td>
<td>Leg amputation</td>
<td>Cardiac arrest</td>
<td>1</td>
<td>3000</td>
<td>Y</td>
</tr>
<tr>
<td>36</td>
<td>M</td>
<td>3</td>
<td>?</td>
<td>?</td>
<td>Cardiac arrest</td>
<td>9</td>
<td>5000</td>
<td>Y</td>
</tr>
<tr>
<td>30</td>
<td>F</td>
<td>4</td>
<td>5</td>
<td>Septic abortion</td>
<td>Sepsis, cardiac arrest</td>
<td>5</td>
<td>3000</td>
<td>Y</td>
</tr>
<tr>
<td>38</td>
<td>F</td>
<td>3</td>
<td>10</td>
<td>Minor Cut right foot</td>
<td>Sepsis, HAP</td>
<td>28</td>
<td>2000</td>
<td>Y</td>
</tr>
</tbody>
</table>
DISCUSSION

- Young adult males were mainly affected.
- Developed countries: reported in the elderly with poor immunity.
  - 43 cases per year in US. (1)
  - 3 cases in 1997.
  - 2 cases in 1998 in Canada (2)

TETANUS TRENDS IN DEVELOPED COUNTRIES

Tetanus – Number of Cases and Deaths, 1924-2000

Report of Public Health agency of Canada. Vaccine preventable diseases
VACCINATION STATUS IN PAKISTAN

- No patient vaccinated, including age group 15–25.
- EPI launched in 70’s.
- Is it effective?
- Evaluation of EPI 2000 by UNICEF, 70% immunization of children (Target 95%)
- Status of vaccination among women 15 to 45yrs 56% 2002, 57% 2003, 45% 2004 (3)

(3) Knowledge and attitude of reproductive age females about tetanus toxoid vaccine: Amna Zeb JCPS2006, vol 16(12)
Twenty-two tetanus deaths reported in Pakistan quake zone
27 oct 2005  associate press.

144 tetanus cases including 41 dead;
Consolidated health situation bulletin #3  . 8 Nov.2005
BENEFITS OF EFFECTIVE VACCINATION

- Medical experience of university hospital in Turkey after the 1999 Marmara earth quake.
  

  “All patients received Tetanus prophylaxis. There was no case of gas gangrene or tetanus”
ROLE OF PASSIVE IMMUNIZATION

- Therapeutic dose HTIG 150 units/kg.
- Recommended dose 500 to 5000 iu.
- Give HTIG as early as possible.
- Single dose is effective. Half life of TIG > than 21 days.
- Intrathecal administration of HTIG of unproven benefit (4).
- Local infiltration of the HTIG of unproven value.
- Equine antitoxin or pooled IVIG may be used when HTIG is not available.
- Tetanus td at time injury gives no protection in the incubation period.

4) Miranda-Filho, B, Ximenes. Randomized controlled trial of tetanus treatment with antitetanus immunoglobulin by intrathecal or intramuscular route. BMJ 2004;328:615
ROLE OF ANTIMICROBIAL THERAPY.

- Surgical debridement essential.
- Role of antibiotics controversial.
- Penicillin G traditionally recommended.
- Metronidazole is the alternate choice.
- Penicillin vs metronidazole the mortality was less for Met (5)
- Comparison of pen. and met. no difference in mortality (6)
- Study of 364 patients no difference in mortality between those who received antibiotics and those who did not. (7)

SEDATION AND PARALYSIS

- 85% required deep sedation with curarization

- Deep sedation and paralysis, makes the difference between conservative and ICU management

- Analysis of 641 cases before and after ICU care showed;

- Resp.Failure 80% in conservative group. 15% in ICU treated group. (9)

MAGNESIUM SULPHATE IN TETANUS

- Magnesium sulfate:
  - causes pre synaptic neuromuscular blockade
  - blocks catecholamine release from the nerves
  - decreases responsiveness to catecholamines.
- In a pilot study (8 cases) high dose MgSO4 (5g bolus - 2-3g/h). Sedation and artificial vent. could be avoided.
- Prospective study (40 cases) N-M blockade avoided, 17/40 (43%) needed mech. vent. (9)
- Used as adjunctive therapy,
- Brady arrhythmias may limit use of high doses.

9) Attygalle D, Rodrigo. Magnesium as first line therapy in the management of tetanus: Anesthesia 2002;57;811
Comparison of mortality before and after ICU

- Analysis of 641 patients over 28 yrs (1956-84)
  - 335 before ICU (1956-68) Mortality 43%
  - 306 after ICU (1968-84) Mortality 15%(10)
- Analysis of 236 patients over 20 yrs (1981-2001)
  - 126 before ICU (1981-93) Mortality 36.5%


COMPLICATIONS

- Freq of HAP 80% alarmingly high. Others report freq. of 42% (12) and 36% (13) in Honduras and S. Africa.
- Sudden Cardiac Death a feature of severe tetanus.
- Caused by loss of symp.drive or P/sym storm.
- 3 of 20 (15%) patients in our study had cardiac arrest.
- Cause of death for 3/5 (60%) of our patients.
- Cardiac arrest and acute MI accounted for 49% (9) and 73% (12) mortality in other studies.

## COMPARISON OF MORTALITY (other ICUs)

<table>
<thead>
<tr>
<th>Ref.</th>
<th>place</th>
<th>time</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>M H Trujillo (9)</td>
<td>Venezuela</td>
<td>1968-84</td>
<td>46/306</td>
<td>15</td>
</tr>
<tr>
<td>Anuradh S (14)</td>
<td>Delhi</td>
<td>1991-99</td>
<td>82/217</td>
<td>37</td>
</tr>
<tr>
<td>Brauber JS (10)</td>
<td>Brazil</td>
<td>1993-2000</td>
<td>20/110</td>
<td>18</td>
</tr>
<tr>
<td>N Saltugo (15)</td>
<td>Turkey</td>
<td>1994-2000</td>
<td>27/53</td>
<td>52</td>
</tr>
<tr>
<td>Al-Kaabi (16)</td>
<td>Oman</td>
<td>1991-99</td>
<td>1/10</td>
<td>10</td>
</tr>
<tr>
<td>C Fernandez (13)</td>
<td>SA</td>
<td>1998-2002</td>
<td>5/11</td>
<td>45</td>
</tr>
<tr>
<td>Present study</td>
<td>Ibid</td>
<td>2005-06</td>
<td>5/20</td>
<td>25</td>
</tr>
</tbody>
</table>
CONCLUSIONS

- Tetanus result of failure of preventive vaccination.
- Untreated the mortality is high.
- Management in ICU decreases mortality.
- Treatment is prolonged, expensive.
- ICU treatment associated with high incidence of infective complications.
- Cardiac complications are main cause of mortality in ICU.
RECOMMENDATIONS:

- Immunization programmes for all age groups.

- Simple schedules that reach all segments of the population.

- Primary care and emergency room physicians to ensure appropriate wound care (tetanus toxoid and prophylactic immunoglobulins).

- Public awareness about tetanus.
**Wound management & tetanus prophylaxis**

*Guide for adult immunization Philadelphia, American College of Physicians, 1994*

<table>
<thead>
<tr>
<th>Clean and minor wounds</th>
<th>Previously received 3 or more doses of tetanus toxoid or tetanus Diphtheria td.</th>
<th>Uncertain whether 3 doses of tetanus toxoid or TD have ever been administered.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Td if last dose more than 10 yrs ago</td>
<td>Start primary series: 1 dose now, 2 in one month, 3 in 12 month</td>
</tr>
<tr>
<td>All other wounds</td>
<td>Td if last dose was 5 yrs ago</td>
<td>TIG 250 iu I/m and start primary series.</td>
</tr>
<tr>
<td>SCHEDULE</td>
<td>CHILDREN</td>
<td>ADULTS</td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Primary course</td>
<td>3 doses of vaccine (as DTaP) at 2, 3, 4 months of age</td>
<td>3 doses of vaccine as Td one month apart</td>
</tr>
<tr>
<td>4th dose</td>
<td>3 years after the primary course usually pre-school entry.</td>
<td>10 years after primary course as Td</td>
</tr>
<tr>
<td>5th dose</td>
<td>Aged 13-18 years before leaving school as Td/IPV</td>
<td>10 years after 4th dose as Td.</td>
</tr>
</tbody>
</table>
THANK YOU