Brief Communication

Usage of pioglitazone at Medanta, the Medicity

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ABSTRACT

Pioglitazone improves glycemic control by acting as an insulin sensitizer and is used in the management of Type 2 diabetes mellitus. Pioglitazone has recently been at the center of a controversy with regards to its safety. There is no clear consensus on how, when and in what dose the drug should be used in the management of diabetes. We have summarized our strategy on pioglitazone use in Type 2 diabetes in a large private tertiary care center - Medanta, the Medicity- which may help in generating further thought about positioning of this anti-diabetic molecule. We use pioglitazone as the fourth in the pecking order of oral anti-diabetic agents. We typically use pioglitazone in a dose of 15 mg/day. We avoid using pioglitazone with insulin. We do not use pioglitazone under following situations: In the presence of significant or proven cardiac disease, in patients who are struggling with their weight or need to lose weight, in patients at high risk for osteoporotic fractures, in patients with macular edema, in patients with pre-existing bladder cancer and would discontinue in case hematuria or any other symptom of bladder cancer develops. We continue to use the drug in patients well controlled on it without any evident side-effects or contraindications.

Key words: Pioglitazone, type 2 diabetes, medanta

Introduction

Recently there has been a lot of controversy generated over the positioning and use of pioglitazone in India. Sudden banning of the molecule and subsequent revocation of the ban has left many prescribers and patients confused about its actual usage. There is no clear consensus on how, when and in what dose the drug should be used in the management of diabetes. Different countries and associations have taken varying positions on its place in therapy.[1] Overall, however, the usage of thiazolidinediones has declined globally ever since the rosiglitazone fiasco. They are no longer the darling of endocrinologists and cardiologists -as was the case a decade ago.

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.126588

At Medanta Medicity, which has a large diabetes and endocrine service (>300 out-patient and inpatient visits daily) we do use pioglitazone, but its use is limited to some specific situations. The following points enumerate our strategy for use of pioglitazone. This is just the opinion of our group and does not in any way attempt to be a guideline for our expert colleagues, but maybe it will help in generating further thought about positioning of this anti-diabetic molecule.

1. We use pioglitazone as the fourth in the pecking order of oral anti-diabetic agents. It is used after metformin, incretin-based therapies and sulphonylureas. Since we almost never use four oral agents, pioglitazone is used if any of the first three cannot be used either because of contraindications, side-effects or economic reasons. One example of where we use pioglitazone is the lean type 2 diabetic who is losing weight with metformin and is unwilling to take insulin.
2. We typically use pioglitazone in a dose of 15 mg/day. We avoid higher doses and have virtually no experience with lower doses like 7.5 mg.
3. We avoid using pioglitazone with insulin because of increased risk of fluid retention.
4. We do not use pioglitazone in the presence of significant

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or proven cardiac disease - certainly not in the presence of heart failure, but even otherwise because of fear of water retention and aggravating/precipitating failure.[2] Our cardiologists concur with this. A substantial proportion of our diabetic patients fall in this group.

5. We do not use pioglitazone in patients who are struggling with their weight or need to lose weight. Another large chunk of North Indian/Delhi patients belong to this category.
6. We do not use pioglitazone in patients at high risk for osteoporotic fractures – typically postmenopausal women, but also others who are at high risk such as elderly men.[3] Such patients also form a substantial proportion of our patient population.
7. We do not use pioglitazone in patients with macular edema.
8. We explain to the patient about the possibility of weight gain and water retention. So far we have not been discussing bladder cancer with our patients since the jury is still out.[4-5] However, "discussing" bladder cancer is tantamount to not prescribing the drug as no patient will agree to take a drug, which has the word "cancer" associated with it, even remotely. (Remember what happened to hormone replacement therapy? despite no data on younger postmenopausal women, it was junked overnight! Now it is trying to make a comeback). Our prescribing patterns have not been majorly influenced by bladder cancer as yet. Obviously we do not use the drug in patients with pre-existing bladder cancer and would discontinue in case hematuria or any other symptom of bladder cancer develops (we have not seen this so far). If current and past smokers are excluded too (we are not doing so at present), as suggested in the government notification, another large chunk of patients will be excluded. A large observational study in India is required regarding bladder cancer, but will be extremely hard to carry out.
9. We do not discontinue the drug in patients well controlled on it without any evident side-effects or contraindications. If we do plan to discontinue pioglitazone, we do it gradually with introduction or up titration of other anti – diabetic agents. Sudden withdrawal results in high blood glucose values and the full impact of withdrawing pioglitazone may not be evident for a couple of weeks.
10. We feel that the use of pioglitazone in triple drug combinations should be restricted to those who actually require all three drugs and not as a single tablet to initiate therapy, which is how it is commonly prescribed in India.

Given the aforementioned criteria, a limited number of patients in our clinical practice are actually initiated on pioglitazone since it is possible that some of our concerns may be reduced with the use of low-dose pioglitazone (7.5 mg), as observed by some colleagues, we feel that a well-designed study comparing efficacy of different doses is called for so that it can be firmly established if Indians respond well and with less/minimal side-effects to 7.5 mg pioglitazone as compared with higher doses. We also need to know more about the beneficial pleotropic effects of pioglitazone – whether they still occur at low-doses. The low cost and proven anti-hyperglycemic efficacy of pioglitazone make it an attractive option for some patients, so we need to prove this – either way.

We understand that some of our colleagues use pioglitazone more frequently and particularly earlier in the course of disease with the aim of preserving beta cells. Others use it commonly in cardiac patients with preserved ejection fraction to make use of the proposed pleiotropic cardioprotective effects of the drug. We also know that some of our colleagues do not use it all for fear of bladder cancer.

We believe that that pioglitazone has a role in diabetes management although it is limited to selected patients. The future of this molecule will depend on further data regarding bladder cancer.

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Cite this article as: Mithal A, Kaur P, Bansal B, Mishra SK, Wasir JS, Jevalikar G, Mahendru S. Usage of pioglitazone at Medanta, the Medicity. Indian J Endocr Metab 2014;18:111-2.

Source of Support: Nil, **Conflict of Interest:** None declared.