

continuous subcutaneous insulin infusion and insulin pumps, but these are relatively costly, and being significantly different molecules/modes of administration comparison with the earlier insulins is no longer strictly comparison of like with like.

At the recent APICON meeting in Kolkata, 2012, I shared notes with several diabetologists and they also have anecdotally confirmed an increase in average insulin requirements, and I would therefore suggest that a formal documentation of average daily total insulin requirements be analysed from clinic data at various centres.

I had earlier in a letter to your esteemed journal called attention to possible pancreatotoxic chemical/microorganismal factors due to environmental degradation (pollutants/pesticides) as possible factors in India's Diabetes explosion, and also to the markedly increased frequency of pancreatitis in the general patient population in North India including nondiabetics. It is possible that these or similar factors may be driving the increased insulin requirements observed in NIDDM therapy. Factors increasing Insulin resistance over the last 40 years would also need consideration. HOMA or similar model analysis of patients to document beta cell dysfunction and insulin resistance in the same patients would be invaluable, if data were available.

### Reference

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## Eight Cases of Bladder Cancer in Pioglitazone users from India

Sir

The peroxisome proliferator activator receptor gamma (PPAR-γ) agonist pioglitazone is commonly used worldwide for the treatment of type 2 diabetes. Recently, there has been some concern regarding the association of this agent with the development of bladder malignancy. A few retrospective studies, principally based on diabetes registries and adverse event reporting systems, have shown a small increase in the incidence of this form of malignancy in patients, particularly males, who are on pioglitazone.<sup>1</sup> These concerns have led to the suspension of marketing of pioglitazone in France and a recommendation to avoid initiating the drug on new patients in Germany. The USFDA has recommended that a warning be added to the drug prescribing information for pioglitazone in order to reflect this new concern.<sup>2</sup> To date, there have been no reports of bladder cancer among pioglitazone users in India. We report here, eight cases of bladder cancer from India in patients with type 2 diabetes on pioglitazone.

Three of the patients were from Chennai, two from Salem and one each from Belgaum, Hyderabad and Mumbai. Seven of the eight patients were males. The patients ranged in age from 43 years to 76 years. They all had type 2 diabetes and were on pioglitazone for periods ranging from two to nine years. The mean dose of pioglitazone ranged from 15 mg to 30 mg per day. While seven patients had transitional cell (urothelial) carcinoma on biopsy, the nature of malignancy was not clear in the eighth patient. Seven patients are presently on follow up with urologist and oncologist, whereas the eighth patient developed metastases to the liver and lungs and expired in November 2011 after several cycles of chemotherapy and two surgeries. The single female

patient developed bladder cancer seven years ago while on 30 mg of pioglitazone. She underwent surgery for the same in the U.S. and was declared free of malignancy. Since the link of pioglitazone with bladder cancer was not known at that time, she was continued on pioglitazone even after the surgery. She developed recurrence of haematuria and pain 4 months later and had to undergo repeat surgery and chemotherapy.

This is, to the best of our knowledge, the first report on bladder cancer among pioglitazone users in India and one of the first in a female patient. Although one cannot draw any conclusions of causality from these eight cases, the development of this relatively uncommon malignancy in eight patients who were on this particular drug does raise concern about the long term safety of pioglitazone. It is also of interest to note that these patients were on much lower doses of pioglitazone, compared to those from the U.S. studies. This raises the possibility that this particular adverse effect of pioglitazone may manifest at a lower dose in Indians compared to the western population, probably due to smaller body mass index or differences in ethnic susceptibility. Clinicians should therefore exercise extreme caution in the use of this drug. Patients should be made aware of this potential side effect of pioglitazone and should be allowed to make informed choices regarding its use. Finally, a nationwide pharmacovigilance study appears to be justified to see whether these cases of bladder cancer with pioglitazone use are just sporadic ones, or whether they represent the tip of the iceberg with many more unreported cases.

### References

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## Per Oral Endoscopic Myotomy for a patient with Achalasia cardia

Sir,

Achalasia cardia is a benign but debilitating primary esophageal motility disorder characterized by incomplete lower esophageal sphincter (LES) relaxation, increased pressure at the LES and failure of esophageal peristalsis. The clinical presentation is mainly with dysphagia, regurgitation and chest pain. Per Oral Endoscopic Myotomy (POEM) is a new addition in the treatment armamentarium of achalasia cardia.<sup>1</sup> To the best of our knowledge POEM procedure has not yet been reported from India.

We performed this procedure on a 52 years female. Patient was symptomatic for progressive dysphagia since 12 years.