Letter

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The Risk of Bladder Cancer in Korean Diabetic Subjects Treated with Pioglitazone (*Diabetes Metab J* 2012;36: 371-8)

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Dear Editor,

Ever since prospective pioglitazone clinical trial in macrovascular events (PROactive), the very first large randomized trial of pioglitazone, published in 2005 [1], whether this antihyperglycemic agent could increase the risk of bladder cancer was debated by diabetologists and pharmacologists. Despite lack of support from molecular mechanism, several cohorts observed the association between long term application of pioglitazone and the bladder cancer risk [2,3]. Recently, a nested case-control study provided by Azoulay et al. [4] also indicated bladder cancer risk increased 1-fold after 2-year usage of pioglitazone. It appeared no doubt that bladder cancer should be caused by this agent. However, no rational explanation was given by investigators.

In the current study by Song et al. [5], an obviously lower prescription of pioglitazone was reported in diabetic patients with bladder cancer compared with those bladder cancer-free ones (6.4% vs. 15%). Interestingly, the adjusted odds ratio (OR) of bladder cancer incidence was 2.09, which was almost the same with previous reports [1-4], despite failed to reach statistical significance in the current population. This result brought us two questions: Why was the prescription of pioglitazone in diabetic patients with bladder cancer so low compared with controls? What made the result of such difference between the results from univariate and multivariate statistics? As the risk of pioglitazone has been reported for years since 2005 [1], diabetologists all over the world may have already noticed the risk of this agent, and have a mind to prevent the usage in real clinical practice if a patient has a high risk of cancer. Furthermore, a potential selective bias could be hardly prevented in the design of matched case-control study. For the second question, it appears that the multivariate model in the study perfectly adjusted for all potential confounding biases, and the adjusted OR just gave the 'true' risk like previous studies. Among the adjusted factors, co-existing neoplasm would a potential bias, and the reason was mentioned above. However, it required further analysis of the original data to determine whether it is really the very one that explained such difference between the results from univariate and multivariate statistics. It could be of interest that might tell us why there was little prescription of diabetic patients with bladder cancer, and help us understand if it is really pioglitazone which lead to the cancer of urinary bladder.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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