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Incretin-based treatments and cancers of digestive system among patients with type 2 diabetes mellitus: a systematic review and network meta-analysis

Sanbao Chai, Shuqing Yu, Zhirong Yang, Shanshan Wu, Le Gao, Haining Wang, Yuan Zhang, Siyan Zhan, Linong Ji, Feng Sun

Citation

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Review question

To evaluate the risk of cancers of digestive system with incretin-based therapies among patients with type 2 diabetes mellitus.

Searches

MEDLINE, EMBASE and the Cochrane Library were searched from inception through June 23rd, 2017. The limited language is English.

The following search strategy for Ovid-MEDLINE was adapted for other databases:

1.exp (DPP-4 inhibitors or dipeptidyl peptidase 4 inhibitor or glucagon-like peptide-1 agonists)/

2.(DPP-4 or dipeptidyl peptidase 4 or glucagon like peptide* or GLP-1).tw.

3.(exenatide or liraglutide or albiglutide or taspoglutide or lixisenatide or dulaglutide).tw.

4.(Victoza or Byetta or Bydureon).tw

5.(januvia or juvisync or janumet or galvus or equatablets or eucreas or onglyza or kombiglyzexr or nesina or liovel or ondero or jentadueto).tw.

6.(sitagliptin or vildagliptin or saxagliptin or alogliptin or linagliptin or teneligliptin or anagliptin or gemigliptin or trelagliptin).tw.

7.randomized controlled trial.pt.

8.(randomized or randomised).tw.

9.(diabetes mellitus, type 2).sh.

10.(1 or 2 or 3 or 4 or 5 or 6) and (7 or 8) and 9

Types of study to be included

Randomized controlled clinical trials

Condition or domain being studied

Incretins are gut peptides which can augment nutrient-stimulated insulin secretion after dietary intake. Incretin-based therapies include incretin mimetics of glucagon-like peptide-1 receptor agonists and incretin enhancers of dipeptidyl peptidase 4 inhibitors. With the widespread use of these drugs, there are concerns about the safety of the digestive tract. Clinical studies completed thus far are insufficient to confirm or exclude an increased long-term risk of cancers of digestive system with incretin-based therapies. Therefore,

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we conducted a meta-analysis by investigating all randomized controlled clinical trials to evaluate cancer risk of digestive system related with incretin-based therapies in patients with type 2 diabetes mellitus.

Participants/population
Patients with type 2 diabetes mellitus. There are no other restrictions.

Intervention(s), exposure(s)
Analysis of gastrointestinal tumors in all randomized controlled clinical trials studies involving incretin-based therapy.

Comparator(s)/control
Placebo and other traditional anti-diabetic drugs (e.g.Metformin, Insulin, Sulfonylurea, hiazolidinediones and so on).

Context

Main outcome(s)
Incidence of gastrointestinal tumors

Timing and effect measures

Additional outcome(s)
None

Timing and effect measures

Data extraction (selection and coding)
Three investigators will extract data independently in duplicate. Any disagreement will be resolved by consensus. The data being extracted will included the incidence of gastrointestinal tumors and the baseline characteristics of the study to be included.

Risk of bias (quality) assessment
Risk of bias of included studies was assessed according to Cochrane risk of bias tool.

Strategy for data synthesis
Quantitative synthesis based on aggregate data is planned. For traditional meta-analysis, the pooled OR and 95% confidence interval (95% CI) of incidence of digestive system cancer will be calculated by random-effects model. I^2 is used to describe the heterogeneity between pair-wise comparisons. For network meta-analysis, we will use the frequentist framework to perform a random effect network meta-analysis. Pooled OR and 95% CI will be also summarized. Next we will estimate the ranking probabilities of each treatment being at order. To assess the publication bias, a comparison-adjusted funnel plot will be used to detect the small-study effects. Finally, we will check the assumptions in the NMA including inconsistency and heterogeneity. We will use STATA 13.1 and R 3.5.0 software for the above analysis.

Analysis of subgroups or subsets
We will conduct meta-regression by baseline FPG, age, BMI and so on.

Contact details for further information
Sanbao Chai
chaisb@126.com

Organisational affiliation of the review
Peking University International Hospital

Review team members and their organisational affiliations
Dr Sanbao Chai. Peking University International Hospital
Ms Shuqing Yu. Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Centre
Ms Zhirong Yang. Primary Care Unit, School of Clinical Medicine, University of Cambridge

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Dr Shanshan Wu. National Clinical Research Center of Digestive Disease, Beijing Friendship Hospital, Capital Medical University
Ms Le Gao. Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Centre
Professor Haining Wang. Department of Endocrinology and Metabolism, Peking University Third Hospital
Dr Yuan Zhang. Department of Clinical Epidemiology and Biostatistics, McMaster University
Professor Siyan Zhan. Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Centre
Professor Linong Ji. Department of Endocrinology and Metabolism, Peking University People's Hospital
Professor Feng Sun. Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Centre

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Conflicts of interest

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English

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China

Stage of review
Review_Ongoing

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Subject indexing assigned by CRD

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Diabetes Mellitus, Type 2; Digestive System; Humans; Incretins; Neoplasms; Network Meta-Analysis

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Details of any existing review of the same topic by the same authors

Stage of review at time of this submission

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Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Versions

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