

Blood copper and arsenic levels and the occurrence of colorectal cancer

Piotr Baszuk^{1,2,*}, Paulina Stadnik¹, Wojciech Marciniak^{1,2}, Róża Derkacz^{1,2}, Anna Jakubowska¹, Cezary Cybulski^{1,2}, Tomasz Huzarski^{1,2,3}, Jacek Gronwald^{1,2}, Tadeusz Dębniak¹, Katarzyna Białkowska¹, Magdalena Muszyńska^{1,2,3}, Sandra Pietrzak¹, Józef Kładny⁴, Rodney J. Scott^{5,6,7}, Steven A. Narod^{8,9}, Jan Lubiński^{1,2}, Marcin R. Lener¹.

1. International Hereditary Cancer Center, Department of Genetics and Pathology, Pomeranian Medical University in Szczecin, ul. Unii Lubelskiej 1, 71-252 Szczecin, Poland.
2. Read-Gene, Grzeczynica, ul. Alabastrowa 8, 72-003 Grzeczynica, Dobra (Szczecińska), Poland.
3. Department of Clinical Genetics and Pathology, University of Zielona Góra, ul. Zyty 28, 65-046 Zielona Góra, Poland.
4. Department of General Surgery and Surgical Oncology, First Clinical Hospital of Pomeranian Medical University in Szczecin, ul. Unii Lubelskiej 1, 71-252 Szczecin, Poland.
5. Priority Research Centre for Cancer Research, Innovation and Translation, Hunter Medical Research Institute, New Lambton Heights, NSW 2308, Australia.
6. School of Biomedical Sciences and Pharmacy, Faculty of Health and Medicine, University of Newcastle, Callaghan, NSW 2308, Australia.
7. Division of Molecular Medicine, Pathology North, John Hunter Hospital, New Lambton, NSW 2305, Australia.
8. Women's College Research Institute, Toronto, ON M5G 1N8, Canada.
9. Dalla Lana School of Public Health, University of Toronto, Toronto, ON M5T 3M7, Canada.

*Speaker

Abstract:

Colorectal cancer is one of the most common types of cancer in both men and women. There are several approaches to detect early colorectal cancer including testing relevant markers in stool or blood (proteins; DNA; mRNA and long non-coding RNA; microRNA; metabolites, gut microbiome and platelets) as well as algorithms using machine learning techniques. Invasive methods of early detection of colorectal cancer include: colonoscopy, sigmoidoscopy and colonography based on computed tomography. There is a need to identify new markers for early detection of colorectal cancer. The influence of elements and inherited changes in genes on cancer risk and incidence has been one of the issues studied in the last decades.

In this study we examined whether blood arsenic and/or copper levels combined with specific polymorphisms can be used as a marker for colorectal cancer detection.

A retrospective case-control studies were performed among 187 colorectal cancer patients and 187 matched controls. All participants provided written informed consent to be enrolled into the following study. Information about: age, sex, smoking status and familial aggregation of cancer was obtained from all participants. All diagnosed participants were asked about additional clinical data related with colorectal cancer. From each study participant pre-treatment peripheral blood was collected for arsenic and copper level measurements using inductively coupled-plasma mass spectrometry (ICP-MS) and for genotyping. Selected variants in ten genes were genotyped: rs13181 in *ERCC2*, rs1799782 in *XRCC1*, rs7191779 in *MTIB*, rs1695 in *GSTP1*, rs2032582 in *ABCBI*, rs1800566 in *NQO1*, rs12915189 in *CRTC3*, rs1050450 in *GPXI*, rs4880 in *SOD2*, and rs1001179 in *CAT*.

According to the study results – a low blood arsenic level (0.27–0.67µg/L) was associated with an increased frequency of colorectal cancer among women (OR: 3.69; $p=0.005$). This correlation was significantly greater among women carrying functional polymorphisms: *CAT* rs1001179–nonCC (OR: 19.4; $p=0.001$); *ABCBI* rs2032582–CC (OR: 14.8; $p=0.024$); *GPXI* rs1050450–CC (OR: 11.6; $p=0.002$) and *CRTC3* rs12915189–nonGG (OR: 10.3; $p=0.003$).

As a result of the research performed, it was also observed that high blood copper level (931–2 043µg/L) is associated with an increased incidence of colorectal cancer (OR: 12.7; 95% CI: 4.98–32.3; $p<0.001$). This correlation was significantly greater among study participants carrying particular gene variants: *ABCBI* rs2032582–nonCC (OR: 33.7; 95% CI: 4.04–281; $p=0.001$); *MTIB* rs7191779–nonGG (OR: 16.6; 95% CI: 3.32–83.4; $p<0.001$); *CAT* rs1001179–CC (OR: 16.1; 95% CI: 3.68–70.7; $p<0.001$); *SOD2* rs4880–nonGG (OR: 15.9; 95% CI: 3.27–77.0; $p<0.001$); *GSTP1* rs1695–nonAA (OR: 15.9; 95% CI: 1.54–164; $p=0.02$) and *XRCC1* rs1799782–CC (OR: 15.6; 95% CI: 5.00–48.5; $p<0.001$).

Based on above studies it can be stated that blood arsenic and copper level measurements can be valuable marker in order to select patients for further colorectal cancer diagnostics. Selection effect for colorectal cancer diagnosis can be stronger among individuals with particular gene polymorphisms.