

Glucocrinology of Modern Sulfonylureas

**Clinical Evidence and Practice
Based Opinion**

Glucocrinology

"Glucocrinology is the study of medicine that relates to the relationship of glycaemia with the endocrine system"

Glucocrinology

- In the management of DM, a holistic approach encompassing vasculo-metabolic aspects and endocrine facets of diabetes is very important.
- The concept of glucocrinology focuses on the association of various endocrine glands and diabetes, the role of endocrinopathic drugs in unmasking latent diabetes, and the role of antidiabetic drugs in modulating endocrine disease.
- The concept of glucocrinology emphasizes the consideration of endocrine aspects in the management of diabetes.
- It promotes a comprehensive assessment of and aids in the quest for novel targets in the management of DM.

Nobel prizes in Glucocrinology

Year	Nobel Laureate	Contribution
1923	Frederick Banting John Macleod	Discovery of insulin.
1947	Bernardo Alberto Houssay	Role of anterior pituitary hormone in sugar metabolism.
1947	Carl Ferdinand Cori Gerty Theresa Cori, née Radnitz	Discovery of the catalytic conversion of glycogen, described the Cori cycle.
1950	Edward Calvin Kendall Tadeus Reichstein Philip Showalter Hench	Discoveries relating to hormones of adrenal cortex, their structure and biological effects.
1953	Hans Adolf Crebs	Discovery of the citric acid cycle in generation of ATP.
1953	Fritz Albert Lipmann	Discovery of co-enzyme A and its importance in intermediary metabolism.
1971	Earl W Southerland Jr	Mechanism of action of hormones and their second messengers.
1977	Rosalyn Yalow	Development of Radioimmunoassay. Demonstrated through use of radioactive iodine that type 2 diabetes is caused by body's inefficient use of insulin.
1985	Michael S Brown Joseph L Goldstein	Discovery concerning the regulation of cholesterol metabolism.

Nobel laureates for Physiology or Medicine whose work was related to the field of glucocrinology.

Diabetes Mellitus

- Diabetes mellitus is a complex syndrome, characterized by hyperglycaemia.
- The earlier understanding was that diabetes is a state of decreased insulin secretion and/ or insulin resistance with hyperglycaemia as the core abnormality.
- Diabetes is now recognized to be a multisystem disorder involving metabolic dysfunction, adiposopathy, chronic inflammation, endothelial dysfunction and oxidative stress and increased cardiovascular risk.

Endocrine Impact on Glucose Regulation

- Endocrine glands play a pivotal role in the development of diabetes
- Diabetes is primarily understood as a disease of the endocrine pancreas.
- Other endocrine glands including adipose tissue, gastrointestinal endocrine system, pituitary, parathyroid, thyroid, adrenals and gonads are associated with diabetes in multiple ways, in both the etiopathogenesis of diabetes and development of comorbid states.

Various aspects of glucocrinology

- Endocrinopathies may cause secondary diabetes:
 - Acromegaly
 - Cushing's syndrome
 - Glucagonoma
 - Pheochromocytoma
 - Somatostatinoma
 - VIPoma
 - Hyperthyroidism
 - Hyperaldosteronism
 - Hyperparathyroidism
 - Insulin resistance syndromes, type A and B
 - Lipodystrophy

Various aspects of glucocrinology

Endocrinopathies may be associated with Metabolic syndrome:

- Polycystic ovary syndrome (PCOS)
- Hypothyroidism
- Subclinical Cushing's syndrome

Endocrine dysfunction and diabetes may coexist:

- Autoimmune polyglandular syndromes
- Multiple endocrine neoplasia
- DIDMOAD syndrome
- Mitochondrial disorders, including MELAS
- Chance association

Various aspects of glucocrinology

Endocrine dysfunction may be the etiology of refractory hyperglycemia in diabetes:

- Hyperthyroidism
- Cushing's syndrome
- Acromegaly

Comorbidities/ complications of diabetes may delay the diagnosis of endocrine dysfunction:

- Hypertension - delayed diagnosis of pheochromocytoma or hyperaldosteronism
- Neuropathy - delayed diagnosis of hypothyroidism
- Obesity and metabolic syndrome - delayed diagnosis of Cushing's syndrome

Various aspects of glucocrinology

Endocrinopathies associated with increased risk of hypoglycaemia with diabetes treatment:

- Adrenal insufficiency
- Hypothyroidism
- Growth hormone deficiency
- Combined pituitary hormone deficiency

Endocrinotropic drugs may worsen diabetes/ exacerbate hyperglycaemia:

- Glucocorticoids
- Thyroid hormones
- Inotropes
- Growth hormone
- Oestrogen (high dose)
- Somatostatin/ Octreotide

Various aspects of glucocrinology

Endocrinotropic drugs may be used to manage diabetes:

- Bromocriptine
- Mifepristone
- 11- β HS1 Inhibitors

Glucose lowering drugs may exhibit endocrine exaptation:

- Metformin reduces serum TSH
- Treatment of endocrine dysfunction may unmask latent diabetes:
- Addison's disease
- Hypothyroidism

Glucocrinology: Concept of Interplay and Interlink of Glucose Homeostasis and Endocrine Glands

1. Endocrinopathies may cause secondary diabetes:

- Acromegaly
- Cushing syndrome
- Pheochromocytoma
- Hyperthyroidism
- Hyperaldosteronism
- Hyperparathyroidism

Glucocrinology: Concept of Interplay and Interlink of Glucose Homeostasis and Endocrine Glands

2. Endocrinopathies may be associated with metabolic syndrome:

- Polycystic ovary syndrome
- Hypothyroidism
- Subclinical Cushing syndrome

3. Endocrine dysfunction and diabetes may coexist:

- Autoimmune polyglandular syndromes
- Multiple endocrine neoplasia
- Mitochondrial disorders

Glucocrinology: Concept of Interplay and Interlink of Glucose Homeostasis and Endocrine Glands

4. Endocrine dysfunction may be the etiology of refractory hyperglycemia in diabetes:

- Hyperthyroidism
- Cushing syndrome
- Acromegaly

5. Endocrinopathies associated with an increased risk of hypoglycemia with diabetes treatment:

- Adrenal insufficiency
- Hypothyroidism
- Growth hormone deficiency

Glucocrinology: Concept of Interplay and Interlink of Glucose Homeostasis and Endocrine Glands

6. Endocrinopathic drugs may worsen diabetes:

- Glucocorticoids
- Thyroid hormones
- Inotropes
- Growth hormone
- Estrogen
- Somatostatin analogs

Sulfonylureas: An Established Treatment of DM

Guideline Recommendation

- **American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) Recommendations for SUs in T2DM Management**
- Modern SUs confer a lower risk of hypoglycemia and have favorable cost, efficacy, and safety profiles.



REVIEW

Glucocrinology of Modern Sulfonylureas: Clinical Evidence and Practice-Based Opinion from an International Expert Group

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Clinical Evidence and Practice-Based Opinion from an International Expert Group

Modern SUs (such as glimepiride and gliclazide MR) should be preferred to conventional SUs especially in

- Overweight/obese T2DM patients
- Patients at a high risk of hypoglycemia
- Patients at a high risk of CV diseases

Modern SUs (such as glimeperide and gliclazide MR) should be preferred to conventional SUs with the aim to reduce mortality, bring better outcomes, and preserve renal function

Clinical Evidence and Practice-Based Opinion from an International Expert Group

- The panel suggests that the patients/family members should be educated on the appropriate use (dose, time, route, and adherence) of modern Sus
- The pleiotropic effects of modern SUs, including beneficial effects on the pancreas, extra-pancreatic effects, immunomodulatory effects, and other effects on endocrine functions, were reinforced in the meeting

Clinical Evidence and Practice-Based Opinion from an International Expert Group

Cardiovascular Effects of Sus

- The Clinical Expert Group Endorsed Newer SUs. Because of CV Safety Since modern SUs (such as gliclazide MR and glimepiride) are associated with a lower risk of all-cause and CV-related mortality compared to conventional SUs in T2DM patients.

Clinical Evidence and Practice-Based Opinion from an International Expert Group

The Clinical Expert Group Endorsed Newer SUs Because of CV Safety

- The clinical expert group opinion suggests that the modern SUs can be used in T2DM patients with CV risk, myocardial infarction, or stroke
- Modern SUs (such as gliclazide MR and glimepiride) are associated with a lower risk of all-cause and CV-related mortality compared to conventional SUs in T2DM patients

Clinical Evidence and Practice-Based Opinion from an International Expert Group

Affordability and Improved Adherence with Modern SUs

- Modern SUs offer superior glycemic efficacy and are also available at a reasonable cost
- Treatment with modern SUs is associated with a lower economic burden, and hence they are an effective alternative to other newer antidiabetic drugs.

Summary

- The concept of glucocrinology revives the importance of endocrinology and endocrinologists in diabetes management
- It enhances the understanding of a multifaceted disorder, while opening new therapeutic and preventive targets.
- It also promotes a comprehensive and complete assessment and management of diabetes
- The concept of glucocrinology to be implemented in the management of diabetes to achieve holistic care and best clinical outcomes.



Thank You