JCD

REVIEW ARTICLE

The Comparative Effect of Metformin, Voglibose Alone and in Combination on Body Mass Index in Non-diabetic Obese Subjects

Dr. Jyoti Bobde[a], Dr Rajesh Kadam[b], Dr Deepak Bhosle[c]

[a.b.c] MGM Medical Collage, Aurangabad 431003

Address for correspondence: MGM Medical Collage, Aurangabad 431003

Keywords : Oral antidiabetics, BMI, Metformin, Voglibose

INTRODUCTION

Throughout most of the human history, obesity has been viewed as a sign of health and prosperity. But now it has been termed as an epidemic and asocial burden, with increasing prevalence worldwide.[1] Obesity is also defined as an abnormal growth of the adipose tissue due to an enlargement of fat cell size (hypertrophic obesity) or an increase in fat cell number (hyper plastic obesity) or a combination of both;[2] or is defined "as a condition of abnormal or excessive fat accumulation in adipose tissue, to the extent that health may be impaired to produce adverse health consequences and is associated with increased morbidity and mortality."[3]

According to the World Health Organization estimates, 1.6 billion adults (aged 15 years and above) were overweight and 400 million were obese in 2005 and the figures are predicted to rise to 2.3 billion overweight and over 700 million obese adults by 2015.[4] Surprisingly, obesity is often neglected, though it is associated with a serious, life-threatening complications like increasing risk of cardio-metabolic illness.[5,6] According to National Family Health Survey (NFHS)-3 prevalence of overweight or obesity in India is 12.1% in males and 16% in females, and in Maharashtra it is 15.9% in males and 18.1% in females.[7] Obesity is caused by a complex interaction among the environment, the genetic predisposition, and human behavior, but the relative contribution of these factors is still poorly understood. Though changes in genetic makeup of populations may not be fully responsible for this rapid rise in obesity, but genetic predisposition does play a vital role in its development.[8,9]

Body mass index (BMI) provides a simple and convenient anthropometric index for classification of obesity. The World Health Organization (WHO), the US Preventive Services Task Force and the International Obesity Task Force define overweight "as a BMI between 25.0 and 29.9 kg/m^2 and obesity as a BMI 30.0 kg/m^2".[10–13]

Parameter	WHO Criteria	Indian Criteria
Normal	18.5–24.9 kg/m^2	18.0-22.9 kg/m^2
Over-weight	25.0–29.9 kg/m^2	23.0–24.9 kg/m^2
Obese	>30 kg/m^2	>25 kg/m^2

Table 1 Body Mass Index Classification.[14]

An excess accumulation of body fat is responsible for most obesity-associated health risks.[15]

Therapeutic approach for a non-diabetic obese patient starts with comprehensive lifestyle management i.e. very low calorie diet, physical activity and behaviour modification and if needed anti-obesity drugs. Bariatric surgery is suggested for those who are at greater risk of obesity. There are many examples of drugs used historically for weight loss that have been removed owing to significant side effects, like sibutramine, rimonabant. Sibutramine in 1997 had been approved for the management of obesity. But in October 2010, after Sibutramine Cardiovascular Outcomes Trial (SCOUT) result, it was withdrawn from the market because of an association with increased cardiovascular events and strokes.[16] The first selective Endocannabinoid Receptor blocker, Rimonabant, was available as an anti-obesity drug in 56 countries; from 2006 it was also withdrawn from the market, because of an increased risk of psychiatric adverse events, including depression, anxiety and suicidal tendencies.[17] FDA approved Orlistat as an anti-obesity drug in 1999. It reduces intestinal fat absorption by inhibiting pancreatic lipase. Orlistat is notorious for its gastrointestinal side effects which include steatorrhea. Though they are the most frequently reported adverse effect of the drug, but they tend to decrease with time. But, its over-the-counter approval was controversial in the United States, with consumer advocacy group Public Citizen repeatedly opposing it on safety and efficacy grounds.[18]

FDA approved few new anti-obesity as adjunctive therapy for chronic weight management: lorcaserin approved in 2012; and phentermine/topiramate extended-release formulation also approved in 2012.[19]

Metformin, the biguanide, is most widely used for the treatment of type 2 diabetes mellitus (T2DM). In diabetic patients, it suppresses endogenous glucose production and may also act as an insulin sensitizer. It also helps diabetic patients to lose weight or at least keep their weight stable.[20–22] The weight loss effects have been attributed by lipolytic and anorectic effects; also suppressing glucose production by liver.[23] Metformin activates AMP-activated protein kinase (AMPK), a liver enzyme that plays an important role in insulin signaling, whole body energy balance and in the metabolism of glucose and fats.[24] Recent study suggests that the effect of metformin on AMPK dependent lipolysis in adipocytes may lead to lower plasma levels of fatty acids and improve adipose tissue function.[25]

Voglibose is the recent alpha glycosidase inhibitor. Though voglibose has similar efficacy to acarbose, it has much weaker effect on alpha-amylase when given in a pharmacological dose. Hence, it has better tolerability.[26,27] It has shown strong anti-obesity and anti-diabetic activities and has been found to significantly reduce postprandial blood glucose concentration and weight in some animals.[28,29] It delays the digestion and absorption of carbohydrates, thereby inhibiting postprandial hyperglycemia. Administration of voglibose, increases the secretion of glucagon-like peptide (GLP)-1. GLP 1 is an incretin type of hormone, which causes early satiety. Also, it decreases plasma dipeptidyl peptidase-4 (DPP-4) activity.[30] A study by Xiaoling Cai et al. shows weight reduction with alpha glucosidase inhibitors on type 2 diabetes patients.[31] An animal study done by Hyun Ju Do shows weight reduction in non-diabetic mice with voglibose.[32]

Some studies have revealed that there is significant weight reduction in non-diabetic subjects with metformin.[33] Also some studies have revealed weight reduction with voglibse in T2DM patients. In a study done on non-diabetic animals with obesity, there was weight reduction with voglibose.[31,32] Considering the findings of above studies, we have undertaken this study to see the effect of voglibose on weight in non-diabetic subjects.

At present, no clinical studies have been reported of metformin and voglibose in head to head comparison for non-diabetic obesity. Therefore, the present study was planned to compare and evaluate the effect of metformin and voglibose on BMI in non-diabetic obese individuals.

Primary Objectives

The comparative effect of metformin and voglibose alone and in combination on BMI of non-diabetic obese subjects.

Secondary Objectives

- To study the effect of metformin alone on BMI of non-diabetic obese subjects.
- To study the effect of voglibose alone on BMI of non-diabetic obese subjects.
- To study effect of combination of metformin and voglibose on BMI of non-diabetic obese subjects.
- To compare safety profile of metformin and voglibose as per se in terms of patients reported adverse effects.

MATERIALS AND METHODS

The present study was carried out in the Department of Pharmacology in collaboration with the Department of Medicine at MGM Medical College and Hospital, Aurangabad.

Patient Selection

The subjects enrolled for this study were selected after screening for HbA1c according to the inclusion and exclusion criteria. Written informed consent was obtained from each patient.

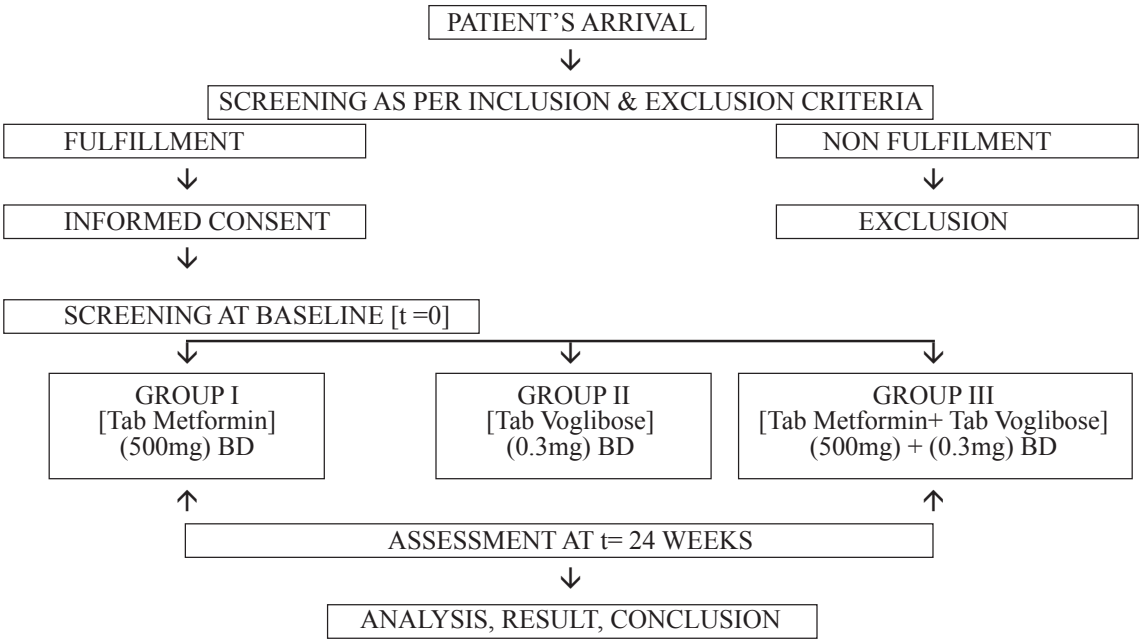
Inclusion Criteria

- Willing to participate in the study
- Must be able and willing to give written informed consent prior to any study-related procedures and to comply with the requirements of the study protocol.
- Age group of 20–60 years of either gender.
- Obese or overweight determined by a BMI of>25 kg/m^2.

Exclusion Criteria

- Patients with HbA1c <5.7%
- Pregnant and lactating women.
- Patients with known allergic to drugs and sensitive to drugs.

STUDY FLOW CHART



Study Period: September 2015–February 2016 (6 months)

Study Drugs: Metformin; 500mg and Voglibose; 0.3mg

Study Groups:

Group A: Voglibose

Group B: Metformin

Group C: Combination (Voglibose+ Metformin)

- Patient concurrently taking other medication which is known to affect the obesity.
- Smoker, alcoholic and tobacco chewer.
- Patients with gastrointestinal disorders like inflammatory bowel disease, gastric deranged liver function test, kidney function test.
- Patient with hypothyroidism.

Experimental Phase

Volunteers were assessed at baseline for HbA1c for screening of non-diabetic subjects. Healthy non-diabetic obese subjects were enrolled and assessed at baseline and at end of study for BMI.

HbA1C by High Performance Liquid Chromatography (HPLC) NGSP Certified

Principle

HPLC separates mixture of compounds based on polarity. Polarity states that the greater the difference in electron affinity i.e. electro negativity between atoms in covalent bond, the more polar the bond. Partial negative charges are found on the most electro negative atoms, the others are partially positive. The molecular electro stat potential energy of a hydrogen ion at a particular location near a molecule negative electrostatic potential corresponds to: partial negative charges. Positive electrostatic potential corresponds to partial positive charges. It is used to analyze, identify, purify and quantify compounds.

Procedure

It has a mobile phase, a stationary phase and detector. The mobile phase is continuously pumped at a fixed flow rate through the system and mixed by the pump. The injector is used to introduce a plug of a sample into the mobile phase without having to stop the mobile phase flow and without introducing air into the system. The mixture of components is carried in a narrow band to the top of the column. Some compounds in the sample mixture will have greater preference for stationary phase than the mobile phase and will be retained in the column longer.

Pointsto Remember

"Like attracts Like" i.e. if the column is non-polar the compound to elute first will be the most polar one. Those components that are not retained as strongly as are carried by the mobile phase down the column. The detector is then used to respond to a physico-chemical property of analyses; this response is digitally amplified and sent to a data system where it is recorded as a 'chromatogram'.

Assessments

1. General physical examination
2. Laboratory investigations at base line: HbA1c level
3. Blood sugar level- fasting and post meal at base line
4. BMI at base line and after 6 months
5. BMI was calculated by the following formula:

$$BMI = \frac{mass(kg)}{height\ (m))^2}$$

Statistical Phase

The statistical evaluation was done by Student's t-test with the help of SPSS (Statistical Package for Social Service version 19) value less than $p<0.05$ was taken as significant.

Ethical Approval

This study is conducted in accordance with the ethical principles that have their origin in the declaration of Helsinki and that are consistent with GCP and applicable laws and regulations.

This study is approved by MGM Ethics Committee for Research on Human Subjects.

Observation and Results

The present study, done on 60 non-diabetic obese subjects (n=60) volunteers completed the study,'Comparative effect of metformin and voglibose alone and in combination on BMI'. Evaluation was done after 6 months. All the groups were matched in baseline characteristics i.e. age, sex and weight. The BMI decreased significantly when compared to baseline value in all three groups. For the result and calculation we applied student t-test, both paired and unpaired.

Intragroup Comparison

The results of paired t-test is given in Table 1.

Table 1 | Paired t-test

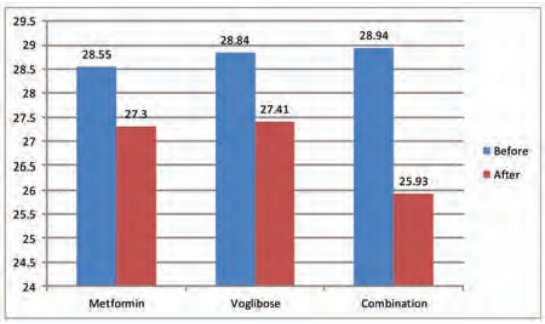
Group	BMI			P value
	Mean value ±SD			
	Before therapy	After therapy	Mean difference	
A	28.55± 2.19	27.84±2.08	1.26±1.07	0.00
B	28.84±2.73	27.41±2.83	1.44±0.68	0.00
C	28.94±2.005	25.93±1.86	3.00±1.03	0.00

(Note:P< 0.05**: Statistically significant. P <0.001***: Statistically highly significant).

Group A: Metformin, Group B: Voglibose, Group C: Combination (Voglibose+ Metformin)

Metformin and voglibose alone and in combination, before and after therapy on BMI values (Graph 1).

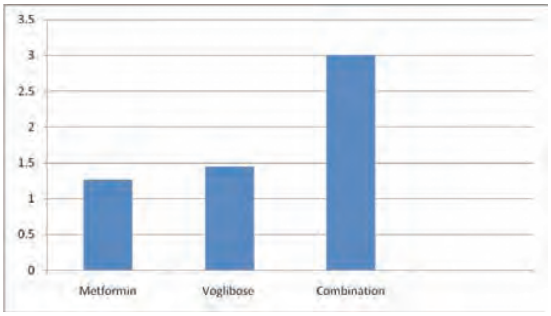
Graph 1 Comparison of baseline values of BMI before and after therapy in three groups.



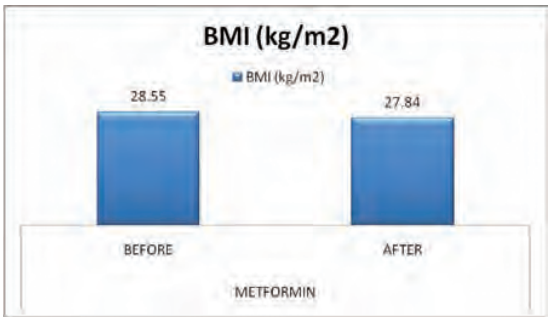
Intragroup comparison of voglibose and metformin at baseline and after 6 months was found to be significant but a highly significant result was found in combination group (voglibose+ metformin) (Graph 2).

Graph 2: Mean difference between the treatment groups before and after 6 months in three groups.

Mean Difference of BMI

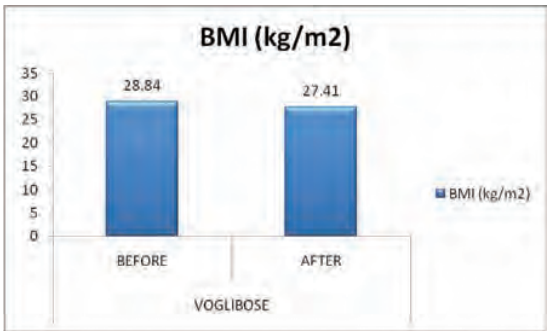


Graph 3: Comparative effect of metformin before and after therapy on BMI values.



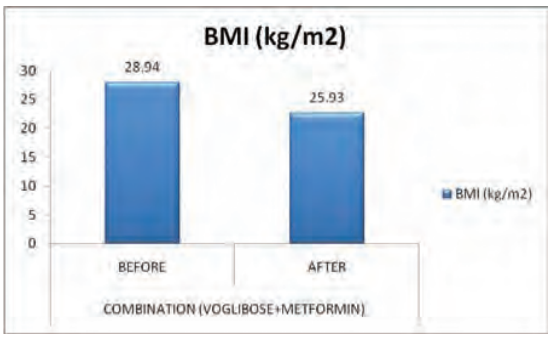
Graph 3 shows that after 6 months of therapy with metformin, significant difference in BMI values was observed.

Graph 4: Comparative effect of voglibose before and after therapy on BMI values



Graph 4 depicts that after 3 months of therapy with voglibose, significant difference in BMI values was observed.

Graph 5: Comparative effect of combination (metformin + voglibose) before and after therapy on BMI values.



Graph 5 shows that after 6 months of therapy with combination (metformin + voglibose), significant difference in BMI values were observed.

Inter Group Comparison

For inter group, in three groups comparison we used unpaired t-test (Table 2).

Table 2 | Unpaired t-test for comparison of BMI

Groups	Mean Difference ± SD	P value
A vs. B	0.1±2.37	0.88
A vs. C	1.4 ± 1.97	0.035**
B vs. C	1.5 ± 2.28	0.048**

(Note:P> 0.05*: Not Statistically significant, P< 0.05**: Statistically significant).

Metformin and Voglibose

Inter group comparison between group metformin and voglibose showed (0.1±2.37) no statistical difference in BMI when compared by using unpaired t-test and was found to be statistically non-significant with a p value >0.05.

Metfornin alone and in combination group (voglibose and metformin)

Inter group comparison between metformin group and combination group (1.4 ± 1.97) showed statistical difference in BMI when compared by using unpaired t-test and was found to be statistically significant with a p value <0.05.

Voglibose alone and in combination (voglibose and metformin)

Inter group comparison between voglibose group and combination group (1.5± 2.28) showed statistical difference in BMI when compared by using unpaired t-test and was found to be statistically significant with a p value <0.05.

ADVERSE EFFECTS

Most common adverse drug reaction reported in all the three groups were related to gastrointestinal disturbances (Table 3). In two patients (10%) in metformin group had shown adverse drug reactions, in voglibose group four patients (20%) and in combination group five patients (25%).

In metformin group, adverse drug reaction seen was bloating of abdomen in two patients (10%). With voglibose group, gastrointestinal adverse drug reactions seen were,nausea in one patient (5%), flatulence in two patients (10%)and diarrhoea in one patient (5%). In combination group, adverse drug reactions seen were, nausea in one patient (5%), bloating of abdomen in two patients (10%), diarrhoea in one patient (5%) and abdominal pain in one patient (5%).

Table 3: | Comparison of ADRs in treatment with metformin, voglibose and combination groups

ADRs	Group A	Group B	Group C
Nausea	—	5%	5%
Abdominal bloating	10%	—	10%
Flatulence	—	10%	—
Diarrhoea	—	5%	5%
Abdominal Pain	—	—	5%
Total	10%	20%	25%

DISCUSSION

The incidence of obesity has dramatically increased over the past decade reaching epidemic proportions across the globe.[1] Multiple causative factors like genetic, environmental, nutritional, physiological, psychological, social and cultural have been linked to development and progression of obesity and associated morbidities. Obesity and being overweight poses a major risk for chronic diseases including T2DM, cardiovascular disease, hypertension, stroke and certain forms of cancer.[11,12] Currently there are many FDA approved drugs for obesity. As they are not cost effective and have some severe side effects;there is need of better treatment options.[34,35]

Both the study drugs are widely used in the treatment of diabetic patients. Some studies have revealed effectiveness of metformin in weight reduction,[33] not only in diabetic but also in non-diabetic patients. Similarly, administration of voglibose in diabetic patients has shown weight reduction. Another study involving use of voglibose in non-diabetic obese animals showed weight reduction.[30] Due to above considerations, this study was undertaken. Moreover,at present no clinical studies have been reported on metformin and voglibose in head-to-head comparison for non-diabetic obesity. Therefore, the present study was planned.

The objective of our study was to observe the effect of metformin and voglibose on BMI, as it provides a simple and convenient anthropometric index for classification of obesity. Sixtynon-diabetic obese subjects were selected based on inclusion and exclusion criteria, and divided into three groups of 20 subjects each. The first group received metformin 500mg BD, second group received voglibose 0.3 mg and the third group received a combination of metformin 500mg and voglibose 0.3mg. For the comparison we applied paired and unpairedt-test. Paired t-test was applied for intra group comparison and unpaired t-test was applied for inter group comparison.

When we applied paired t-test for metfomin group,it showed significant reduction in BMI after 6 months of treatment as compared to baseline values. These findings are similar to a study conducted by Seifarth et al. on non-diabetic obese (n= 154) patients with a body mass index ≥27 kg/m^2 showed mean weight loss in the metformin treated group of 5.8±7.0 kg (5.6±6.5%) over 6 months.[33] Probable mechanisms of metformin for weight reduction is its lipolytic and anorectic action.[23] Other possible mechanism is its actions it increases GLP 1. Also weight loss through AMP-activated protein kinase (AMPK) leads to lower plasma fatty acid level and improves adipose tissue function.[24]

In TODY study to manage T2DM in youth showed gastrointestinal disturbances were most common adverse event (41%) in metformin treatment group. In our study, though drug was well tolerated as there was only one type of ADR reported i.e. the bloating of abdomen in two patients.

Similarly, there was significant reduction in BMI values from baseline in voglibose group (0.3 mg BD) in our group after 6 months of treatment(1.44 ±0.68) P < 0.00. Study by Xiaoling Cai et al. showed weight reduction from baseline was significantly more with voglibose treatment (n= 216) compared with placebo (n= 210) in Asians (WMD, 21.00 kg;).[31] Also another study done by Hyun Ju Do, exhibited weight reduction in non-diabetic obese mice with voglibose.[29] The probable weight reduction mechanism is increase in the secretion of glucagon-like peptide (GLP)-1, causing early satiety. Also it delays the digestion and absorption of carbohydrates, thereby inhibiting postprandial hyperglycemia.[30]

In a study by Iwamoto Y et al. in a Japanese patient with T2DM, the most common drug-related ADRs with voglibose group were gastrointestinal disorders with an incidence of 32.8%.[36] In our study ADRs with voglibose group were,nausea in one patient, flatulence in two patients and diarrhoea in one patient.

In our study we found significant weight reduction with combination group which is more as compared to other groups;this is because of additive effect of combination of metformin with voglibose. In this group, ADRs were seen i.e. nausea in one patient, bloating of abdomen in two patients, diarrhoea in one patient and abdominal pain in one patient.

Inter group comparison shows the following findings:

Inter group comparison between metformin alone and voglibose alone groups showed no statistical significant difference in BMI value when compared by using unpaired t-test (0.1±2.37) with a p value >0.05.

Inter group comparison between metformin alone group and combination group showed statistical difference in BMI value when compared by using unpaired t-test with a (1.4 ± 1.97) p value <0.05.

Inter group comparison between voglibose alone group and combination group showed statistical difference in BMI when compared by using unpaired t-test with a (1.5± 2.28) p value <0.05.

SUMMARY AND CONCLUSION

After 6 months of treatment with metformin 500mg BD alone, voglibose 0.3mg BD alone, and metformin 500mg with voglibose 0.3mg BD in combination, all three groups showed statically significant reduction in BMI values from baseline. When we compared results of metformin group with voglibose group there was no statistically significant difference. But when we compared results of metformin alone with metformin and voglibose combination and voglibose alone with metformin and voglibose combination,

the combination group showed statically significant reduction in BMI base line values.

There was only a single ADR associated with metformin group i.e. bloating of abdomen in two patients. In voglibose group, there was nausea in one patient, flatulence in two patients and diarrhoea in one patient. While in the combination group, ADRs were nausea in one patient, blotting of abdomen in two patients, diarrhoea in one patient and abdominal pain in one patient.

Although ADRs associated with the combination of voglibose and metformin are comparatively more they are not serious and subside with time; therefore it can be concluded that the use of metformin and voglibose in combination has greater efficacy in reducing the BMI in non-diabetic obese subjects than drugs when given alone. Therefore, it can be concluded that metformin + voglibose combination is very effective in reducing body weight, but further long-term studies with large sample size are needed to assess the safety and efficacy of metformin+voglibose combination in treatment of obesity in non-diabetic population.

References

1. World Health Organisation Obesity: Preventing & Managing Global Epidemic. Geneva: WHO 1998.
2. Park K. Park's Textbook of Preventive and Social Medicine,18th edn. MP, India: Banarsidas Bhanot Publishers, 2005.
3. Haslam D, James WPT. Obesity. Lancet 2005; 366: 1197–209.
4. World Health Organisation Factsheet. (http://www.who.int/mediacentre/factsheets/fs311/en/index.htm)
5. Henegar JR, Bigler SA, Henegar LK et al. Functional and structural changes in the kidney in the early stages of obesity. J Am Soc Nephrol 2001; 12: 1211–7.
6. King H, Aubert RE,Herman WH. Global burden of diabetes, 1995–2025: prevalence,numerical estimates,and projections. Diabetes Care 1998;21:1414-–31.
7. National Family Health Survey, *2005–06*.
8. Fru¨hbeck G, Diez-Caballero A, Go´mez-Ambrosi J, Cienfuegos JA, Salvador J. Preventing obesity. Doctors underestimate obesity. BMJ 2003; 326: 102–3.
9. Fru¨hbeck G. Screening and interventions for obesity in adults. Ann Intern Med 2004; 141: 245–6.
10. World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995; 854: 1–452.
11. US Preventive Services Task Force. Screening for obesity in adults: recommendations and rationale. Ann Intern Med 2003; 139: 930–2.
12. International Obesity Task Force, 2009.
13. Poirier P, Giles TD, Bray GA, Hong Y, Stern JS, Pi-Sunyer FX et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation 2006; 113: 898–918.
14. Rakesh Kumar Sahay; KD Modi Manual of Clinical Endocrinology, 1 stedn, 2012.
15. Kahn BB, Flier JS. Obesity and insulin resistance. J Clin Invest 2000; 106:473–81
16. James WP, Caterson ID, Coutinho W, Finer N, Van Gaal LF, Maggioni AP, Torp-Pedersen C, Sharma AM, Shepherd GM, Rode RA, Renz CL. SCOUT Investigators. Effect of sibutramine on cardiovascular outcomes in overweight and obese subjects. N Engl J Med 2010; 363:905–17.
17. Christensen R, Kristensen PK, Bartels EM, Bliddal H, Astrup A. Efficacy and safety of the weight-loss drug rimonabant: a meta-analysis of randomised trials. Lancet 2007; 370:1706–13.
18. Schmid, Randolph E (9 February 2007). "FDA OKs First Nonprescription Diet Pill".USA Today. Retrieved 2009-06-09.
19. Kim GW, Lin JE, Blomain ES, Waldman SA. New advances in models and strategies for developing anti-obesity drugs. Expert Opin Drug Discov 2013; 8: 655–71.
20. Clinical Guidelines Task Force, International Diabetes Federation (2005). "Glucose control: oral therapy". In: Global Guideline for Type 2 Diabetes. Brussels: International Diabetes Federation, 35–8. Retrieved on November 6, 2007.
21. National Collaborating Centre for Chronic Conditions. Type 2 diabetes: national clinical guideline for management in primary and secondary care. London: Royal College of Physicians; 2008. ISBN 978-1-86016-333-3.p. 86.
22. American Diabetes Association. Standards of medical care in Diabetes—2009. Diabetes Care 2009;32 Suppl 1:S13–61.
23. Desilets AR, Dhakal-Karki S, Dunican KC. Role of metformin for weight management in patients without type 2 diabetes. Ann Pharmacother 2008; 42:817–26
24. Towler MC, Hardie DG. AMP-activated protein kinase in metabolic control and insulin signaling. Circ Res 2007; 100(3):328–41.
25. Bourron O, Daval M, Hainault I, Hajduch E, Servant JM, Gautier JF, Ferré P, Foufelle F. Biguanides and thiazolidinediones inhibit stimulated lipolysis in human adipocytes through activation of AMP-activated protein kinase. Diabetologia 2010; 53(4): 768–78.
26. Scott Lj, Spencer CM. Miglitol: are view of its therapeutic potential in type 2 diabetes mellitus, Drugs 2000;59:521–49.
27. Matsuo T, Odaka H, Ikeda H**.** Effect of an intestinal disaccharidase inhibitor (AO-128) on obesity and diabetes. Am J Clin Nutr 1992;55 (1 Suppl):314S–7S.
28. Chen X, Zheng Y, Shen Y. Voglibose (basen AO-128) one of the most important alpha-glucosidase inhibitors. Curr Med Chem 2006;13:109–16.
29. Mastsuzawa Y, Kobatake T, Fujioka S,Tokunga K,Tasui S. Abstract of 5th International Congress on Obesity, Jerusalem, Israel 1986 ,50.
30. Moritoh Y, Takeuchi K, Hazama M. Chronic administration

of voglibose, an alpha-glucosidase inhibitor, increases active glucagon-like peptide-1 levels by increasing its secretion and decreasing dipeptidyl peptidase-4 activity in ob/ob mice. J Pharamacol Exp Ther 2009;329:669–76.

31. Cai X, Han X, Luo Y, Ji L. Comparisons of the efficacy of alpha glucosidase inhibitors on type 2 diabetes patients between Asian and Caucasian. Endocrinology & Metabolism Department, Peking University People's Hospital, Beijing, China.
32. Do HJ. Voglibose administration regulates body weight and energy intake in high fat-induced obese mice. Biochemical and Biophysical Research Communication 2014 Jan 17; 443(3): 1110–7.
33. Seifarth C, Schehler B, Schneide HJ. Effectiveness of metformin on weight loss in non-diabetic individuals with obesity. Exp Clin Endocrinol Diabetes 2013; 121(01): 27–31.
34. Loannides-Demos LL, Piccenna L, McNeil JJ. Pharmacotherapies for obesity: past, current, and future therapies. Jobes 2011; 2011: 179674.
35. Kim GW, Lin JE, Blomain ES, Waldman SA. Anti obesity pharmacotherapy: new drugs and emerging targets. Clin Pharmacol Ther 2014; 95(1): 53–66.
36. Iwamoto Y, Kashiwagi A, Yamada N, Terao S, Mimori N, Tachibana H, et al. Efficacy and safety of vildagliptin and voglibose in Japanese patients with type 2 diabetes: a 12-week, randomized, double-blind, active-controlled study. Diabetes Obes Metab 2010; 12(8): 700–8.