Contraindications to Cisplatin based chemotherapy in the treatment of cervical cancer in Sub-Saharan Africa

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Contraindications to cisplatin based chemoradiotherapy in the treatment of cervical cancer in Sub-Saharan Africa

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Introduction

• The majority of Cervical cancer patients live in developing World (Parkin et al, 2002)
• Uganda incidence is 44.1/100,000 (11) compared to 4-11/100,000 in the developed world
• Multiple social-economic factors lead to late presentation of Cervical cancer
• Co-existing HIV and other infections, poor nutritional status and anemia make treatment difficult in Sub-Saharan Africa
Introduction

• Concomitant chemoradiotherapy confers an overall survival of 10-16% (Lukka et al 2002, Green et al, 2005)
• Now standard of care
• It however presents multiple challenges with implications for allocation of scanty resources in Sub-Saharan Africa with a low resource setting.
• We conducted a prospective study to assess the proportion of patients with cervical cancer considered suitable for chemotherapy in our department in Kampala, Uganda
Materials and Methods

• All patients presenting with biopsy proven cervical cancer from Aug 2005 – June 2006 were eligible for the study.
• They had standard work up to assess suitability including: H&E, KPS, EUA, CBC, RFTS and LFTS, USS (Abdomen and Pelvis) and whenever possible HIV testing.
Exclusion criteria for Cisplatin

• Stage 1A and stage IV A & B
• HIV status positive,
• KPS less than 60
• Age > 70 years
• Hydronephrosis
• Haemoglobin < 8 gm/dl
• WBC < 2,000/ µL
• Platelets < 100,000/µL
• Creatinine > 97µmol/L
• Previous surgery (as it is difficult to assess extent of surgery & positive margins from the reports)
Results

- 314 patients were referred in the 10 months study period
- Only 47 patients (15.1%) were eligible
- 190 patients were NOT eligible
- In 77 cases (24.4%) eligibility could not be established as work up was incomplete
- 37 patients (11.6%) were proven to be HIV positive but in 38.4% HIV sero-status was not established
## Frequency of exclusion criteria

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>No (=314)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1A</td>
<td>4</td>
<td>1.1</td>
</tr>
<tr>
<td>Stage IV A &amp; B</td>
<td>44</td>
<td>14.0</td>
</tr>
<tr>
<td>Age &gt; 70 years</td>
<td>11</td>
<td>3.5</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>99</td>
<td>31.4</td>
</tr>
<tr>
<td>HIV positive</td>
<td>37</td>
<td>11.6</td>
</tr>
<tr>
<td>Haemoglobin &lt; 8gm/dl</td>
<td>55</td>
<td>17.4</td>
</tr>
<tr>
<td>WBC &lt; 2,000/µL</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Platelets &lt; 100,000/µL</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Postoperative cases</td>
<td>41</td>
<td>12.8</td>
</tr>
<tr>
<td>Creatinine &gt; 97µmol/L</td>
<td>47</td>
<td>15.1</td>
</tr>
</tbody>
</table>
Multiple exclusion criteria

• The most frequently encountered exclusion criteria were hydronephrosis and anaemia
• Cut off point of 8 gm/dl led to exclusion of 55 pts, if 10 g/dl used → additional 11 pts
• Hydronephrosis was in 99 pts, 44% of which had bilateral hydronephrosis
• 29 pts (29.3%) of those with hydronephrosis had abnormal creatinine levels
• 96 pts (50.5%) of the 190 pts had multiple exclusion criteria (HIV positive pts were more likely to have multiple criteria (p=0.0000001))
### Frequency of multiple exclusion criteria

<table>
<thead>
<tr>
<th>No of exclusion criteria</th>
<th>HIV positive n=37</th>
<th>HIV negative n=153</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (%)</td>
<td>No (%)</td>
</tr>
<tr>
<td>1</td>
<td>4 (11)</td>
<td>90 (59)</td>
</tr>
<tr>
<td>2</td>
<td>19 (51)</td>
<td>33 (22)</td>
</tr>
<tr>
<td>3</td>
<td>11 (30)</td>
<td>26 (17)</td>
</tr>
<tr>
<td>4</td>
<td>3 (8)</td>
<td>4 (3)</td>
</tr>
</tbody>
</table>
Discussion

• 35-40% of dept workload at Mulago Hospital, Kampala is composed of cervical cancer
• Exclusion criteria were selected with a view of selecting the patients most likely to benefit from chemoradiation while minimizing its side effects as the facilities for supportive care are limited
• 60.5% of our cervical cancer patients were not suitable for chemoradiation at presentation
• Apart from anemia & hydronephrosis, most of the other criteria are not easily modified by clinical intervention
Anemia and hydronephrosis

- Anemia represents a double disadvantage for our pts as it prevents the chemotherapy while it is itself associated with poorer treatment outcomes (2,6,7).
- Cut off at 8 g/dL was chosen because at this level transfusion with 2-3 units can reverse the anemia. In practice transfusion is not readily available & multiple transfusions difficult.
- 99 pts had hydronephrosis & in our setting placing of ureteral stents is not possible.
Stage IVA and age above 70 years

- These are not absolute contraindications
- Represents only a pragmatic & cautious approach on our part
- Omitting these criteria increases the total eligible patients by 29 (9.2%) leaving the ineligible ones at 47.7%
HIV/AIDS

- 11.6% of our patients were HIV patients (UNAIDS reported HIV prevalence of 6.7% in general population in Uganda in 2005)
- At present there is no proven survival benefit for chemoradiation in HIV positive cervical cancer patients
- Radiation therapy alone has been shown to produce increased toxicity in HIV positive patients & chemoradiation has clear implications (2,9).
- HIV/AIDS pts are treated with chemoradiation as part of an ongoing IAEA coordinated multinational randomized controlled trial (CRP 13120) in our dept.
Radiotherapy alone?

• There are however reports which show impressive results that can be achieved with radiotherapy alone in the developing world setting (Saibishkumar EP et al, 2006)
Conclusions

• Our study showed that only a small proportion of our patients were likely to benefit from chemoradiotherapy with weekly Cisplatin.

• This illustrates difficulties of applying a “standard” cervical cancer treatment to the developing world where the majority of these cancers exist.

• Introduction of chemoradiotherapy might therefore not have as a major effect on treatment outcomes for the group as a whole.

• Alternative chemotherapy agents especially those not associated with potential renal complications of Cisplatin should be investigated.
Conclusions - 2

• The provision of accessible radiotherapy facilities for the treatment of existing disease and

• The introduction of national screening / vaccination programmes to prevent cervical cancer and to catch it while it is in its early stages should be the major priorities in the developing world setting.
Acknowledgements & references

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References


THANK YOU FOR YOUR ATTENTION