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# Study on safety of insulin add on therapy and oral hypoglycemic agents (ohgas) in type - II diabetes patients

D.Ashalatha[1], C.Roop kumar[1], K.Prem Raj[1], V.Vani[1], P.Narayana Swamy[2], Sankara Lakshmikanth[3].

[1] Pharm.D V year of Jagan's institute of pharmaceutical science, spsp Nellore, Andhra Pradesh,India.

[2] Department of Pharmacy Practice, Jagan's institute of pharmaceutical science, spsp Nellore, Andhra Pradesh,India.

[3] PTO(Senior Technical Assistant), NIN, Telangana, National TB Prevelence Survey,ICMR-NIRT.

ABSTRACT

Objectives**:** A clinical observational investigation directed to look at the security of Insulin add-on treatment and Hypoglycemic Agents in polypharmacy and to advance safe utilization of insulin and hypoglycemic agents in Type II Diabetes patients, through patient guiding by Clinical drug specialist at Jayabharath hospital, Nellore.Methods**:** A Prospective Observational investigation was directed on Type -2 Diabetes mellitus patients in the General Medicine office in a tertiary consideration emergency clinic, during the time of June – December 2019. The work was completed by utilizing quiet information assortment structures and a Diabetes survey.Results**:** Among 193 investigation populace with Type -2 Diabetes, hypoglycemic agents in polypharmacy 46.25% (n=108) was discovered to be more than Insulin alone, and Insulin add on treatment. Conclusion: From the examination, it was discovered that patients who are on hypoglycemic agents in polypharmacy were exposed to GI unsettling influences and who are on Insulin treatment was exposed to hypoglycemic scenes. Considering the key job of drug specialists the security of antidiabetic prescriptions and adherence was improved through patient directing.

Key words:
Insulin, Hypoglycemic agents, type-2 DM.

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*Corresponding Author
Name: Sankara Lakshmikanth
Email: drlakshmikanth08@gmail.com

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## INTRODUCTION

Diabetes is a chronic disease, which occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin that it produces. This leads to an increased concentration of glucose in the blood (hyperglycaemia).The primary objective of diabetes management is to achieve satisfactory levels of glycaemic control, which reduces the risk of associated serious, long-term complications [1, 2]. Literature suggests that the majority of people with type 2 diabetes (T2D) worldwide are not achieving targeted glycemic levels [3]. The T2D is characterised by progressive loss of beta cell function requires concurrent changes in treatment to maintain adequate glycemic control, mostly require insulin therapy to achieve this [4]. Due to distinguished pharmacodynamic and pharmacokinetic profile and based on evidence of their efficacy and safety in clinical trials, now a day's insulin analogues are gaining wide acceptance and are frequently prescribed [5]. Most patients begin treatment with diet and exercise with or without treatment regimen but, unfortunately most patients are unsuccessful in controlling type 2 diabetes through lifestyle modification alone and require antidiabetic agents. In poorly controlled diabetics there is a requirement for intensified and multidrug regimens, ultimately, oral agents alone cannot be the mainstay treatment for glycaemic control in many individuals and therapy must be added by the addition of insulin. Therefore this study is conducted with the aim to compare the safety (adverse effects, contraindications and Drug-Drug interactions) of the two possible approaches i.e OHGAs polypharmacy and insulin add on therapy for managing failure of combination therapy with oral medication only [6].

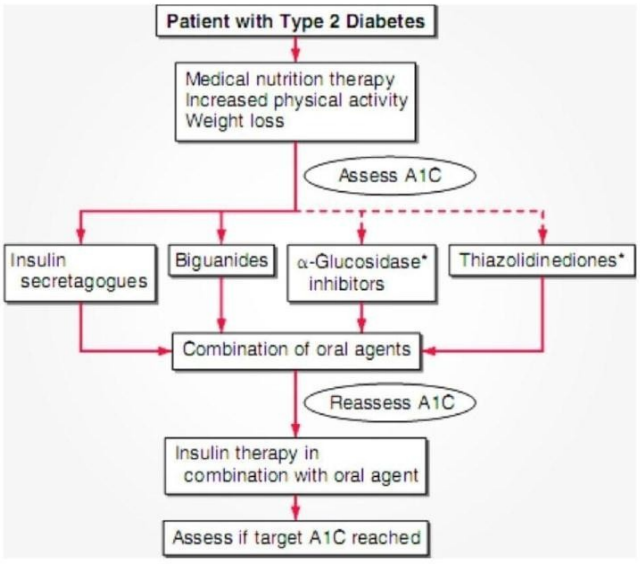



**Figure 01: Standard Treatment Guidelines for Type 2 Diabetes Mellitus**

**Note:** The broken line indicates that biguanides or insulin secretagogues, but not glucosidase inhibitors or thiazolidinediones, are preferred for initial therapy [1].

**Table 01: Nutrition Therapy for Diabetes Mellitus**

| **MEDICAL NUTRITION THERAPY** | |
|---|---|
| Nutrition therapy for all patients with diabetes as part of overall treatment plan | |
| Prediabetes or diabetes Individualized medical nutrition therapy as needed to achieve treatment targets, preferably provided by registered dietitian. | |
| **INDIVIDUALS AT HIGH RISK FOR DEVELOPING TYPE 2 DIABETES** | |
| Being structured program emphasizing life style changes, | • Moderate weight loss ( 7% body weight)<br>• Regular physical activity ( 150 min/ wk) with dietary strategies |
| including - | including reduced calorie and fat intake. |
| Achieve dietary fiber intake of 14g/1000 k cal and whole grains 50% of grain intake | |

**Table 02: Physical Activity in Type Ii Diabetes Mellitus**

| **PHYSICAL ACTIVITY** |
|---|
| **Adults with diabetes** |
| Exercise programs should include<br>• ≥ 150min/wk moderate – intensity aerobic activity ( 50% - 70% max heart rate), spread over<br>• ≥ 3 days/wk with no more than 2 consecutive days with out exercise.<br>• Resistance training ≥ 2 times/wk ( in absence of contraindications) |
| Evaluate patients for contraindications prohibiting certain types of exercise before recommending exercise program. |
| Consider age and previous level of physical activity. |
| Children with diabetes/ prediabetes - ≥ 60 min hysical activity/day. |

**Table 03: Oral Hypoglycemic Agents**

| MEDICATION | MECHANISM OF ACTION | SIDE EFFECTS | CONTRAINDICATIONS |
|---|---|---|---|
| **Biguanides**<br>Metformin | Reduce gluconeogenesis, increase glucose uutilisation | Lactic acidosis, anorexia, Vit B12 deficiency, nausea, diarrhoea, GI dyscomfort | Hepatic or renal impairment, alcoholism, advanced age |
| **Sulphonyl ureas**<br>Glibenclamide glimepride Glipizide Gliclazide | Stimulates release of endogenous insulin | Significant hypoglycaemia, nausea, GI dyscomfort | Hepatic or renal impairement |
| Thiazolidinediones | Increase peripheral | Increased TG, | Liver disease |
| Rosiglitazone Pioglitazone | insulin sensitivity, reduce gluconeogenesis | weight gain, hepatotoxicity, anemia | Congestive heart failure |
| **Meglitinides**<br>Repaglinide | Stimulate release of endogenous insulin | Less frequent hypoglycemia | Hypersensitivity Diabetid ketoacidosis |
| **Alpha glucosidase inhibitors**<br>Acarbose | Decrease the absorption of carbohydrates | Flatulence, abdominal cramping, diarrhoea | Hypersensitivity, DKA, IBD |

**Table 04: Hypoglycemia Management**

| At risk patients | Ask about symptomatic and asymptomatic hypoglycemia at each encounter |
|---|---|
| Preferred treatment: glucose(15-20 g)<br>• After 15 mins of treatment, repeat if hypoglycemia continues(per SMBG)<br>• When SMBG normal: patient should consume meal or snack to prevent recurrence | |
| Prescribe glucagon if significant risk of severe hypoglycemia | |
| Hypoglycemia unwareness or episode of severe hypoglycemia | Reevaluate treatment regimen<br>Insulin-treated patients: raise glycemic targets for several weeks to partially reverse hypoglycemia unawareness and reduce<br>Recurrence |
| Low or declining cognition | Continually assess cognitive function with increased vigilance for hypoglycemia.[9] |

A reasonable initial dose is 20 g of glucose. If neuroglycopenia precludes oral feedings, parenteral therapy is necessary. Intravenous glucose (25 g) should be given using a 50% solution followed by a constant infusion of 5 or 10% dextrose. If intravenous therapy is not practical, subcutaneous or intramuscular glucagon can be used, particularly in patients with type 1 diabetes mellitus. Because it acts primarily by stimulating glycogenolysis, glucagon is ineffective in glycogen-depleted individuals (e.g., those with alcohol-induced hypoglycemia). It also stimulates insulin secretion and is therefore less useful in type 2 diabetes mellitus. These treatments raise plasma glucose concentrations only transiently, and patients should be encouraged to eat as soon as practical to replete glycogen stores [7].

## AIMS AND OBJECTIVES

### AIMS

A clinical observational study on safety of Insulin add on therapy and OHGA poly pharmacy in type 2 diabetic patients attending general medicine ward in Jayabharath hospital, Nellore from June – December 2019.

### OBJECTIVES

- To compare safety of insulin add on therapy and Oral hypoglycemic agents poly pharmacy.
- To promote safe use of insulin through patient counseling by clinical pharmacist.

### PLAN OF WORK

The work is planned to carry out as following:

- To include type 2 diabetes mellitus patients.
- To design a patient data collection form and diabetes questionnaire.
- To collect all the data required for the study from general medicine ward
- To analyse the data and provide the feedback of results to the physician (prescriber) and submit the safety data of insulin add on therapy and OHA's polypharmacy in type-2 DM
- To counsel the patients regarding the usage of medications.

## METHODOLOGY

### STUDY SITE

A Non experimental prospective observational study was conducted on type-2 diabetes mellitus patients in general medicine department, JAYABHARATH HOSPITAL, Nellore, Andhra Pradesh.

### STUDY PERIOD

The study is being conducted from to June – December 2019.

### INCLUSION CRITERIA

- Subjects more than 18years of age with Type II diabetes.
- FBS must be > 130 mg/dl.
- Both inpatients and outpatients who consulted the general medicine department.
- The patients who are willing to participate in the study.

### EXCLUSION CRITERIA

- Critically ill patients who cannot participate in the study.
- Subjects with Type I DM.
- Subjects on OHGA monotherapy.
- Patients who are not willing to participate in the study.

### STUDY DESIGN

A prospective observational study.

### STUDY METHOD

- Study is conducted in Jayabharah Hospital, Nellore, a 300 bedded tertiary care hospital.
- All patients with Type 2 diabetes mellitus will be included in the study.
- Most of the patients visiting the hospital are from rural areas
- Patients were screened for FBS/RBS/PPBS level and FBS must be > 130 mg/dl were considered.
- Evaluation of clinical symptoms, FBS/RBS/PPBS levels in patients on Insulin add on therapy and OHGA polypharmacy for better glycemic controland adherence, safety parameters were assessed.

- The baseline knowledge of the patients on the disease, complications, regular blood glucose monitoring, diet, life style modifications and medication adherence is assessed using a questionnaire.
- Patients are then counseled about disease, diet, life style modifications and medication adherence.
- Patients are reviewed periodically (i.e., every 3 months) for the improvement in their blood sugar levels and improvement in general condition.

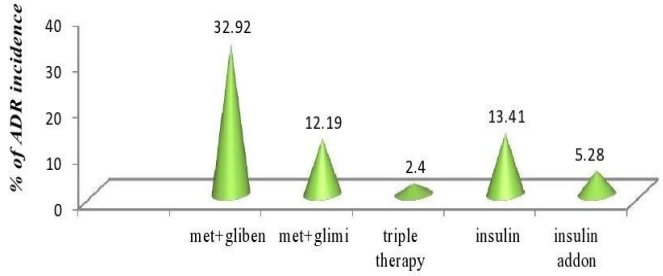
## RESULTS

**Table 05: Current Drug Usage**

| Type of drug | Drug usage in no. persons | % of drug usage |
|---|---|---|
| Insulin | 80 | 55.95 |
| OHGA's poly pharmacy | 108 | 41.45 |
| Insulin addon therapy | 5 | 2.5 |

**Table 06: ADR Occurrence in Different Drug Therapies**

| Type of drug | Overall ADR occurrence | % ADR occurrence |
|---|---|---|
| Metformin+glibenclamide | 81 | 32.92 |
| Metformin+glimipride | 30 | 12.19 |
| Triple therapy | 6 | 2.4 |
| Insulin | 33 | 13.41 |
| Insulin add on therapy | 13 | 5.28 |

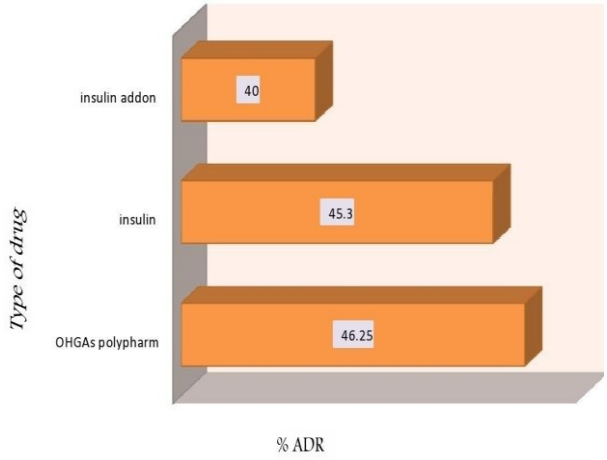



% OF ADR IN CURRENT TREATMENT

**Graph 01: ADR Occurrence in Different Drug Therapies**

**Table 07: % of ADR in Current Treatment**

| Drug | Total no. exposed | ADR occurrence | % ADR |
|---|---|---|---|
| OHGA's Polypharmacy | 80 | 37 | 46.25 |
| Insulin | 108 | 49 | 45.3 |
| Insulin addon therapy | 5 | 2 | 40 |

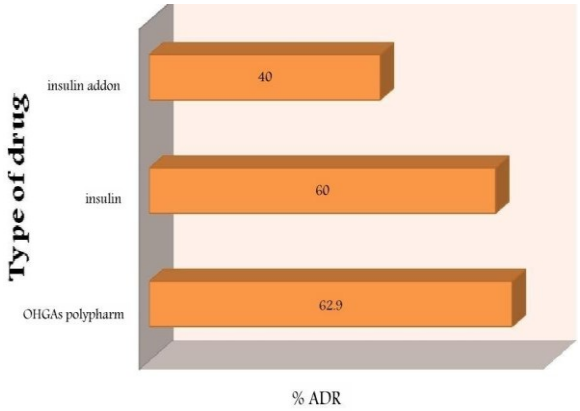



% OF ADR IN PAST TREATMENT

**Graph 02: % of ADR in Current Treatment**

**Table 08: % of ADR in Past Treatment**

| Drug | Total no exposed | ADR occurance | % ADR |
|---|---|---|---|
| OHGAs polypharm | 116 | 73 | 62.9 |
| Insulin | 5 | 3 | 60 |
| Insulin addon therapy | 5 | 2 | 40 |



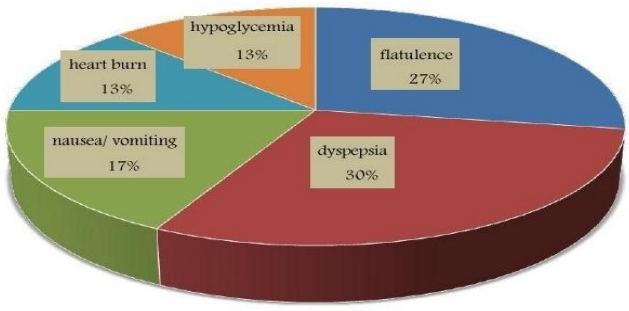

% ADRS OF OHGAS POLYPHARMACY

**Graph 03: % of ADR in Past Treatment**

**Table 09: % ADRS of Ohgas Polypharmacy**

| Type of ADR | ADR occurrence | Polypharmacy |
|---|---|---|
| Flatulence | 22 | 27.5 |
| Dyspepsia | 24 | 30 |
| Nausea/ vomiting | 14 | 17.5 |
| Diarrhoea | 0 | 0 |
| Heart burn | 10 | 12.5 |

| | | |
|---|---|---|
| Hypoglycemia | 10 | 12.5 |

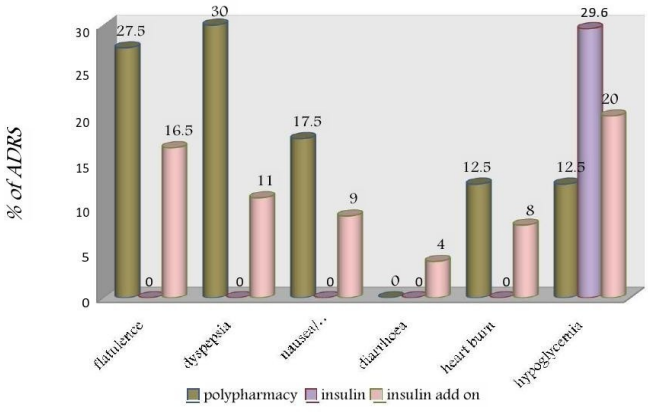



% ADRS OF INSULIN ADD ON THERAPY

**Graph 05: % ADRS of insulin add on therapy**

**Table 11: ADRS of antidiabetic agents**

| Type of ADR | Polypharmacy | Insulin | Insulin addon therapy |
|---|---|---|---|
| Flatulence | 27.5 | 0 | 16.5 |
| Dyspepsia | 30 | 0 | 11 |
| Nausea/ vomiting | 17.5 | 0 | 9 |
| Diarrhoea | 0 | 0 | 4 |
| Heart burn | 12.5 | 0 | 8 |
| Hypoglycemia | 12.5 | 29.6 | 20 |

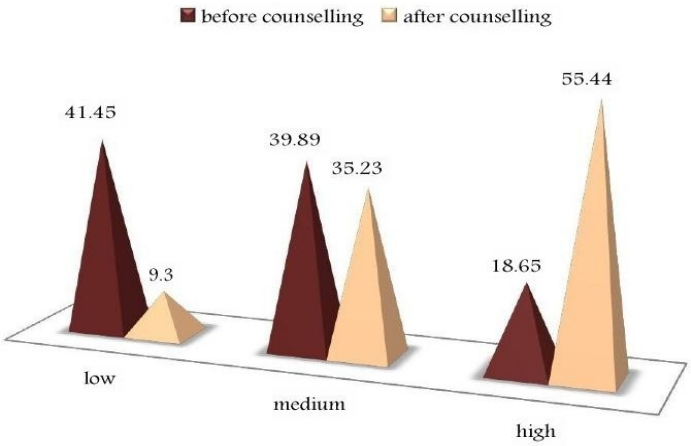



IMPACT OF COUNSELLING ON MEDICATION ADHERENCE

**Graph 06: ADRS of antidiabetic agents**

**Table 12: Impact of counselling on medication adherence**

| Adherence | Before counselling | | After counseling | |
|---|---|---|---|---|
| **Low** | 80 | 41.45 % | 18 | 9.3% |
| **Medium** | 77 | 39.89 % | 68 | 35.23 % |
| **high** | 3 | 18.65 | 1 | 55.44 |




**Graph 07: Impact of counselling on medication adherence**

## DISCUSSION

A prospective observational study done in a tertiary care hospital during the period of June – December, 2019 in type 2 diabetic patients, on safety of Oral hypoglycaemic agents polypharmacy (OHGAs) and insulin add on therapy to OHGAs and promotion of safe use of antidiabetic medications through patient counseling. The OHGAs to which the patient population exposed currently are combination of metformin and glibenclamide; metformin and glimepride; metformin and glipizide; metformin, glimipride and pioglitazone; metformin, glimipride and voglibose, insulin alone and insulin add on therapy with OHGAs. Considering the antidiabetic usage currently OHGAs polypharmacy (108 out of 193) was found to be more than insulin alone ( 80 out of 193) and insulin add on therapy ( 5 out of 193) responsible increased occurrence of ADRs like flatulence (27.5%), dyspepsia(30%), nausea/vomiting(17.5%), heart burn(12.5%), hypoglycaemia(12.5%) in OHGAs polypharmacy and flatulence (24%), dyspepsia(16%), nausea/vomiting(13%), diarrhoea(6%) heart burn(12%), hypoglycaemia(29%) in insulin add on therapy. Except hypoglycaemia the occurance of all other ADRs were comparatively less in patient population on insulin add on therapy than OHGAs polypharmacy.

## CONCLUSION

Hence the safety assessment i.e. ADR occurrence, sub therapeutic and toxic responses, adherence to medication were carried out in study population who are on antidiabetic agents like OHGAs polypharmacy, insulin alone, insulin add on therapy considering FBS/ RBS , physical symptoms, questionnaire as evaluating parameters. Considering the key role of pharmacist the safety of antidiabetic medications and adherence was improved through patient counselling on disease, proper drug usage ( how to take, when to take, how much to take, how long to take, with what we have to take medication, do's and don'ts while administering antidiabetic medication, possible side effects and contraindications, advantages of taking medication), diet ( daily calorie intake, diet chart, foods to be taken and to be avoided), physical activity ( what to do ?, how long to do?) which reduced the ADRs, economical burden with its management and worsening condition due to withdrawl of medication and promoted the quality of life of patient.

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