COACTION PUBLISHING

The impact of anti-diabetic drugs on colorectal cancer risk in a large cohort of women with diabetes

In order to investigate whether an association between anti-diabetic drugs and the risk of colorectal cancer exists in women with diabetes mellitus (DM) in Taiwan, we designed a population-based cohort study using data from Taiwan National Health Insurance Database. There were 19,863 women aged 20 or older with newly diagnosed DM (International Classification of Diseases (ICD) 9th Revision, ICD-9 codes 250 and A181) and currently using anti-diabetic drugs in 2000–2007 (mean age 54.5 years, standard deviation 12.9 years, and age range 20–93). The index date for each case was defined as the date of diagnosis of colorectal cancer. Subjects diagnosed with cancer before the index date were excluded from the study.

After adjusted for covariates, Cox proportional hazard analysis showed that the hazard ratios (HR) of colorectal cancer were 3.56 (95% CI = 2.02–6.72) in women with ever-use of sulfonylureas and 0.42 (95% CI = 0.28–0.64) in women with ever-use of metformin compared with the non-use group (Table 1).

There is a growing body of evidence to show that metformin is associated with a substantially decreased risk of cancers (1–4). In Decensi et al.'s meta-analysis, a 31% reduction of overall cancer risk (95% CI = 0.61–0.79) is found in patients using metformin compared with the other anti-diabetic drugs (2). The present study also showed women with ever-use of metformin could have a 58% reduced risk of colorectal cancer. Three studies in Japan recently have also revealed the effect of metformin on suppressing colonic epithelial proliferation in mice and in humans, and further inhibiting colorectal carcinogenesis (5–7). The authors suggest that metformin may play a promising role in the chemoprevention of colorectal cancer (5–7).

A retrospective cohort study by Currie et al. in UK (8) revealed that sulfonylurea monotherapy could increase 1.8-fold risk of colorectal cancer (95% CI = 1.29–2.53). In the present study, women with ever-use of sulfonylureas increased 3.6-fold risk of colorectal cancer. Previous studies have supported the hypothesis that hyperinsulinemia may play a key role in colorectal carcinogenesis

Table 1. Cox model hazard ratios (HR) and 95% confidence intervals (CI) of colorectal cancer associated with anti-diabetic drugs and covariates, 2000–2007

Variable	Crude HR	95% CI	Adjusted HR	95% CI
Age group (years)				
20–39	1.00	–	1.00	–
40–64	3.10	0.97–9.90	2.74	0.86–8.77
≥65	6.24	1.94–20.04	5.19	1.61–16.71
Medications				
Sulfonylureas (ever-use vs non-use)	2.47	1.45–4.20	3.56	2.02–6.72
Metformin (ever-use vs non-use)	0.63	0.43–0.93	0.42	0.28–0.64
Insulins (ever-use vs non-use)	0.75	0.38–1.48	–	–
Thiazolidinediones (ever-use vs non-use)	0.88	0.54–1.48	–	–
Alpha-glucosidase inhibitors (ever-use vs non-use)	0.92	0.56–1.51	–	–
Aspirin (ever-use vs non-use)	1.05	0.70–1.57	–	–
Other non-steroidal anti-inflammatory drugs (ever-use vs non-use)	1.25	0.46–3.40	–	–
Statins (ever-use vs non-use)	1.21	0.83–1.76	–	–
Co-morbidities				
Obesity (yes vs no)	1.07	0.26–4.33	–	–
Colorectal adenomas (yes vs no)	1.76	0.25–12.61	–	–
Inflammatory bowel diseases (yes vs no)*	–	–	–	–
Alcoholism (yes vs no)*	–	–	–	–

*No case was found

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(8–10). Because sulfonylureas can stimulate secretion of insulin, it may partially explain why patients using sulfonylureas are at an elevated risk of colorectal cancer.

Because the mechanism of anti-diabetic drugs on the risk of colorectal cancer remains unproven, more prospective intervention trials are required to definitively address this issue.

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