Summer Training

At

JOLLY HEALTHCARE

(1st April to 31st May 2020)

A Report

by

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MBA Pharmaceutical Management

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THE IIHMR UNIVERSITY

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CERTIFICATE

This is to certify that Miss. ADITI APOORVA student of MBA PM 11, Enrolment no. **IIHMR-U/02/2019-21/0163** (academic year 2019-2021) has submitted her project on "**BALILA MARKET SURVEY**" in partial fulfilment for the requirement for the award of **MASTER OF BUSINESS ADMINISTRATION**.

SUPERVISOR

DR. ARPITA BASAK

ASSOCIATE PROFESSOR

SCHOOL OF PHARMACEUTICAL MANAGEMENT

DATE:

PLACE: JAIPUR

ACKNOWLEDGEMENT

It is great pleasure for me to acknowledge all those who have contributed towards the conception, origin and nurturing of this project.

This work was carried out at the School of Pharmaceutical Sciences Pharmaceutics, IIHMR University, Jaipur, Rajasthan.

It is a delightful moment for me, to put into words all my gratitude to my esteemed guide and preceptor **Dr. ARPITA BASAK**, for her inestimable guidance, valuable suggestions and constant encouragement during the course of this study. It is with affection and reverence that I acknowledge my indebtedness to her and her outstanding dedication, often far beyond the call of duty. Apart from guiding me, her unwiring moral support and advice.

At this moment, last but not least, express my heartiest regards to **My family and friends** for their energetic, moral and economical support that boosted my spirits. It was the blessing of them that gave me courage to face the challenges and made my path easier. It is because of them I have reached the place where I am today.

Aditi Apoorva

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EXECUTIVE SUMMARY

The project assigned is **Ballia market survey.**

The point of the investigation is to do the market survey of Diazoxide molecule in different cities across India as organization is going to launch a hypoglycaemic agent i.e. DIAZOXIDE for neonates. The study was conducted by utilising a structured questionnaire for data collection from respondent i.e Paediatricians and Neonatologists of the hospital. Data was analysed & the findings were obtained for the comprehensive review of market situation.

I have surveyed 77 doctors comprises of Paediatricians and Neonatologists. By this survey, I tried to know the various preferences of doctors concerning the diazoxide molecule. I have done my survey in around 6 cities through telephonic/online medium and questions to doctors are asked via questionnaire. The results obtained from the survey is helpful and informative.

This project was carried out in 3 stages:

1. Finding the hospitals which have NICU facility and getting their response over telephone .
2. Conducting primary data collection survey.
3. Data analysis and data interpretation.

COMPANY PROFILE

Jolly Healthcare-Bridging the Unmet Medical Needs!!

From the beginning, the founders envisioned a company that consistently generates fresh intellectual capital to combat challenging diseases

Jolly Pharmaceuticals started operations in 1996—the year Dr. Krishna M. Ella and Mrs. Suchitra Ella returned from the US to line up a corporation dedicated to making innovative vaccines and bio-therapeutics. Dr. Ella was coming back from a search and teaching stint within the US and he wanted the new company to be an intellectual capital powerhouse. within the years that followed, he

assembled a team of bright scientists and led the creation of path-breaking vaccines.

Today, Jolly Pharmaceuticals has over 50 patents. As the number one biotechnology company, we seamlessly straddle the worlds of marketing research and manufacturing to make effective vaccines and therapeutics for patients around world.

"Jolly Healthcare is one of the fastest-growing Pharma Exporter in India with a wide range of pharmaceutical formulations with an assurance of quality and reliability for both Domestic and Export (Indian Subcontinent & Africa) market. The Company has contract-manufacturing tie-up with a state-of-the-art WHO-GMP certified manufacturing Unit at Haridwar. Jolly Healthcare observes Safety Health Environment (SHE), U.K.-M.H.R.A. and U.S.-FDA. Norms. Our product portfolio covers almost all therapeutic segments like Anti-malarial, Analgesics, Anti-diabetics, Gastro-intestinal, Anti-allergic, Cough & cold preparations, Anti-fungal, Antibiotics, Sedatives, Tranquilizers, Anti-amoebic, Anti-diarrheal, Erectile Dysfunction tablet, Hypertension tablets, Anti-fungal, Anti-HIV, Anti-Cancer, Vitamins, Corticosteroids, Anti-ulcers, Hormonal Preparations, Ointments & Cosmetics and Herbals and Nutraceuticals & Food Supplements. At Jolly Healthcare we supply formulations in practically all dosage forms, i.e. Tablets, Capsules, Soft Gels, Dry Syrups, Liquid Orals, Powder in Sachet, Dry & Liquid Injections, Pre-filled Syringes, Large Volume Parenteral, Eye / Ear / Nasal Drops. JOLLY HEALTHCARE strengths lie in developing Quality & Affordable Products with QC certificates-COA report and COPP certificates. We have the finest team for the Product Dossiers and have 100% success rate in Dossier Approval. We have developed a new drug delivery system for 100 % Timely Delivery of Products to our Valuable Importers. Our

pharmaceutical formulations have gained huge acknowledgement for their unsurpassed effectiveness and highly competitive rates."

Our Mission- To become No. 1 shortage and orphan drug company in India by 2020.

Our Vision- Availability of life-saving drugs and diagnostics for the neglected across the globe.

Our USP- Essential ingredients of Exports possessed by Jolly Healthcare-

1. Quality
2. Capacity & Timely delivery
3. Competitive price
4. Sound Financial Status
5. Well defined systems of production
6. WHO-GMP, ISO-9001, ISO-14001, SHE & International Bar Coding.
7. Exports to Bhutan, Sri Lanka, Africa etc
8. Manufacturing & Marketing Shortage & Orphan Drugs

Our strengths-

1. WHO-GMP Approved & UKMHRA Compliant Manufacturing Unit
2. Anabolic Steroid Manufacturer
3. Best ACTD/CTD dossier
4. Timely Delivery
5. Comfortable payment terms
6. Affordable Pricing

Our plant is approved by the following authority:

- WHO GMP CERTIFICATE- With more than 900 COPP
- NAFDAC, Ministry of Health, Nigeria
- MOH-ZAMBIA

- DOMINIC REPUBLIC
- MOLDOVA
- SRILANKA
- ANVISA

Trade affiliations-

- PHARMEXCIL
- DGFT
- Company of Registrar
- Indian Pharmaceutical Association
- WHO-GMP

Trade show we participate-

- CPhi India
- CPhi SEA
- Middle East Gateway for the Medical & Pharmaceutical Industries

Transparency in Dealings-

1. Transparent & honest dealings
2. Ethics of business
3. Corporate governance
4. Fair dealings
5. Fast communication
6. 100% Dossier approval
7. QC certificates-COA report and COPP certificates
8. 100 % Timely Delivery of Products

I. Product Portfolio

A. Anti-HIV

a) Cytoflu (Flucytosine)

b) Valgaids (Vanganciclovir)

B. Antibiotics

a) Jolltrim (Trimethoprim + Sulfamethoxazole)

b) Jolclo (Cloxacillin)

c) Jollpen (PenicillinG)

d) Huelin (Benzathine Penicillin)

e) Nostof (Cefazolin Sodium)

f) Sulphaz (Sulphadiazine)

C. Analgesic

a) Cabaza (Pentoxifyline)

D. Antifungal

a) Mycoflu (Amphoterecin-B)

E. Diagnostics

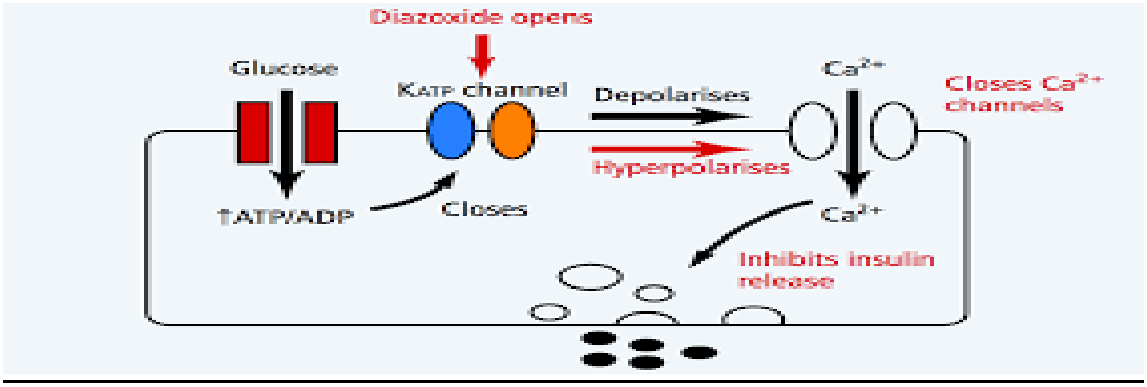
a) Exacto (HIV test kit)

INTRODUCTION

Hypoglycaemia is when the extent of sugar (glucose) within the blood is simply too low. Glucose is the main source of fuel for the brain and therefore the body. during a new-born infant, low glucose can happen for several reasons. It can cause problems like shakiness, blue tint to the skin, and feeding and breathing problems.

MECHANISM OF ACTION

Diazoxide increases the permeability of the membrane to potassium ions in vascular smooth muscle, thereby stabilizing the membrane electrical discharge and preventing the contraction of vascular smooth muscle; this finishes up in peripheral vasodilatation and reduces in peripheral vascular resistance. This hypoglycaemic agent also inhibits the release of insulin by interacting with ATP-sensitive potassium channels of islet beta-cells of the **pancreas.**



Neonatal hypoglycemia happens when the neonate's blood glucose level is not exactly the infant's body prerequisites for components, for example, cell vitality

and digestion. There is irregularity globally for indicative limits. In the US, hypoglycemia is the point at which the blood glucose level is underneath 30 mg/dl inside the initial 24 hours of life and beneath 45 mg/dl from that point. In the UK, in any case, lower and progressively factor edges are utilized (<18 mg/dl whenever OR infant with unusual clinical signs and a solitary worth <45 mg/dl OR infant in danger of disabled metabolic adjustment however without irregular clinical signs and an estimation <36 mg/dl and remaining <36 mg/dl at next estimation). The neonate's gestational age, birth weight, metabolic requirements, and health condition of the infant substantially affect the neonate's blood glucose level. There are realized hazard factors that can be both maternal and neonatal. This is a treatable condition. Its treatment relies upon the reason for the hypoglycemia. Even though it is treatable, it very well may be lethal whenever gone undetected. Hypoglycemia is the most widely recognized metabolic issue in infants.

Hyper-insulinemic hypoglycaemia (HH) has continuously been seen as an explanation behind headstrong hypoglycemia in neonates and infant youngsters. HH happens on account of uncontrolled discharge of insulin from β-cells of islets of Langerhans in the pancreas. Small for gestational age (SGA) babies and macrosomic infant of diabetic mothers (IDM) are the two most essential social affairs of infant kids at risk for hypoglycaemia in the neonatal period. Glucose is crucial essentialness hotspot for the new-born cerebrum and hypoglycaemia is known to cause irreversible neuronal injury when it is dreary and genuine; so speedy affirmation and treatment of these infant youngsters with HH is indispensable.

HH is of two kinds i.e. transient and congenital. Data on blood glucose homeostasis and fitting assessments for centre individual metabolites throughout a scene of hypoglycaemia is the establishment for investigation and the administrators of HH. The organization of therapeutically dormant HH regardless

of everything remains a test. Data on genetic changes, more forward-thinking imaging modalities like Fluorine 18L-3, 4 dihydroxyphenylalanine positron transmission tomography (18F-DOPA-PET) yield and availability of histological division of focal and diffuse kinds of consistent HH have streamlined the organization of Congenital Hyperinsulinism (CHI).

I] What causes hypoglycemia in an infant?

Hypoglycemia can be brought about by conditions, for example,

1. Poor sustenance for the mother during pregnancy

2. Making an excessive amount of insulin in light of the fact that the mother has inadequately controlled diabetes

3. Incompatible blood classifications of mother and child (extreme hemolytic sickness of the infant)

4. More insulin in the child's stool for different reasons, for example, a tumour of the pancreas

5. Birth imperfections

6. Congenital metabolic maladies or hormone insufficiencies. A portion of these disagreement families.

7. Not enough oxygen during childbirth (birth asphyxia)

8. Liver malady

9. Infection

II] Which babies are in danger for hypoglycemia?

Infants are bound to have hypoglycemia include:

1. Babies destined to moms with diabetes

2. Babies who are little for gestational age or development confined

3. Preterm infants, particularly those with low birth loads

4. Babies brought into the world under critical pressure

5.Babies with moms rewarded with specific medications, for example, terbutaline

6. Babies who are huge for their gestational age

III] What are the indications of hypoglycemia in an infant?

Indications of low glucose may not be clear in infants. The most well-known signs include:

1. Shakiness

2. Blue color to skin and lips (cyanosis)

3. Stopping breathing (apnea)

4. Low internal heat level (hypothermia)

5. Floppy muscles (poor muscle tone)

6. Not keen on taking care of

7. Lack of development and vitality (laziness)

8. Seizures

IV] Management of Hyperinsulinemic Hypoglycemia with Diazoxide

Diazoxide, a Potassium-Adenosine Tri Phosphate channel activator, its a pillar of clinical treatment in delayed HH. Diazoxide forestalls alpha-cell layer depolarization, what's more, represses insulin discharge by keeping a Potassium-Adenosine Tri Phosphate channels open. It is administered via oral route with a dose of 5-20 milligram per kg per day in three partitioned dosages. Once utilizing diazoxide in babies having hepatic brokenness or hypoalbuminemia, use lower dosages of 3 milligrams per kg per day as it is profoundly protein-bound (more than 90%). Additionally, lower dosages are more secure in SGA babies as they are touchy to diazoxide. Diazoxide is ordinarily joined with thiazide diuretics to balance its most normal reaction of liquid maintenance in neonates. Hypertrichosis is also a significant normal intricacy of this molecule which for the most part returns following the end of treatment. Diazoxide effect is noted when baby can quick properly for age, keeps up ordinary glucose levels and shows ascend in serum unsaturated fats and ketone bodies toward the finish of quick. Nifedipine, a Ca^{+2} channel antagonist, has been utilized in barely any diazoxide inert instances of CHI, however, a lot of such patients fails to show any response.

V] About the product – BALILA

Diazoxide enables the release of insulin from pancreas by opening the potassium channel. Hence it increases the potassium ion permeability through the membrane and causes the hyperpolarization eliciting the relaxation of the local smooth muscles (because of which voltage-gated calcium ion channel switches off leading to inhibition of action potential generation).

It also acts as a peripheral vasodilator hence used for hypertensive emergencies (it relaxes articular smooth muscles and decreases the vascular resistance). Diazoxide is an antidiuretic hence increase the reabsorption or retention of sodium and water/fluid in the body (therefore it may precipitate the CHF in cardiac patients).

Fig.1- Balila Pamphlet

The pharmacokinetics of the drug is as follows-

1) Absorption- readily absorbed in the body following the oral route of administration.

2) Distribution- Dispersed all through the body; the most significant level is found in kidneys, liver, and adrenal organs; it passes through the placental barrier and blood-cerebrum barrier. It has high protein-philic affinity i.e. around 90% to serum proteins, in this manner, it has a half-life of around 25 to 35 hours in typical grown-ups.

3) Metabolism- partially metabolised in the liver.

4) Excretion- discharged gradually by the kidneys in urine.

Consecutive administration of benzothiazide and in presence of hypokalaemia condition the hyperglycaemic activity of diazoxide gets enhanced. The hyperglycaemic activity of diazoxide can be antagonized by the administration of insulin, tolbutamide and alpha-blockers (like prazosin terazosin and doxazosin etc).

Diazoxide is commonly recommended for grown-ups who have inoperable islet cell adenoma or carcinoma or extra pancreatic danger. It can likewise be utilized in babies and youngsters which are experiencing leucine affectability, islet cell hyperplasia, nesidioblastosis and extra pancreatic danger.

It is contraindicated in patients with hypersensitivity towards diazoxide or to other thiazides. It should also not prescribe in case of improper renal functioning, functional hypoglycaemia, pregnancy (due to severe teratogenic effects).

Diazoxide requires close clinical oversight with cautious checking of blood glucose and clinical reaction so portion alteration should be possible appropriately.

Some ADR's related to the drug is as follows-

1) Hirsutism
2) Diabetic ketoacidosis
3) Hyperosmolar non-ketonic coma
4) Na+ ion and water retention
5) GI intolerance like nausea, vomiting.
6) Hypotension
7) Cataract
8) Fever
9) Gout
10) Acute Pancreatitis

Overdose of diazoxide can be treated with prompt insulin administration and Restoration of electrolyte balance and fluid. It also requires prolonged surveillance for up to 7 days due to the long half-life of the drug. It shows a drug-drug interaction with a diuretic, coumarin anticoagulants, diphenylhydantoin, and chlorpromazine.

Usual daily dosage for adults and children is 3 to 8 mg per KG and for infants and new-borns, it is 8-15 milligram per kilogram separated into 2 or 3 equivalent quantities every 8 or 12 hrs. To maintain its stability ideally it must be stored at room temperature ranging between 15-30 C.

Literature Review

Shrenik Vora, Khalid Hussain And Victor Samuel Rajadurai, Suresh Chandran

"Assessment of blood tests, assembled at the hour of hypoglycemic scenes, for delegate metabolites and hormones is essential for finding and treatment. Extended care among clinicians about infant youngsters "in harm's way" of hypoglycemia and late advances in the genetic investigation has made an imperative responsibility to the assurance and the leading body of hyperinsulinism. Increasingly flow drugs like lanreotide (long-acting somatostatin straightforward) and sirolimus (mammalian target of rapamycin (mTOR) blocker) appear to be encouraging as patients with the diffuse ailment can be managed adequately without subtotal pancreatectomy, restricting the long stretch sequelae of diabetes and pancreatic lack. More state-of-the-art bits of information in understanding the sub-nuclear and histological reason and upgrades in imaging and cautious systems will change the best approach to manage patients with natural hyperinsulinism."

Paul J. Rozance, MD

"Management of neonatal hypoglycemia remains controversial due to inconsistent definitions and a lack of high-quality interventional trials [1;63]. No new studies addressed these deficiencies. However, new studies have been published describing the incidence of low glucose concentrations in the four most at-risk group of asymptomatic neonates and showing that repetitive low glucose concentrations are not associated with adverse long-term outcomes. But the serious consequences of hypoglycemia, especially due to hyperinsulinism, have been confirmed and advances made in the diagnosis and management of these patients. Finally, newer studies continue to demonstrate the promise of CGMS for improving research and clinical care in this area."

Siddique A.A., Saleem A.M.

"According to our observation, the incidence of hypoglycemia in low birth weight neonates in the present study is 24%. Small for gestational age is a significant determinant for hypoglycemia. The point that study adding to the existing knowledge - Hypoglycemic episodes were significantly noticed in the first 24 hours as compared to another time interval. Various co-morbidities were analyzed in normoglycemic and hypoglycemic infants of which sepsis was significantly noticed after hypoglycemia."

OBJECTIVES OF PROJECT

To investigate the market of Diazoxide in multiple cities of India.

RESEARCH METHODOLOGY

Sample Design- Descriptive Study

Sampling Method- Non -probability (purposive) sampling

Sample Population-paediatrics and neonatologist

Sample Size- 77

Sampling Area- Jodhpur , Patna ,Delhi Mumbai ,Nashik ,Pune

Tool Used- Telephonic and online survey using a questionnaire

Data Analysis and Interpretation**:**

Analysis and interpretation of the data have been carried out to deduce the conclusions with the aid of appropriate statistical tools

Results & Discussions

1) No. of Doctors responded?

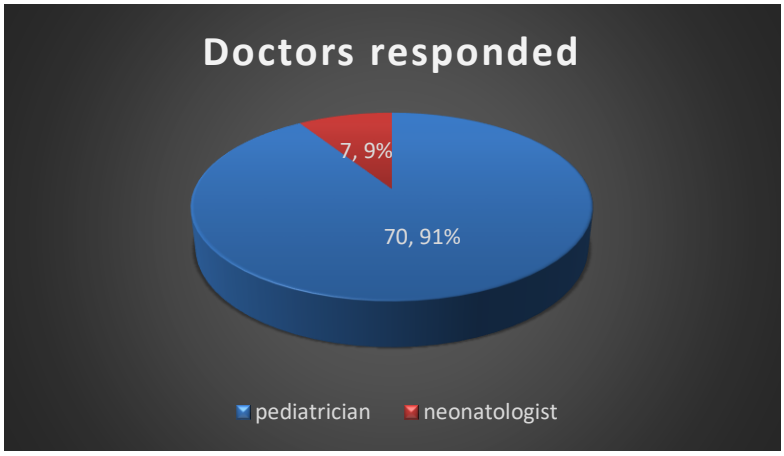


Fig.2- Depiction of Doctor's responded to the survey questionnaire.

Interpretation – From fig.2 it was observed that 91% paediatrician and 9%neonatologist responded.

2) Type of Hospitals covered?

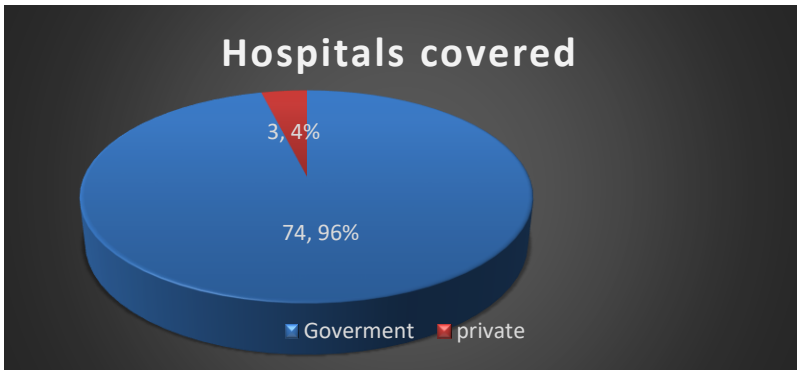


Fig.3- Depiction of Hospitals covered during the survey.

Interpretation – From fig.3 it was observed that 96% were Private hospitals and 4% were Government hospitals.

3.How many NICU bed your hospital have?

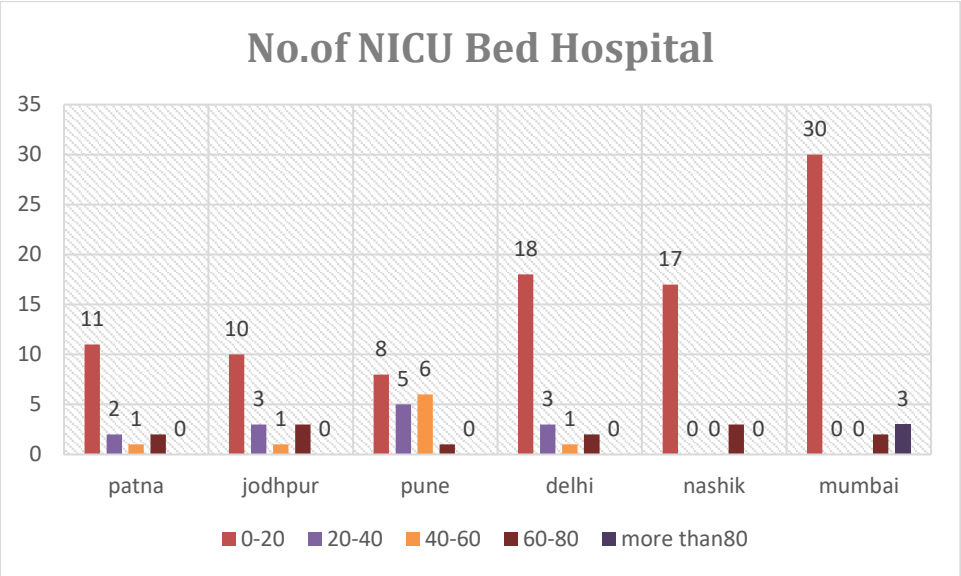


Fig.4: Depiction of city on the basis of NICU bed.

Interpretation – From fig.4 it was observed that product should launched in Mumbai followed by Delhi.

4)In which condition(s) you preferred the Diazoxide molecule

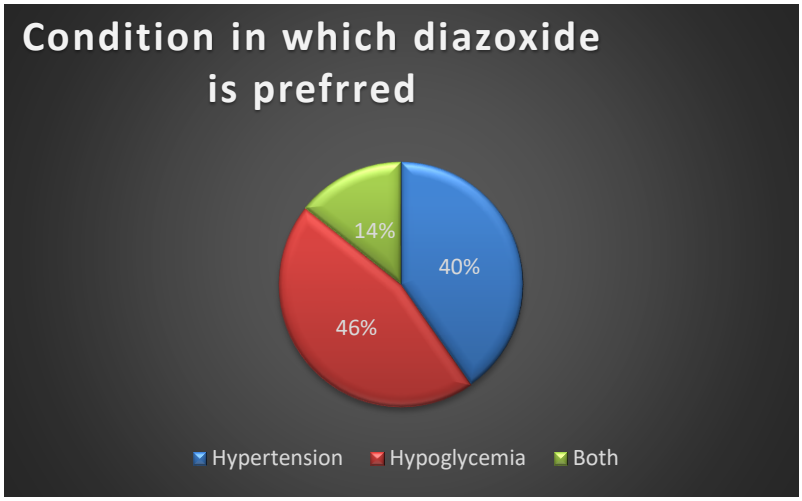


Fig.5- Depiction of indications used for Diazoxide.

Interpretation – From fig.5 it was observed that diazoxide was preferred by 46% responded for Hypoglycemia followed by 40% respondent for Hypertension.

5)Which is the most preferred form of administration by patients?

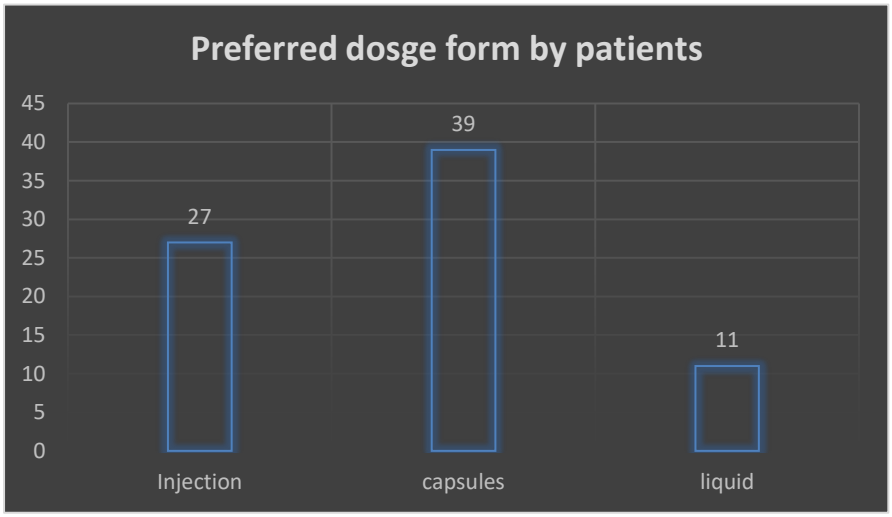


Fig.6- Depiction of preferred dosage forms.

Interpretation – From fig.6 it was observed that most preferred dosage form by the patient was capsules followed by injection and then liquid form.

6) **Which of the following attributes influences your prescription?**

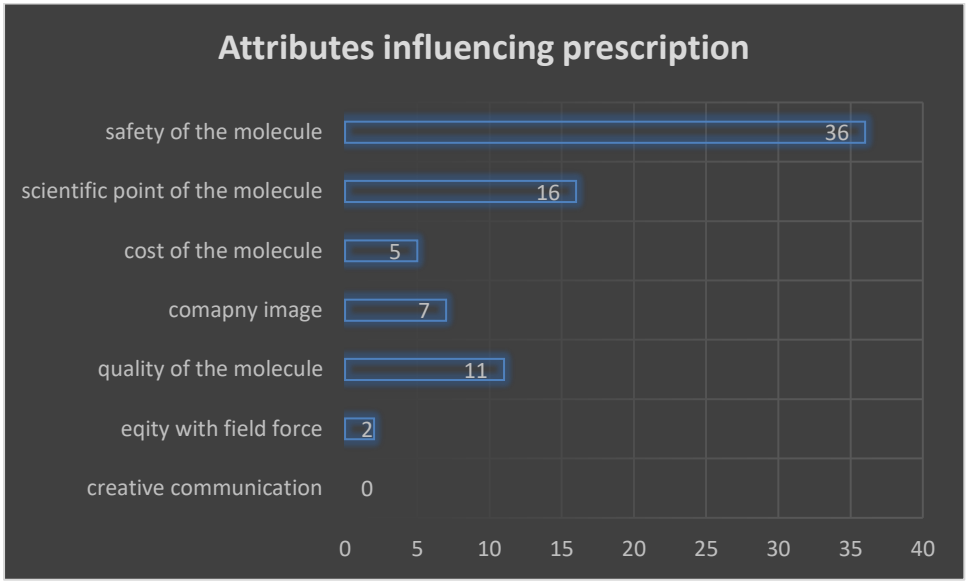


Fig.7- Depiction of attributes influencing the prescriptions.

Interpretation – From fig.7 it was observed that Safety of the molecule and Scientific point of the molecules are two major attributes that influence the prescription of respondents.

7)Which of the following activity will help you in prescribing the Drug molecule?

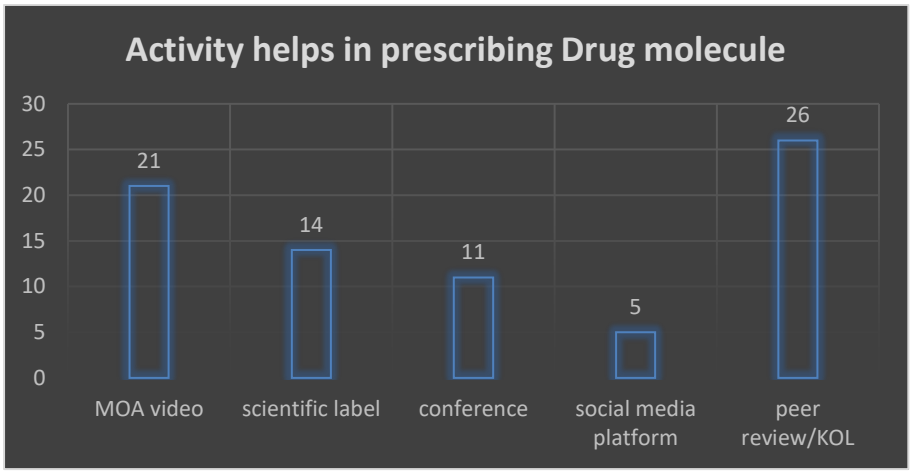


Fig.8- Depiction of activities that help in Prescribing Diazoxide.

Interpretation – From fig.8 it was observed that the KOL/peer review followed by MOA VIDEO is the two major activities that help in prescribing the drug.

8)How do you mostly treat Severe Hypoglycemia patients?

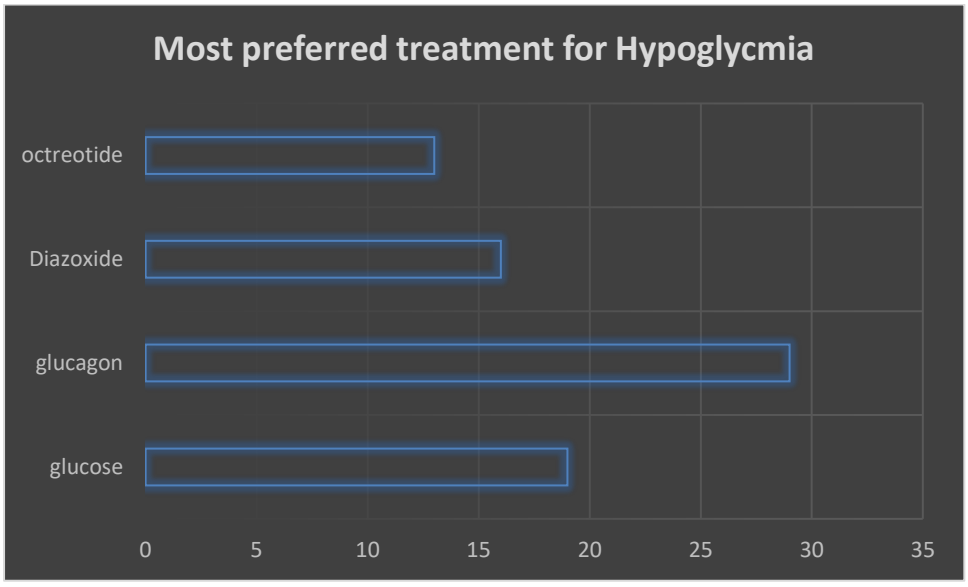


Fig.9- Depiction of preferred treatment for severe hypoglycaemia

Interpretation – From fig.9 it was observed that Glucagon and Glucose (IV) are most preferred for severe hypoglycaemia conditions.

9) what is the most preferred treatment in mild/moderate hypoglycaemia?

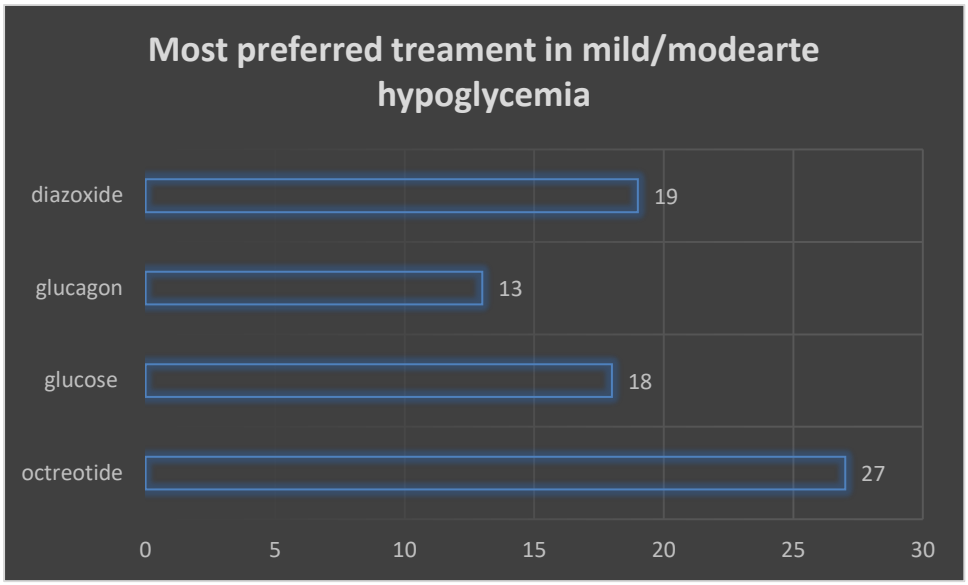


Fig.10 Depiction of preferred treatment for mild/moderate hypoglycaemia.

Interpretation – From fig.10 it was observed that octreotide and diazoxide are most preferred for mild/moderate hypoglycaemia conditions.

CONCLUSION

To conclude diazoxide is an effective treatment for Hyperinsulinemic hypoglycemia and malignant hypertension. Hyperinsulinemic hypoglycemia majorly occurs due to excessive endogenous or injected insulin. Malignant hypertension has a BP that is commonly over 180/120 while the normal range is 120/80. Malignant hypertension ought to be treated as a health-related crisis or a medical emergency. India can be a hub of malignant hypertension due to a large number of Hypertensive patients and its association with Diabetic pool in the country. Hence there can be a potentially untapped market for this molecule. Jolly Healthcare is one of the best companies in the orphan drug market which provides quality and efficacious products to doctors and patients at a competitive price.

And there are less competitors present in the market for orphan drugs which provide quality and effective drugs to the doctor

RECOMMENDATION

- According to respondents, Diazoxide is a potent molecule which can be used in Hyperinsulinemic Hypoglycemia and severe hypertension conditions.
- According to respondents, KOL opinions can drive prescription behaviour
- Strong scientific knowledge backed representative can bring good Top line growth.
- The dosage form of the drug can play a pivotal role since the drug can be targeted to all age segments i.e. from Neonates to Adults.
- Safety of the molecules is a major source of concern for respondents towards their patients therefore lesser side effects molecule or a drug with a precise amount of active ingredient will be most suitable.
- According to No. of NICU beds in hospital , we should target the hospital which have more NICU bed so that we can target more consumers and according to this drug should launched in Mumbai followed by Delhi.

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