Biological Trace Element Research

Copper Levels in Patients with Unexplained Dysplastic Cytopenia

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Supplementary Materials

ESM1 Inclusion and exclusion criteria

Inclusion criteria	***Exclusion criteria***
Patient had one or more persistent cytopenia(s) or macrocytosis	Bone marrow blasts found to be increased in excess of >5%
Patient had had a bone marrow examination performed to investigate persistent and unexplained cytopenia(s) or macrocytosis, and a diagnosis of ICUS, IDUS or MDS was made	Patient found to have a clonal cytogenetic or molecular abnormality (with the exception of deletion of chromosome Y)
Patient was over 18 years of age.	Patient had been started on treatment for MDS (excluding transfusion, erythropoietin and/or steroid therapy).
Patient had given consent to participate.	Patient unable or unwilling to give consent.
Patient was under the care of haematology at Hammersmith Hospital.	Patients who received copper replacement therapy in the past 12 months.

ESM2 Participant demographics

Demographic		***Frequency (%)***
Age		
	50 to 59	2 (12%)
	60 to 69	2 (12%)
	70 to 79	6 (35%)
	80 to 89	7 (41%)
Sex		
	Male	9 (53%)
	Female	8 (47%)
Ethnicity		
	Black Caribbean	4 (24%)
	Greek	1 (6%)
	Indian	1 (6%)
	Middle Eastern	2 (12%)
	Moroccan	1 (6%)
	Turkish	1 (6%)
	White British	5 (29%)
	White Irish	2 (12%)
BMI		
	<18.5	2 (12%)
	18.5 to 24.9	6 (35%)
	25.0 to 29.9	6 (35%)
	>30.0	3 (18%)

ESM3 Full blood count results at time of inclusion. All participants had at least one cytopenia M – males; F – females

Blood test	***Mean value (median)***	***Range***	***(Reference Range)***
Red cell count	*M:* 4.17 (3.95) *F:* 3.38 (3.49)	*M:* 2.85 to 6.05 *F:* 2.32 to 4.61	*(M:* 4.7 to 6.1 x10^{12}/L) *(F:* 4.2 to 5.4 x10^{12}/L)
Haemoglobin	*M:* 115 (118.0) *F:* 104.3 (107.5)	*M:* 95 to 127 *F:* 74 to 135	*(M:* 130 to 180 g/L) *(F:* 114-165 g/L)
Mean Cell Volume	92.6 (96.4)	58.9 to 109.9	(83.5 to 99.5 fL)
Platelets	127.2 (113.0)	34 to 387	(130 to 370 x10^{9}/L)
White Cell Count	4.6 (4.1)	2.2 to 8.1	(4.2 to 10.6 x10^{9}/L)
Neutrophils	2.2 (2.6)	0.6 to 6.0	(2.0 to 7.1 x10^{9}/L)

ESM4 Findings for each patient BMI – Body Mass Index, Cu – serum copper level, Hb – haemoglobin, RCC – red cell count, MCV – mean cell volume, WCC – white cell count, Neut – neutrophils, Plts – platelets, CRP – C-reactive protein, PPI – proton pump inhibitor

Patient	*Gender*	*Age*	*BMI*	*Cu*	*Hb*	*RCC*	*MCV*	*WCC*	*Neut*	*Plts*	*CRP*	*Dysplastic lineage(s)*	*Risk factors*
1	Male	79	21.30	11.3	113	6.05	58.9	2.9	1.5	36	0.6	Erythroid & Megakaryoblastic	
2	Male	78	28.10	13.3	119	5.74	62.4	3.6	1.4	133	1.0	Erythroid	
3	Male	81	31.60	14.7	127	4.47	82.7	4.1	0.7	116	No CRP	Trilineage	
4	Female	71	24.20	15.3	114	3.44	104.9	4.1	2.5	68	0.3	Erythroid & Megakaryoblastic	Dialysis, PPI
5	Male	82	32.50	16.8	124	4.15	101.0	4.2	2.8	126	2.5	Erythroid	Dialysis, PPI
6	Female	80	21.00	17.1	95	3.04	97.0	8.1	5.0	387	2.0	Declined marrow	
7	Male	67	27.40	18.9	104	3.45	92.0	4.9	2.2	194	No CRP	Trilineage	Low copper diet
8	Male	64	34.30	19	110	3.60	96.4	7.7	6.0	82	9.8	Erythroid	PPI
9	Female	84	17.90	19.5	111	3.65	101.4	2.3	1.6	87	1.1	Trilineage	PPI
10	Female	76	17.90	19.7	135	4.61	89.2	6.0	3.4	111	0.4	Megakaryoblastic	PPI, low copper diet
11	Male	83	21.10	19.7	118	3.25	107.7	3.2	2.2	151	2.9	Erythroid	
12	Female	55	27.18	20.6	81	2.32	109.9	4.0	2.0	34	1.4	Erythroid & Megakaryoblastic	
13	Male	83	27.40	20.9	125	3.95	95.9	5.7	2.8	113	0.3	Myeloid	PPI, multivitamins
14	Male	84	28.30	21.8	95	2.85	103.5	2.3	0.9	76	32.5	Myeloid & Megakaryoblastic	Multivitamin, neuropathy
15	Female	75	28.60	22.0	74	2.52	82.5	2.2	0.6	49	58.8	Trilineage	PPI
16	Female	59	20.10	22.8	104	3.88	83.0	8.0	4.6	200	3.9	Trilineage	
17	Female	72	20.80	23.6	121	3.54	105.4	5.3	3.7	199	2.4	Megakaryoblastic	

ESM5 Risk factors for copper deficiency in our population

Risk factor	***Frequency (%)***
Dialysis	2 (12%)
Proton pump inhibitor use	7 (41%)
Nutrition & Metabolic	
Low copper intake	2 (12%)
Alcohol excess	0 (0%)
Zinc-containing supplements	2 (12%)
Enteral nutrition, Total parenteral nutrition	0 (0%)
Copper metabolism defects e.g. Menkes, Wilson's	0 (0%)
Gastrointestinal	
Upper bowel resection, Bariatric surgery	0 (0%)
Short bowel syndrome	0 (0%)
Chronic diarrhoea	0 (0%)
Inflammatory bowel disease	0 (0%)
Neurology	
Optic neuropathy	1 (6%)
Peripheral neuropathy	1 (6%)

ESM6 Health Questionnaire used to gather patient information

Imperial College Healthcare NHS Trust

Imperial College London

Health Questionnaire

For the participants of the study: Reviewing the prevalence of copper deficiency in patients with suspect myelodysplastic syndromes

Please answer as many questions as you wish. The information you provide will only be available to researchers in this study, who will anonymise this information when it is entered into a password-protected document on an Imperial College Healthcare NHS Trust computer. This form will be disposed of in a confidential waste bin.

Full name: _____

Date of birth: _____

Gender: _____

Occupation: _____

Are you exposed to any hazardous chemicals at work? Yes/No. If yes, please specify:

_____

Ethnic Origin:

This is not about nationality, place of birth or citizenship. It is about the group to which you perceive you belong. Please circle the appropriate answer.

Prefer not to say

White: English/Welsh/Scottish/Northern Irish/Irish/British/Other, please specify: _____

Mixed/multiple ethnic groups: White and Black Caribbean/White and Black African/White and Asian/Other mixed background, please specify:

_____

Asian: Indian/Pakistani/Bangladeshi/Chinese/Asian British/Other, please specify: _____

Black: Black/African/Caribbean/Black British/Other, please specify:

_____

Any other ethnic group, please specify:

_____

Height: _____ **Weight:** _____

Current medications:

_____

_____

_____

_____

Are you currently undergoing any form of dialysis? Yes/No. If yes, please give details and the length of time you have been on dialysis:

_____

_____

Are you currently involved in any other research studies? Yes/No. If yes, please give details of the other study/studies:

_____

_____

Diet:

Are you vegetarian/vegan (please delete as appropriate)? Yes/No.

Do you follow a specific diet plan? Yes/No. If yes, please give details of your diet:

_____

_____

_____

_____

Do you take any vitamins or supplements e.g. zinc supplements? Yes/No. If yes, please specify:

_____

_____

_____

Have you received enteral nutrition (i.e. received food through a tube that is attached directly to your intestinal tract) or intravenous nutrition in the past 3 months? Yes/No. Please specify why you had this type of nutrition and for how long:

_____

_____

_____

How much alcohol do you drink in a typical week?

None (please circle if appropriate)

Beer _____ pints

Cider _____ pints

Wine _____ bottles

Spirits _____ bottles

For how many years has this level of drinking been typical?

_____

Medical History:

Have you ever had gastrointestinal surgery e.g. bowel resection, bariatric surgery? Yes/No. If yes, please specify:

_____

_____

Do you suffer from any of the following?

Coeliac Disease. Yes/No.

Cystic Fibrosis. Yes/No.

Short Bowel Syndrome. Yes/No.

Chronic Diarrhoea. Yes/No

Any other digestive or malabsorption condition (please specify):

_____

_____

Peripheral neuropathy. Yes/No.

Myeloneuropathy. Yes/No.

Spasticity. Yes/No.

Any other neurological condition (please specify):

_____

_____

Any visual impairment (please specify):

_____

_____

Wilson's Disease. Yes/No.

Menkes Disease. Yes/No.

Have you ever been diagnosed with any other conditions of copper metabolism? Yes/No. If yes, please specify:

_____

_____

Many thanks for any information you have provided and for your participation in our study.