Effect of insulin therapy and obesity on colon adenoma and advanced adenoma among type II diabetes mellitus population

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Abstract

Insulin is a debatable risk factor for colon adenoma (Ad) among type II diabetes mellitus (DM II) patients. Obesity is an important confounding variable. The study involved chart review of DM II patients undergoing screening colonoscopy. Study population was divided into obese [body mass index (BMI) ≥30] and non-obese (BMI <30) groups which were further divided into insulin and non-insulin subgroup. Colonoscopy and pathology reports were used to calculate Ad detection rate (ADR) and AAd detection rate (AADR). A total of 538 subjects satisfied the inclusion and exclusion criteria. The study population composed of 52.8% obese and 47.2% non-obese subjects. Obese group had 28.9% insulin and 71.1% non-insulin subjects. Non-obese group composed of 29.9% insulin and 70.1% non-insulin subjects. ADR for non-obese insulin and non-insulin subgroup was 31.6% and 37.1% respectively. AADR for non-obese insulin and non-insulin subgroup was 13.2% and 11.2% respectively. ADR for obese insulin and non-insulin subgroup was 41.5% and 34.2% respectively. AADR for obese insulin and non-insulin subgroup was 15.9% and 16.3% respectively. Insulin exposure lacked statistically significant association with ADR or AADR among obese and non-obese DM II subjects.

Introduction

Colorectal cancer (CRC) is a result of malignant growth of epithelial cells of colon or rectum. Over 95% of CRC are believed to arise in benign adenomatous polyps that grow very slowly over many years.1 Disrupting the classic adenoma-carcinoma sequence by polypectomy is the basis for offering screening colonoscopy to reduce the incidence of CRC.

There are multiple known risk factors for adenomatous colon polyps. Some of the risk factors like age (>50 years in general and >45 years for African Americans), race (African American), gender (male), dietary habits (red meat), lifestyle (sedentary/smoking/alcohol), past medical history of polyps/CRC/inflammatory bowel disease (IBD), syndromes like familial adenomatous polyposis (FAP)/hereditary non-polyposis colorectal cancer (HNPPC) and family history of CRC have been proven to increase the risk of adenoma (Ad) and CRC and therefore are taken into account before planning CRC screening strategy for patients.2,3 Other factors like, obesity, diabetes mellitus (DM), insulin exposure have been debated over last few years and the evidence is not strong enough to have an impact on the current CRC screening and surveillance guidelines.2,3

The type II DM (DM II) population has been shown to have a higher incidence of colon Ad and advanced adenoma (AAd) related to endogenous hyperinsulinemia and high levels of insulin growth factor-1 (IGF-1).4-7 Few studies have shown positive correlation between exogenous insulin exposure and colon Ad among the DM II population.8 But none of these studies took obesity into consideration which we think is an important confounding variable in the interpretation of above study results.

The prevalence of overweight [body mass index (BMI) between 25 and 30 kg/m²] and obesity (BMI ≥30 kg/m²) is on rise worldwide.9 Consequently, DM II prevalence is expected to rise.2,3 There is 30-70% increased risk of colon cancer in men who are obese, whereas the association is less consistent in women.10 Similar trends exist for colorectal Ad, although the risk appears lower.10 There is evidence to suggest obesity as an independent risk factor for colon Ad, AAd and CRC.11,12

Materials and Methods

The objective of the study was to determine the effect of exogenous insulin exposure on colon Ad and AAd among DM II subjects after controlling for the effect of obesity.

The study had retrospective design and was conducted at an urban teaching hospital. The study was approved by the Institutional Review Board.

The inclusion criteria were: patients who underwent outpatient screening colonoscopy over a time span of 18 months. Screening Colonoscopy was defined as: i) patient 45 years of age or older; ii) absence of any gastrointestinal sign, or symptom(s); iii) absence of any personal history of colon cancer or polyps. The exclusion criteria were: i) family history (FH) of CRC; ii) past medical history (PMH) of CRC/FAP/HNPPC/IBD/colectomy; iii) incomplete colonoscopy (lack of cecum intubation); iv) poor quality of bowel preparation.

Study method

This was a retrospective study and no intervention or deviation from standard practice protocols for patients were done for the study purposes. It involved chart review of patients, who had undergone outpatient colonoscopy at our center over a time span of 18 months. A list of eligible patients with their names and medical record numbers was obtained from the medical records department. A study identifier was then given to each subject. The master list of eligible patients was deleted after data was collected and checked.

Each subject’s electronic medical record was reviewed to extract relevant data (age, gender, race, weight, height, DM II, Insulin use, PMH of CRC/FAP/HNPPC/IBD or FH of CRC). Weight and height of the individual subjects was used to calculate respective BMI. Colonoscopy reports of each subject were reviewed to collect data related to bowel preparation, indication for colonoscopy, cecum intubation, number and size of polyps. Inclusion and exclusion criteria were then applied to the initial population. Study population was divided into Obese...
A total of 538 subjects, with a mean age of 60.2 years and male to female ratio of 1:1.4 satisfied the inclusion criteria. The study population composed of 284 (52.8%) obese and 254 (47.2%) non-obese subjects. ADR for obese and non-obese group was 36.3% and 35.4% (P=0.66) (Table 3 and Figure 1). ADR for obese and non-obese subgroup was 13.2 and 11.2% respectively (P=0.40) (Table 3 and Figure 1). AADR for non-obese insulin and non-insulin subgroup was 15.9 and 16.3% respectively (P=0.92) (Table 4 and Figure 2).

**Results**

A total of 538 subjects, with a mean age of 60.2 years and male to female ratio of 1:1.4 satisfied the inclusion criteria. The study population composed of 284 (52.8%) obese and 254 (47.2%) non-obese subjects. ADR for obese and non-obese group was 36.3% and 35.4% respectively. AADR for obese and non-obese type II diabetes mellitus group had 82 (28.9%) insulin and 202 (71.1%) non-insulin subjects. Non-obese group composed of 76 (29.9%) insulin and 178 (70.1%) non-insulin subjects. Baseline population characteristics for insulin and non-insulin subgroups of non-obese and obese groups have been summarized in Table 1 and 2 respectively. ADR for non-obese insulin and non-insulin subgroup was 31.6 and 37.1% respectively (P=0.24) (Table 4 and Figure 2).

**Statistical analysis**

Microsoft Office for MAC (version 2011) was used to analyze data. Chi-square (for Race and Gender) and Mann-whitney U test (for Age and BMI) was used to compare baseline population characteristics across insulin and non-insulin subgroups of obese and non-obese category. ADR and AADR for subgroups were compared using Chi-square tests. P value of less than 0.05 was used to determine statistical significance.
Discussion and Conclusions

Many observational studies have shown positive association between DM II and CRC.\(^1\) This association has been attributed to underlying hyperinsulinemia.\(^14,15\) In early stages of DM II, endogenous hyperinsulinemia is seen in response to peripheral insulin resistance.\(^14\) Insulin raises serum IGF-1 level, which is a regulator of growth and is known to play an important role in carcinogenesis through regulating cell proliferation and apoptosis.\(^16\) Conditions with high circulating levels of IGF-1, such as acromegaly, have been associated with an increased risk of CRC.\(^17\) The association between IGF-1 and adenomatous polyps is well supported.\(^18-21\)

With growing evidence for reduction in micro-vascular complications with earlier introduction of insulin therapy,\(^22,23\) there is a rapid increase in proportion of diabetics on insulin. Among patients with DM II, exogenous insulin therapy augments the endogenous insulin production, as shown by 24-hour plasma insulin levels.\(^24\) Chung and colleagues reported a 3-fold increase in colorectal Ad risk in patients with at least one year of insulin therapy in a Korean-based population.\(^25\) Schoen and colleagues, reported that the association between insulin and IGF-1 levels and colorectal Ad is more pronounced among AAd compared.\(^21\) Furthermore, subjects with high fasting blood sugar and fasting insulin levels have been reported to have higher odds for colorectal adenoma.\(^26,27\)

In last 20 years, the obesity prevalence has risen dramatically in the United States and other developed countries.\(^28,29\) Abdominal obesity, such as acromegaly, has been associated with an increased risk of CRC.\(^30\) The association between IGF-1 and adenomatous polyps is well supported.\(^18-21\)

Table 3. Adenoma detection rate and advanced adenoma detection rate for insulin and non-insulin subgroup of non-obese type II diabetes mellitus group [non-obese (BMI<30 Kg/m\(^2\)) (N=254)].

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Insulin subgroup (N=76)</th>
<th>Non-insulin subgroup (N=178)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma, N (%)</td>
<td>24 (31.6)</td>
<td>66 (37.1)</td>
<td>0.400</td>
</tr>
<tr>
<td>Advanced adenoma, N (%)</td>
<td>10 (13.2)</td>
<td>20 (11.2)</td>
<td>0.667</td>
</tr>
</tbody>
</table>

Table 4. Adenoma detection rate and advanced adenoma detection rate for insulin and non-insulin subgroup of obese type II diabetes mellitus group [obese (BMI≥30 Kg/m\(^2\)) (N=284)].

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Insulin subgroup (N=82)</th>
<th>Non-insulin subgroup (N=202)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma, n (%)</td>
<td>34 (41.5)</td>
<td>69 (34.2)</td>
<td>0.246</td>
</tr>
<tr>
<td>Advanced adenoma, n (%)</td>
<td>13 (15.9)</td>
<td>33 (16.3)</td>
<td>0.920</td>
</tr>
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</table>

References


