International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.10 No.10, pp 356-360, 2017

Efficacy of Metformin In Obese young people In Secondary care: A Systematic Review And Meta-Analysis From Randomized Controlled Trials

Ram Kumar Sahu[1], Deepak Prashar[2]*

[1]Department of Pharmacy, Columbia Institute of Pharmacy, Raipur (CG), India
[2]Paher University, Udaipur (RJ), India

Abstract : Metformin is one among the premium medicine used in the treatment of NIDDM. The patients still feel comfortable utilizing the oral drugs instead of parenteral. Most of the time diabetes is associated with the co-morbidities. Among all those co-morbidities obesity is one. However, there are many young candidates getting obese but still devoid of diabetes. The present research work tries to highlight the efficacy of metformin in reducing the BMI in non-obese patients using Systematic and Meta-Analysis approach.
Keywords : Randomized controlled trials (RCTs), Metformin, Body Mass Index, Obesity.

Introduction

Metformin is an oral anti-hyperglycemic agent used for treating non-insulin-dependent diabetes mellitus (NIDDM). It improves glucose tolerance in patients by lowering both basal and postprandial plasma glucose. Metformin decreases blood glucose levels by decreasing hepatic glucose production, decreasing intestinal absorption of glucose, and improving insulin sensitivity by increasing peripheral glucose uptake and utilization. These effects are mediated by the preliminary activation by metformin of AMP-activated protein kinase (AMPK) enzyme in the liver. Utilization of metformin is allied with modest weight loss. Atabek and Pirgon[1] carried out a 6-month, randomized, double-blind, placebo-controlled clinical trial Using the metformin in obese adolescents with hyperinsulinemia. The results of the study suggested that metformin treatment is effective in reducing insulin resistance and also ameliorating metabolic complications of insulin resistance syndrome in obese adolescents with hyperinsulinemia. Freemark and Bursey[2] studied the effects of metformin on body mass index and glucose tolerance in obese adolescents with fasting hyperinsulinemia and a family history of type-II diabetes. Through their interventions they concluded that metformin is not so effective in reducing weight in persons with family history of type-II diabetes. Srinivasan *et al*[3] also carried a randomized, controlled trial of metformin for obesity and insulin resistance in children and adolescents. Yanovski *et al*[4] studied the effects of metformin on body weight and body composition in obese insulin-resistant children through a randomized clinical trial. Wiegand *et al*[5] too carried the similar type of placebo-controlled, randomized study with addition of previous unsuccessful lifestyle intervention. Kendall*et al*[6] carried a study to assess the effect of metformin on body mass index sd score (BMI-SDS), metabolic risk factors, and adipokines. The outcome of the study positively indicates the effect of metformin in weight reduction. Another study was carried by Burgert *et al*[7] to predict the short-term metabolic and cardiovascular effects of metformin in markedly obese adolescents with normal glucose tolerance. The conclusion of the study was the reduced BMI.

Materials and Methods

The current research work was carried on obese group without diabetes to investigate the efficacy of metformin for reducing BMI. The study was carried out through a systematic review of randomized controlled trials (RCTs). The databases like MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) along with the Meta Register of Controlled Trials, WHO clinical trials registry platform and the US Clinical trials registry was searched for RCTs published from 1996 to February 2015.The inclusion criteria involved the publications with double-blind randomized RCTs investigating the efficacy of met form in for BMI reduction in young people aged≤19 years without diabetes, with treatment duration≥6months. The open-label cross over trials and studies those published only in abstract form were excluded. The QUOROM (Quality of Reporting of Meta-analysis) guideline was used for carrying the present work.

Results

Total 862 publications were identified and 165 duplicate publications were initially excluded. 655 studies after title screening were too excluded which does not matches the study criteria.Further 34 articles were rejected after going through the abstract. Only 8 articles were included in the research. Those studies were included under research in which all trials lasted ≥6 months with metformin doses from 1,000-2000 mg/day except one (4 months). Dosage of metformin varied in the different trials ranging from 1000mg to 2000mg per day. Some studies recruited participants of different ethnicity.The pooled analysis based on 8 studies, there is a statistically significant BMI reduction with metformin treatment compared to placebo after 6 months use (Figure 1(a)).

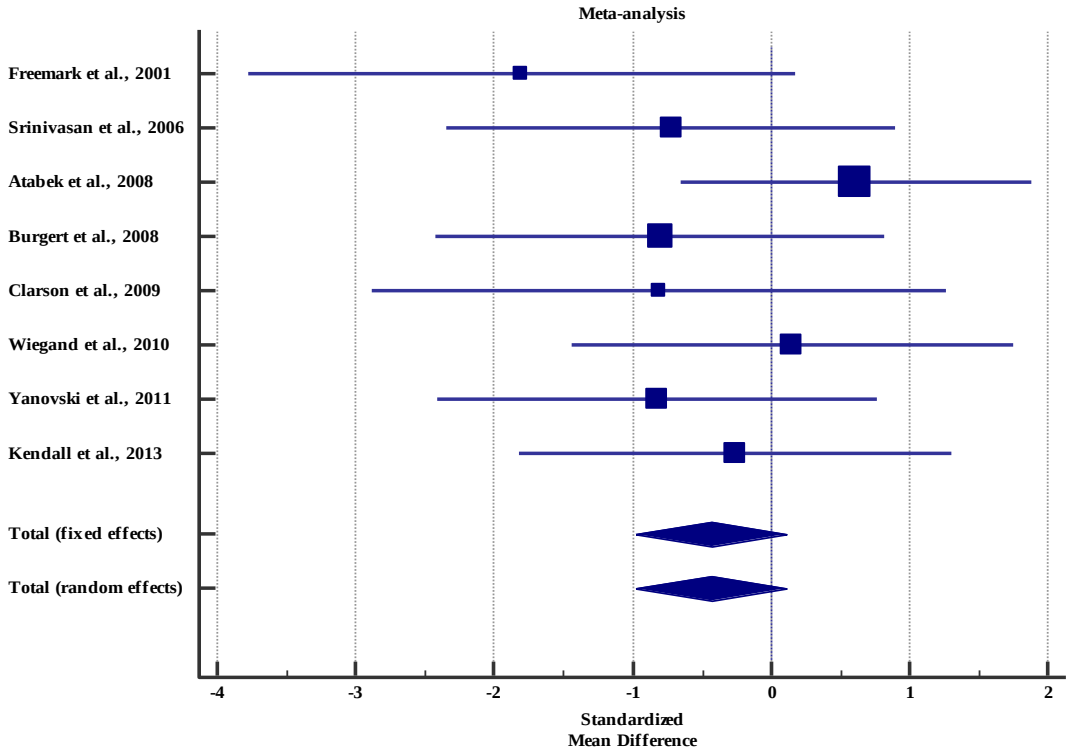

Figure 1 (a): Forest plot comparing change in BMI (kg/m^2) in metformin and placebo groups (a)

Pooled metformin effect on the BMI was found to be significant, but the difference did not reach statistical significance (Figure 1 (b)). Reduction in fasting insulin was greater in metformin than placebo group in all the studies, with a significant reduction. Analysis did not provide strong evidence for a treatment effect on weight reduction, fasting glucose, cholesterol, or triglyceride level. Pooled metformin effect on HDL was found to be valid if the one study by Freemark (2001) (outlier result) was excluded. The overall estimated effect was presented in Table 1, which remains statistically significant ($p<0.05$).

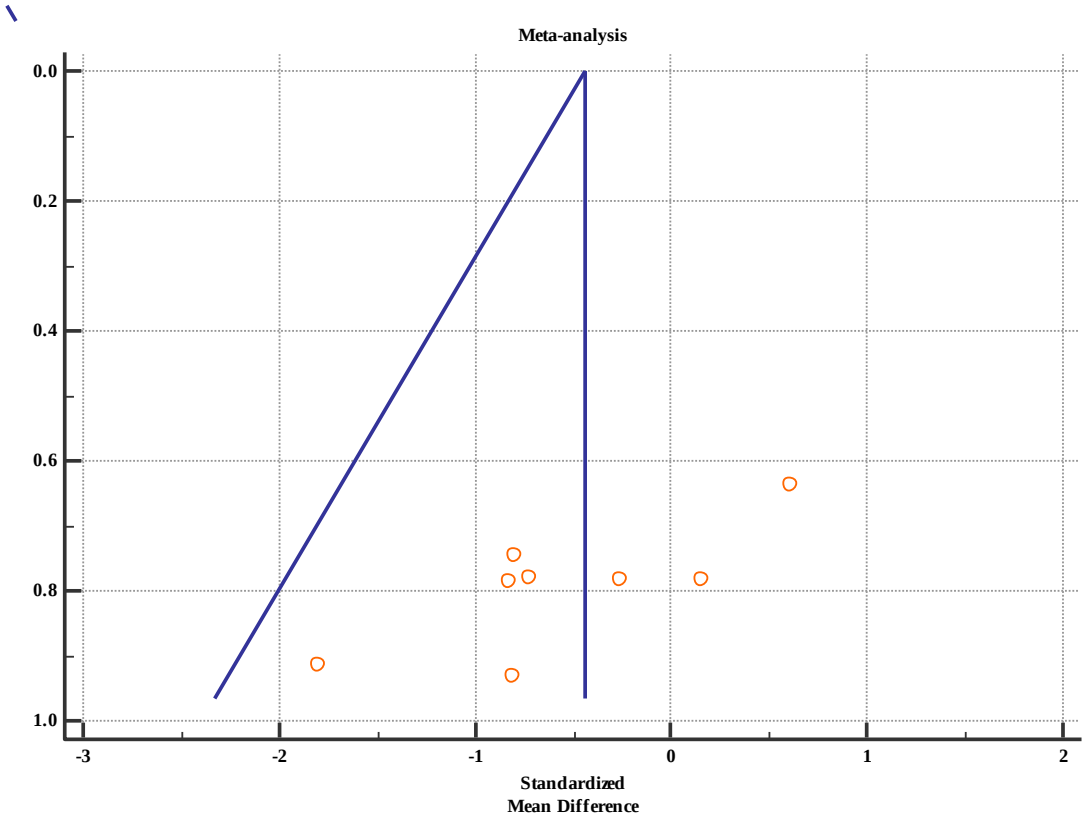

Figure 1 (b): Forest plot comparing change in BMI (kg/m^2) in metformin and placebo groups (b)

Table 1. Meta-analysis: continuous measure

Study	N1	N2	Total	SMD	SE	95% CI	t	P	Weight (%)	
									Fixed	Random
Freemark et al., 2001	14	1	15	-1.803	0.915	-3.780 to 0.174			9.10	9.10
Srinivasan et al., 2006	22	1	23	-0.724	0.779	-2.345 to 0.897			12.54	12.54
Atabek et al., 2008	90	2	92	0.610	0.637	-0.656 to 1.877			18.75	18.75
Burgert et al., 2008	13	1	14	-0.802	0.745	-2.425 to 0.822			13.72	13.72
Clarson et al.[8], 2009	11	1	12	-0.806	0.931	-2.879 to 1.268			8.79	8.79
Wiegand et al., 2010	36	1	37	0.155	0.784	-1.437 to 1.747			12.39	12.39
Yanovski et al., 2011	45	1	46	-0.822	0.786	-2.407 to 0.762			12.32	12.32
Kendall et al., 2013	74	1	75	-0.257	0.784	-1.820 to 1.305			12.39	12.39
Total (fixed effects)	305	9	314	-0.435	0.276	-0.978 to 0.108	-1.577	0.116	100.00	100.00
Total (random effects)	305	9	314	-0.435	0.276	-0.978 to 0.108	-1.577	0.116	100.00	100.00

Test for heterogeneity

Q	6.3241
DF	7
Significance level	P = 0.5025
I^2 (inconsistency)	0.00%
95% CI for I^2	0.00 to 64.49

Gastrointestinal problems (diarrhoea, nausea, and abdominal pain) were the most commonly reported adverse events and were more frequently reported in the metformin than in the placebo group. One study reported gastrointestinal problems as the reason for participants leaving studies (Wiegand*et al*., 2010). In addition to gastrointestinal adverse events, the German study also reported unspecific events such as weakness or fatigue for a short time though with spontaneous remission in both the metformin (n=3) and placebo (n=4) groups (Wiegand*et al*., 2010).

Discussion:

In this systematic review and meta-analysis, 8 RCTs on metformin treatment in non-diabetic obese population were included in the analysis. Compared with placebo, metformin reduced BMI significantly in this population. Fasting insulin was improved in the metformin-treated obese young people compared to those treated with placebo, with a comparable reduction, and no statistically significant heterogeneity amongst individual studies. Also there was a reduction of HOMA-IR in metformin treated obese young people compared with the placebo group. There were no serious adverse reactions reported in any of the included studies. The most commonly reported adverse events were gastrointestinal problems.

Conclusion:

Metformin was found to cause a decrease in BMI in non-diabetic obese young people from short-term RCTs after 6 months of treatment. Metformin may be efficacious in reducing BMI amongst obese children and adolescents in short-term RCT. However, this treatment effect may not be clinically relevant in terms of improving cardiovascular risk for obese young people. Further, RCTs with longer treatment periods and larger sample sizes are needed. In addition, it is difficult to extrapolate findings from RCTs to real-life clinical practice. Therefore, newer prospective cohort studies need to be initiated in regional clinics to investigate the effect of metformin on weight loss in obese young people.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Atabek ME, Pirgon O.Use of metformin in obese adolescents with hyperinsulinemia: a 6-month, randomized, double-blind, placebo-controlled clinical trial.Journal of Pediatric Endocrinology and Metabolism 2008;21(4):339-348.
2. Freemark M, Bursey D.The Effects of Metformin on Body Mass Index and Glucose Tolerance in Obese Adolescents with Fasting Hyperinsulinemia and a Family History of Type 2 Diabetes.Pediatrics2001; 107 (4): 1-7.
3. Srinivasan S, Ambler GR, Baur LA, Garnett SP, Tepsa M, Yap F, Ward GM, Cowell CT. Randomized, controlled trial of metformin for obesity and insulin resistance in children and adolescents:improvement in body composition and fasting insulin. Journal of Clinical Endocrinology and Metabolism 2006;91:2074–2080.

4. Yanovski JA, Krakoff J, Salaita CG, McDuffie JR, Kozlosky M,Sebring NG,Reynolds JC, Brady SM, Calis KA.Effects of Metformin on Body Weight and Body Composition in Obese Insulin-Resistant Children: A Randomized Clinical Trial Diabetes. 2011; 60(2): 477–485.
5. Wiegand S, Allemand D, Hubel H, Krude H, Burmann M, Martus P, Gruters A, Holl RW.Metformin and placebo therapy both improve weight management and fasting insulin in obese insulin-resistant adolescents: a prospective, placebo-controlled, randomized study. European Journal of Endocrinology 2010;163(4):585-592.
6. Kendall D, Vail A, Amin R, Barrett T, Dimitri P, Ivison F, Kibirige M, Mathew V, Matyka K, McGovern A, Stirling H, Tetlow L, Wales J, Wright N, Clayton P, Hall C.Metformin in obese children and adolescents: the MOCA trial. Journal of Clinical Endocrinology and Metabolism. 2013;98(1):322-329.
7. Burgert TS, Duran EJ, Goldberg-Gell R, Dziura J, Yeckel CW, Katz S, Tamborlane WV, Caprio S. Short-term metabolic and cardiovascular effects of metformin in markedly obese adolescents with normal glucose tolerance.Pediatric Diabetes 2008;9(6):567-576.
8. Clarson CL, Mahmud FH, Baker JE, Clark HE, Mckay WM, Schauteet VD, Hill DJ. Metformin in combination with structured lifestyle intervention improved body mass index in obese adolescents, but did not improve insulin resistance. Endocrine 2009; 36(1):141–146.

*****