

Standard population screening for diabetes mellitus has low sensitivity in identifying diabetes in adult survivors of childhood bone marrow transplantation with total body irradiation

Christina Wei ^{1,2,3}, Rebecca Unsworth ¹, Nikki Davis ^{1,2,4}, Karin Bradley^{2,5}, Rachel Cox ¹, Michael Stevens ^{1,2}, Elizabeth Crowne ^{1,2}

1. Bristol Royal Hospital for Children, 2. University of Bristol, 3. St Georges Hospital, St Georges Health Care NHS Trust, 4. University Hospital Southampton NHS Foundation Trust, 5 Bristol Royal Infirmary.

Background

Adult survivors of childhood leukaemia treated with bone marrow transplantation and total body irradiation (BMT/TBI) have an increased risk of developing diabetes mellitus ¹. Guidance on the appropriate method of screening for diabetes in these survivors is lacking.

In the U.K., the National Institute of Clinical Excellence (NICE) guidelines recommend the use of fasting glucose (FG) levels and glycated haemoglobin (HbA1c) to identify patients with diabetes and those at increased risk in the general population (table 1) ²

Table 1: NICE definitions of diabetes and increased risk of diabetes

Diagnosis	Fasting glucose	HbA1c
Diabetes	>7mmol/L	>48 mmol/mol (6.5%)
High risk of diabetes	5.5-6.9mmol/L	42-47mmol/mol (6-6.4%)

However, individuals with reduced peripheral insulin sensitivity or abnormal insulin secretion due to pancreatic beta-cell dysfunction, but relatively normal hepatic insulin sensitivity, may exhibit post-prandial hyperglycaemia with normal fasting glucose levels ³. In addition, HbA1c assumes normal red blood cell turn over and may not be an accurate measure in some patients with chronic ill health.

Objectives

To evaluate the sensitivity of the U.K. national screening criteria in the diagnosis of diabetes in survivors of childhood BMT/TBI.

Methods & Materials

Subjects:

- 37 (Male =19) BMT/TBI survivors
- Single UK tertiary Paediatric Oncology centre, 2006-2013.
- Mean age (SD): 18.9 (3.1)years
- Diagnosis:
 - acute lymphoblastic leukaemia (n=31)
 - acute myeloid leukaemia (n=6)
- Mean age at BMT/TBI: 7.9 (3.8) years of age

Outcome measures:

- Demographic and treatment details
- Oral Glucose Tolerance test (OGTT)
 - Fasting glucose at baseline
 - Post stimulated glucose at 120 minutes
- HbA1c
- Prevalence of
 - Hypertension (>130/85)
 - Hypertriglyceridaemia (>1.7mol/L)
 - Reduced high density lipoprotein (HDL) (M<1.03,F<1.29 mmol/L).

Results

Results of OGTT :

- Diabetes Mellitus (120 minute glucose > 11.1 mmol/L): n=6 (16%)
- Impaired glucose tolerance (120 minute glucose >7.8-11.0 mmol/L): n=13 (35%)
- BMT/TBI survivors have high cardiometabolic risk
 - Hypertension (16%), hypertriglyceridaemia (62%), reduced HDL (35%)

References

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Results

Questions:

1) Do the NICE criteria detect the patients with diabetes identified by OGTT ?

a) Using NICE criteria of **FG >7 mmol/L and/or HbA1c >48mmol/mol (6.5%)**

Diabetes on OGTT	FG>7 mmol/L and/or HbA1c >48 mmol/mol (6.5%)*			
	Yes	No	Sensitivity	33%
Yes	2	4	Specificity	100%
No	0	28		

b) Using NICE lower cut off for patients at high risk: **FG ≥ 5.5mmol/L**

Diabetes on OGTT	FG ≥ 5.5 mmol/L			
	Yes	No	Sensitivity	50%
Yes	3	3	Specificity <td>97%</td>	97%
No	1	30		

c) Using NICE lower cut off for patients at high risk: **HbA1c ≥ 42 mmol/mol (6%)**

Diabetes on OGTT	HbA1c ≥ 42 mmol/mol (6%)*			
	Yes	No	Sensitivity	33%
Yes	2	4	Specificity <td>96%</td>	96%
No	1	27		

2) Do the NICE criteria detect the patients at risk of diabetes with impaired glucose tolerance identified by OGTT?

a) Using NICE lower cut off for patients at high risk: **FG ≥ 5.5mmol/L**

IGT on OGTT	FG ≥ 5.5 mmol/L			
	Yes	No	Sensitivity	8%
Yes	1	12	Specificity <td>100%</td>	100%
No	0	18		

b) Using NICE lower cut off for patients at high risk: **HbA1c ≥ 42 mmol/mol (6%)**

IGT on OGTT	HbA1c ≥ 42 mmol/mol (6%)*			
	Yes	No	Sensitivity	0%
Yes	0	10	Specificity <td>94%</td>	94%
No	1	17		

* 3 patients with no HbA1c were excluded

Conclusions & discussion

- BMT/TBI survivors have a high metabolic risk with increased prevalence of diabetes mellitus, impaired glucose tolerance, hypertriglyceridaemia, reduced HDL and hypertension.
- Diabetes mellitus:
 - Standard NICE screening criteria with FG ≥ 7 mmol/L and HbA1c ≥ 48 mmol/mol will miss 67% of those with diabetes.
 - 50% and 66% of patients with diabetes did not even fulfill the criteria for the NICE high risk of diabetes group according to HbA1c (>42 mmol/mol) and FG (<5.5 mmol/L) respectively
- Impaired glucose tolerance:
 - The NICE criteria of FG ≥5.5mmol/L identified 8% and HbA1c ≥ 42 mmol/mol identified none of those with impaired glucose tolerance identified by OGTT.
- Recommendations
 - Diabetes screening in BMT/TBI survivors requires use of standard OGTT although the optimal frequency needs ongoing evaluation.
 - If an OGTT is not always feasible, it would be preferable to perform a FG rather than a HbA1c, as FG is more sensitive for detecting patients with diabetes or impaired glucose tolerance.

Acknowledgements: The study was funded by the IPSEN clinical research fellowship, BSPED research Award, David Telling Research funds, Peel Medical research award, NIHR feasibility & sustainability funds.