Injection of intra arterial methylene blue ex-vivo in colorectal cancer specimens increase lymph node harvest

Colorectal unit – University Hospital of North Tees
Background

• Lymph node positivity is one of the most important predictors of prognosis following resection of colorectal cancer.
• Thus, current guidelines from the American Joint Committee on Cancer (AJCC), the Union Against Cancer (UICC) and the Association of Coloproctology of Great Britain and Northern Ireland (ACPGBI) recommend a minimum of 12 lymph nodes to be examined in order to reliably confirm lymph node negative disease [1,2].

Recently, a new method of lymph node detection has been advocated, using intra-arterial methylene blue injection following the resection of a colorectal cancer, an ex-vivo technique that appears to achieve a significantly higher yield of lymph nodes compared with the standard techniques.
Methodology

- All patients undergoing planned resection of a colorectal cancer in the University Hospital North Tees are included.
- We estimate to obtain 100 cases (randomised in two groups of 50 patients) within a 12-month study period.
- Following discussion with the institutional Research and Development board and pending its approval, we determined that no further ethical approval would be required as the patient’s management and treatment would not be influenced by the trial, and no direct effects would be resulting form the study for the individual.
Specimen preparation

• Following routine surgical resection of the colorectal specimen, the main arterial blood supply of the specimen is cannulated with 16-20 G intravenous catheters, 50 mg Methylene blue diluted to 30 ml with 0.9% Sodium Chloride are injected until the dye is visible on the surface of the specimen.

• Following injection, the specimen is fixed in formaldehyde solution for 24 hours as is standard practice.
Aims

• To determine the value of intra-arterial methylene blue injection in colorectal cancer specimens to increase the number of harvested lymph nodes.
Methods

• Single blinded randomised controlled trial of 100 consecutive patients undergoing elective resection of colorectal cancer.

• Findings of 99 patients, data sheet of 1 patient missing, between May 2012 to Feb 2013
Results

- Mean age 68.8 (35-92) years.
- Median age 70 years.
- Mean age in No dye group 69.9
- Mean age in Dye group 67.7
- P=0.788
Sex

- Male- Dye group- 28(57.1%)
- Male- No dye- 29(58.0%)
- \( p = 0.931 \)
Site

**Intervention Group**
- Right sided resection: 15 (30.6%)
- Left sided resection: 16 (32.7%)
- Rectal cancers: 18 (36.7%)

**Control group**
- Right sided resection: 22 (44%)
- Left sided resection: 12 (24%)
- Rectal cancers: 16 (32%)

\[ p = 0.367 \]
Site

Bar Chart

<table>
<thead>
<tr>
<th>Site</th>
<th>Count Right colon</th>
<th>Count Left colon</th>
<th>Count Rectum / Rectosigmoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right colon</td>
<td>44%</td>
<td>24%</td>
<td>16%</td>
</tr>
<tr>
<td>Left colon</td>
<td>30.6%</td>
<td>32.7%</td>
<td>36.7%</td>
</tr>
<tr>
<td>Rectum / Rectosigmoid</td>
<td>36.7%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p = 0.367
Lymph node harvest

- **Intervention group**
  - Minimum: 5
  - Maximum: 92
  - Mean: 25.7
  - Median: 23

- **Control group**
  - Minimum: 5
  - Maximum: 37
  - Mean: 17.1
  - Median: 15

  *Mann-Whitney U test for mean - p<0.001*
  *Independent sample median - p=0.002*
Positive Lymph Node Yield

- **Intervention Group**
  Total no of cases-49
  Total no of cases with positive lymph node – 22(44.9%)

- **Control Group**
  Total no of cases-50
  Total no of cases with positive lymph node – 20(40%)

p=0.622
## Dukes’ stage

<table>
<thead>
<tr>
<th></th>
<th>No dye</th>
<th>Meth blue</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>14 (28%)</td>
<td>8 (16.3%)</td>
</tr>
<tr>
<td>B</td>
<td>14 (28%)</td>
<td>18 (36.7%)</td>
</tr>
<tr>
<td>C</td>
<td>20 (40%)</td>
<td>22 (44.9%)</td>
</tr>
<tr>
<td>Benign</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

$p=0.502$
Conclusion

• Injecting methylene blue into the supplying artery does increase lymph node harvest but not yield of positive lymph nodes.

• Larger trial may be indicated to explore this further.