Guideline Name: Guideline for the Supplementation of Folic Acid

Guideline Number: __________________________

Guideline Version: __________________________

Developed By: Oonagh Deeney, Senior Renal Dietitian

Approved By:

Date Effective From: April 2009

Review Date: April 2011

Superseded Documents:
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1.0 Aim / Purpose of Guideline.

To provide guidelines & assist the multidisciplinary team in the appropriate supplementation of folic acid to patients receiving haemodialysis or peritoneal dialysis.

2.0 Review History

<table>
<thead>
<tr>
<th>Date</th>
<th>Review No.</th>
<th>Change</th>
<th>Ref. Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2009</td>
<td></td>
<td>Create guideline</td>
<td></td>
</tr>
</tbody>
</table>

3.0 Scope

This guideline applies to the members of the multidisciplinary team involved in the care of patients receiving haemodialysis or peritoneal dialysis.

4.0 Guideline

The objectives of this guideline are to:

- Prevent sub-clinical and frank deficiency.
- Avoid over-supplementation.
- Use therapeutic amounts to prevent additional pathology.

5.0 Definitions / Background

Folic Acid

Folic acid is one of the B vitamins. Adequate folate intake is necessary for the formation of tetraydrofolate (THF). A lack of THF means the one-carbon transfer reactions required for the DNA synthesis are limited.

<table>
<thead>
<tr>
<th>Minor Deficiency symptoms</th>
<th>Major Deficiency symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiredness, Weakness, Irritability,</td>
<td>Anaemia, Muscular cramps,</td>
</tr>
<tr>
<td>Insomnia, Forgetfulness</td>
<td>Confusion</td>
</tr>
</tbody>
</table>
The nutritional intake of the dialysis patient can be suboptimal due to:
The therapeutic dietary restrictions, cooking procedures.
The disease state and co-morbidities, e.g. uraemia causes decreased absorption and/or
activity of vitamins.
Drug nutrient interaction.
Fluid removal during dialysis.

Laboratory and epidemiological data have suggested that Folic Acid supplementation has a
role in both cancer prevention, by having an antineoplastic effect, and cardio-protection by
reducing homocysteine levels. However, more recent randomized controlled trials have
shown that folic acid supplementation does not reduce colorectal adenoma risk and in fact
may increase the risk of advanced lesions and adenoma multiplicity, Cole et al, 2007, Kim
YI, 2007. In relation to Cardio protection, the evidence is weak with a recent randomized
trial showing folic acid supplementation did not reduce a combined end point of total
cardiovascular events despite significantly lowering homocysteine levels, Albert et al, 2008.

Therefore, it is felt it is prudent to avoid excessive supplementation and only provide the
recommended dose to help prevent deficiency.

<table>
<thead>
<tr>
<th>Current recommendations</th>
<th>Renal Dietetic Practice Group</th>
<th>INDI, RIG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folate</td>
<td>1mg</td>
<td>1mg</td>
</tr>
</tbody>
</table>

GMS Listed Folic Acid Supplementation and treatment options:
(1) 5 mg Folic Acid until serum folate levels reach the upper end of the reference range
and then reduce to 5mg once weekly.
(2) 800 mcg Clonfolate (2 tablets) daily.

**6.0 Responsibilities**

The medical team must:
- On commencing dialysis prescribe the recommended 5 mg daily until serum folate
  levels reach the upper end of the reference range and then reduce to 5mg once weekly
  (ideally Sunday – non-dialysis day)

The nursing staff must:
- Routinely monitor serum Folate levels to allow for dose adjustment * need
  consensus on frequency*
The dietitian must:
- Routinely monitor serum Folate levels to allow for dose adjustment.

7.0 Distribution
This policy document should be available to all hospital staff involved with the care of patients receiving dialysis; this includes Consultants, NCHDs, Nursing staff, dietitians and pharmacists.

8.0. Filing
A copy will be filed in the policy and procedure book folder in each unit and available electronically via the hospital intranet.

9.0 Superseded/ Obsolete Documents
This is the first dedicated guideline on the supplementation of folic acid.

10.0 Reference List


11.0 Appendices

Appendix 1.
Table One- Results of random sample of 50 haemodialysis patients & percentage meeting dietary recommendations
Table Two- Serum Folate levels in the latter half of 2008 in all HD, PD and Northern Cross haemodialysis patients.
Table Three- Frequency of serum folate level checks in HD patients in 2008

Appendix 2.
Short summaries of recent studies of Folic Acid supplementation.
### Table One: Random sample of 50 haemodialysis patients & percentage meeting dietary recommendations.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>RNI</th>
<th>Beaumont 2007</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vit B1 (mg)</td>
<td>m = 0.9 - 1.0 f = 0.8</td>
<td>31/33 16/17</td>
<td>94</td>
</tr>
<tr>
<td>Vit B2 (mg)</td>
<td>m = 1.3 f = 1.1</td>
<td>20/33 9/17</td>
<td>58</td>
</tr>
<tr>
<td>Vit B6 (mg)</td>
<td>m = 1.4 f = 1.2</td>
<td>28/33 13/17</td>
<td>82</td>
</tr>
<tr>
<td>Vit B12 (mg)</td>
<td>1.5</td>
<td>49/50</td>
<td>98</td>
</tr>
<tr>
<td>Niacin (mg)</td>
<td>16 - 17</td>
<td>28/33</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>120 - 13</td>
<td>13/17</td>
<td></td>
</tr>
<tr>
<td>Vit C (mg)</td>
<td>40</td>
<td>24/50</td>
<td>48</td>
</tr>
<tr>
<td>Folate (mg)</td>
<td>200</td>
<td>28/50</td>
<td>56</td>
</tr>
</tbody>
</table>

### Table Two: Serum Folate levels in the latter half of 2008.

<table>
<thead>
<tr>
<th></th>
<th>&lt;2.8ug/l</th>
<th>2.8-17ug/l</th>
<th>17-20ug/l</th>
<th>&gt;20ug/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD, n=183</td>
<td>0</td>
<td>23% (42)</td>
<td>1% (2)</td>
<td>76% (139)</td>
</tr>
<tr>
<td>PD, n=34</td>
<td>0</td>
<td>68% (17)</td>
<td>6% (2)</td>
<td>24% (6)</td>
</tr>
<tr>
<td>Northern Cross, n=30</td>
<td>0</td>
<td>20% (6)</td>
<td>3% (2)</td>
<td>73% (22)</td>
</tr>
</tbody>
</table>

### Table Three: Frequency of serum folate level check in HD patients 2008:
73% Quarterly or less
27% >Quarterly (up to 12 times) leading to 119 unnecessary tests.
**APPENDIX 2**

**Cancer Prevention:**
- Randomized clinical trail. 1mg Folic Acid supplement, 1000 pts, f/u 10yrs
  Results: 1) Did not reduce the risk of recurrence. 2) Suggestion of increased risk of advanced lesions and adenoma multiplicity. 3) Higher risk of non-colorectal cancers, specifically prostate cancer. *Cole et al, 2007*

- Critical review of epidemiologic, animal and intervention studies.
  Results: Dual modulatory effects of folate on colorectal carcinogenesis depending on timing and dose of intervention.
  1) In established colorectal neoplasms folate has an inhibitory effect and supplementation a promoting effect.
  2) In normal colorectal mucosa folate deficiency appears to predispose it to neoplastic transformation and moderate supplementation suppress. While supraphysiologic supplemental doses enhance the development of cancer. *Kim, 2007*

  WAFACS, 2.5mg Folic Acid, 5442 women, f/u 7.3 years
  Results: No significant effect on overall risk of total invasive cancer or breast cancer. *Shumin et al, 2008*

**Cardio-protective:**
- WAFACS, 2.5mg Folic Acid, 5442 women, f/u 7.3 years
  Results: Did not reduce a combined end point of cardiovascular morbidity or mortality among high risk women, despite significantly lowering homocysteine levels. *Albert, et al. 2008*

- Hope 2, 5522 subjects, f/u 5 years
  Results: 1) Supplementation failed to significantly lower the risk of a combined outcome of death from cardiovascular causes, MI and stroke. 2) Significant reduction in the secondary end point of stroke. *Lonn et al, 2006*

- VISP
  Results: No benefit where stroke was taken to be the primary end point. *Toole et al, 2004*
- Norvit, recent MI, f/u 40 month
Result: Marginally significant increased risk of recurrent MI, stroke and sudden death.

**Bonna et al, 2006**

- Meta-analysis of randomized controlled trials
Folic Acid has not been shown to reduce the risk of CVD or all cause mortality among participants with a prior history of vascular disease. **Lydia et al, 2006**