Background: There is paucity of data on triple drug combination containing low dose (7.5 mg) pioglitazone in Indian type 2 diabetes patients (T2DM). Objective: Comparative evaluation of efficacy and safety of glimepiride, metformin (GM) plus low dose pioglitazone fixed dose combination (FDC) in T2DM. Material and methods: In this open label study, 75 insulin naïve T2DM subjects inadequately controlled on GM oral therapy were randomized into Group A: FDC of G 1mg + M 500 mg SR + Pioglitazone 7.5 mg; Group B: FDC of G 2mg + M 500 mg SR + Pioglitazone 7.5 mg or Group C: Insulin 70/30 Mix + M 500mg SR. The primary outcome measure was reduction in HbA1c at 180 days. The secondary end points included reduction in fasting plasma glucose (FPG), postprandial plasma glucose (PPG) and change in lipid parameters and weight. Results: At baseline mean age, weight, HbA1c, body weight, FPG, PPG, C peptide level, LDL-C, triglyceride and HDL-C were similar in three groups. All treatments resulted in significant reduction in mean HbA1c. At the end of 180 days, reduction in HbA1c was 1.49%, 1.51% and 1.11% in Group A, B and C respectively. The difference in HbA1c reduction between groups was not statistically significant. At the end of 180 days, the mean reduction in FPG was -66.72+27.12 mg/dl, -79.68+23.87 mg/dl and -69.60+25.34 mg/dl in Group A, B and C respectively. The difference in the reduction of FPG and PPG was not significant between the groups at day 30, 90 and 180. Significant reduction in LDL-C, TG and increase in HDL-C was observed in all groups without significant difference between the groups. No hypoglycemic episodes requiring hospitalization were observed in any group. Change in weight was comparable between groups. Conclusion: Metformin, glimepiride plus low dose pioglitazone FDC is equally efficacious and well tolerated compared to insulin plus metformin in uncontrolled T2DM. This combination may help in postponing insulin therapy.