IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

OBESITY AND ITS INDUCTION MODELS: A REVIEW UPDATE

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ABSTRACT:

Stoutness is a chronic disorder which result in metabolic disfunction in our body, it occur due to various etiology like, genetic, physical parameter and it is related to various environmental factors and socioeconomic factor which include consumption of processed food, Alcoholic beverages etc. The indication of obesity is start with overweight stub burn fat around abdomen and slow metabolic rate in our body. It associated with the risk of several diseases, such type of diseases are "type II diabetes mellitus and cardiovascular disease", It also affect immune system. In this study, we came to know about the various method of induction of obesity in rats such as diet induced obesity it includes 6NCrl mice (High fat diet, high fat, high carbohydrate diet and so on), Matronly overfeeding, drug induced obesity, chemical induced obesity, Surgical Method which include (VMH lesions, oophorectomy, Castration) age related obesity and so on . It is quite common that these are commonly stoutness induced models in rodents. So, this article summarized all the concern factors which causes stoutness and its treatment.

KEYWORDS: Stoutness Model, Metabolic disfunction, Matornly, VMH lesions.

INTRODUCTION:

A Condition that lead to metabolic disorder and increase the fat, cholesterol and weight of our body this disorder is called as stoutness. It can first identify by the body mass index(BMI) by which you can identify that you are under weight or over weight ,this BMI is further divided in to various class such as Type – 1 stoutness is occurred due to uncontrolled food habits, immobile lifestyle and no or less physical activities this is the most common causes .Type-2 stoutness can also be occurred due to some disease such as Hyperthyroidism ,PCOD , Cushing Syndrome this type is found in fewer than 1% of the population. body's fat cells getting bigger which result in childhood and adult stoutness. Stoutness occur when there is imbalance in food consumption, resting metabolic rate and energy expenditure. The major cause of obesity in current scenario changes in culture, finances, and lifestyle, as well as a decline in physical activity and the improvisation of transportation systems and so on. Restoration, urbanization and globalization of food market these are elements that significantly contributed to the obesity. -If we talk about individual level causes of obesity is related to numerous endogenous and surrounding factors, but in most of cases we see that the consumption of calorie substance is high diet and less energy consumption is there and stoutness is also related to the less energy dense meal which having lots of deficiency in them which led to deficiency of many vitamins in our body. In the clinic, anthropomorphic parameters such as skinfold thickness, waist circumference, and total body fat content are employed to evaluate obesity. These are some of the more sophisticated techniques: quantitative magnetic resonance (qMR) measurement, dual-energy X-ray absorptiometry (DXA), bioimpedance analysis, and air displacement plethysmography, hydrostatic weighing, and ultrasonography, which used to measure the thickness of muscle, subcutaneous fat and intra-abdominal dept (Kleinert et al., 2018) Both computer tomography (CT) and magnetic resonance imaging (MRI) can provide an

accurate evaluation of the distribution of body fat. Being stout is linked to a high death rate and a high illness rate, necessitating significant health investments. (Huang et al., 2003; Su et al., 2016) It is also may lead to severe cases such as (CAD), sleep apnea , asthma , hyperlipidemia , high cholesterol level . The major problem is assosicated with the stoutness is that it can led to type -2 Diabetes mellitus, metabolic syndrome hypertension, certain stroke, cancer and osteoarthritis. (Schelbert, 2009; Su et al., 2016). Nowdays, various lifestyle management and diet management, surgeries are there to reduce stoutness but high morbidity rate is drawback.(Fritscher et al., 2007; Giannopoulos et al., 2010; Rodgers et al., 2012) Eating very appetizing food that is loaded in fat and sugar causes the mesolimbic dopamine pathway to be remarkably activated, increasing the desire to eat more calories. Psychostimulants, which increase brain dopamine levels and have been demonstrated to cause anorexia, are sold as supplements to reduce obesity. Among the first pharmaceuticals used for weight reduction were amphetamine derivatives, such as desoxyephedrine, phentermine, and diethylpropion, as well as rimonabant, sibutramine, fenfluramine, and dexfenfluramine. However, these drugs were taken off the market owing to misuse risks and serious adverse effects. The FDA has currently authorized the lipase inhibitor orlistat (Sane, 2019). Increased exercise facilities and a rise in weight-loss products made of herbs and complementary and alternative medicine are other indications..(Chakraborty et al., 2018; Mauro et al., 2008) The current emerging trend generate many anti-obesity drug which shows a remarkable growth in this metabolic disorder. The laboratory rodents show the similar effect as human obesity does the aim of article is to understand the different types of animal model and use of transgenic mice in this disorder it also throw a light on the emerging anti-obesity drugs.

ANIMAL MODEL OF OBESITY:

Diet-Induced Obesity:

The anatomical mechanisms thought to involved in high-fat diet-induced stoutness are linked to increased or excessive consumption of high-fat foods due to their low-satisfying effects, alterations in hormone and enzyme activity that are involved in the balance of stamina, such as hyperleptinemia and hyperinsulinemia is related to high-fat diets and associated with leptin and insulin resistance, and decreased of ghrelin release.(Inui, 2003) The diet-induced obesity model typically takes three to five months to acquire obese(Hariri & Thibault, 2010) There is a effective correlation between body weight or fat accumulation and the amount of fat in the diet. Genetically, C57BL/6 mice are more prone to T2DM, decreased glucose tolerance, and obesity (central adiposity) brought on by a high-fat diet.

The particular fatty foods included in the diets differ between research; examples include peanut butter, calf tallow, Crisco fat, lard, and palm oil. (Buettner et al., 2007)A traditional high-fat diet is less effective in causing obesity and associated co-morbidities than the cafeteria diet, often known as the human Western diet (high-fat, high-salt).(Sato et al., 2010)The technique entails exposing healthy, lean rats or mice to high-fat diets for three to four months. Weight increase is the most often assessed metric. Other physiological parameters include changes in blood pressure, and biochemical indicators include glucose intolerance, insulin resistance, high plasma leptin, elevated total cholesterol, low-density lipoprotein, and triglycerides. (Wolden-Hanson et al., 1998)Drugs for diabetes, hyperlipidemia, and obesity can also be tested in animals ehich are fed with high-fat diet. Animal models for high-fat diets have the advantages of being cheap and dependent on the type of diet used. The model is suitable for researching obesity caused by non-genetic lifestyle factors. One drawback of the diet plan is its length, which is about 16 weeks with a postponed start.

Cafeteria Induced Obesity:

Cafeteria diets (or CDs) are collection of a variety of tasty pieces that favour the western diet of humans, such as sweet, nuts, high fat milk, etc. The primary cause of CD-induced stoutness is hyperphagia, which is increased energy expenditure brought on by diet-induced thermogenesis (DIT), which is caused by sympathetic activation of brown fat. Adiposity, heaptosteatosis, and swelling in the liver, brown fat, and white fat increase in CD-fed rats. The frequency and amount of meals on a cafeteria diet are different from those on a pleasant diet. The model facilitates the quick achievement of insulin resistance and hypertriglyceridemia, as well as the close monitoring of the composition of nutrients. It facilitates comprehension of the connection between body mass, amount of fat ingested, and effects of various fat types**.**

SUBSTANCE-INDUCED OBESITY:

Gaining weight is a typical adverse effect associated with several medicines, particularly antipsychotic and antidepressant treatments. Weight gain is the outcome of decreased sympathetic nervous system activity as well as decreased serotoninergic and dopaminergic activity. The dopaminergic system's role in reward theory may be the cause. The desire to eat and food itself serve as rewards. The hypothalamus controls appetite by producing neuropeptides including NPY, leptin, ghrelin, orexin, and insulin. The majority of medications cause obesity by interfering with these peptides that regulate fat. Dry mouth from the anticholinergic action leads to a rise in calorie-dense beverage consumption. (Hahm et al., 2002) Among the examples are antipsychotic medications such as quetiapine and clozapine; antidepressants like tricyclic antidepressants; antimanic medications like lithium; and anti-convulsant medications like valproate and carbamazepine. Other medicines that come under the category of drug-induced obesity include glucocorticoids, β-adrenergic receptor blockers, anti-diabetic treatments, antimigraine and antihistaminergic drugs, and sex hormones. The model has a delayed onset, which is a drawback, but it is helpful for researching the association with other metabolic disorders.

CHEMICAL INDUCED MODEL:

Obesity caused by “mono-sodium glutamate {MSG}”. When mouse pups are given MSG (4.0 g/kg body weight, s.c.) from the first to the fifth days of life, they become obese by the sixth week and show signs of Vagal hyperactivity and hypoactivity of the sympathoadrenal system, which cause hyperinsulinemia and a rise in white fat. To prevent obesity in the newborn rats, MSG can be given subcutaneously or intraperitoneally, either regularly or as an alternate, in doses ranging from four to ten. MSG raises normal food consumption and induces metabolic disorders in mice, which raise levels of insulin, triglycerides, glucose, and leptin. (17) Rodents that are given gold thioglucose are made obese. After receiving a single intraperitoneal injection of gold thioglucose at a dose of 0.8 mg/gm

or 30–40 mg/kg, mice exhibit stoutness after 15 days. (Houtkooper et al., 2011)Administering gold thio-glucose alters capillary permeability, which allows for a sufficient blood flow to this region and ultimately results in necrosis in the ventromedial section of the hypothalamus. It is thought that the glucose moiety in gold thioglucose plays a significant role in the lesion's formation. Obesity results from hyperphagia brought on by the necrotic lesion. Additionally, it suggests that the ventromedial hypothalamus has unique glucoreceptor cells that regulate food intake. Body fat, body lipogenesis, and triglycerides are all increasing. This model's primary drawbacks are its high death rate and extended time to obesity development.

OBESITY CONNECTED TO AGE:

Another significant factor that significantly affects obesity outcomes is age. Human body weight grows with maturity, reaching a peak for both men and women at around 55 years of age. Insulin resistance has been linked to aging because of an increase in intramuscular and intrahepatic fat storage. It has been suggested that ageing is an independent factor that determines glucose tolerance, which gets poorer with age. As people age, a progressive decrease in androgens and other metabolic hormones also hastens obesity. Many used mouse strain for metabolic research, the C57BL/6J, has a body weight that grows with age; obesity peaks at nine months of age. When compared to young 3-month-old mice, the twenty two month old C57BL/6J mice show decreased lean mass and increased fat mass. Rats are more impacted by glucose tolerance than mice are. Research has indicated that aging rats exhibit elevated levels of body mass, insulin, cholesterol, and leptin levels. (Anisman et al., 2008)

STRESS INDUCED OBESITY:

Repeated exposure to social stresses causes body mass, obesity, and the consumption of high-calorie meals in both human and non-human primates. Under stress, the HPA axis is repeatedly stimulated, which modifies the negative feed-back process and causes metabolic alterations. (Aswar et al., 2017) Numerous studies have demonstrated that chronic stress causes people to eat more and acquire weight and fat. (Kalshetty et al., 2012)It has also been discovered that depression and fat are related. Previous research has shown that in rats with olfactory bulbectomy-induced depression, a high food intake is correlated with an increase in body weight. (Suleiman et al., 2020)

SURGICAL MODELS:

Rat Female Ovariectomies*:*

Preclinical research on a population of rats indicates that sudden hormone deprivation via ovarier tomy lowers estrogen levels, which in turn induces obesity and associated metabolic aftereffects. Leptin resistance is the term for the reduction of early leptin level followed by a rise in the same after 7 weeks following ovariectomy. Studies on ovariectomy in rats have shown a connection between total and LDL cholesterol levels, adiposity, insulin resistance, leptin resistance, and bilat eral ovariectomy, which results in obesity. (Von Diemen et al., 2006) We can learn more about the impact of hormonal alterations on female obesity by utilizing ovariectomy. (Gaur T et al., 2014) The fact that each animal must have surgery and that obesity might develop at different rates are the drawbacks.

Ventromedial - Hypothalamic Nucleus (VMH) Lesion:

"VMH" is the primary brain region responsible for energy balance, satiety, munchies regulation, and obesity. It plays a part in keeping cholesterol and triglyceride levels low and prevents the onset of insulin resistance. Stereotaxic VMH lesioning may be carried out with current intensity of 1mA and 10 s duration. The rat brain coordinates for this lesion are as follows: 1.6 mm anteriorly posterior to the bregma; 0.5 mm transversely lateral to the midsagittal line; and 0.2 mm vertically over the base of the skull. Significant increases in body weight and serum cholesterol are seen after the lesion. (Vickers et al., 2011)

GENETIC MODELS:

The C57BL/6J mouse family, which is inbred and prone to developing extreme obesity, increased A popular model for Diabetes Induces Obesity (DIO) is one that includes modest insulin resistance, glucose intolerance, and obesity.. The aforementioned metabolic alterations experienced during research necessitate that researchers carefully optimize strain selection based on protocol requirements and intended research outcomes. For instance, the C57BL/6N strain rather than the C57BL/6J model may be the better option for researching the relationship between diabetes and obesity since the former seldom experiences hyperglycemia and islet atrophy when fed a high-fat diet, whereas the latter has hepatosteatosis, hyperglycemia, and hyperinsulinemia. The inbred strain C57BL/6J is prone to atherosclerosis, type 2 diabetes, and obesity brought on by food. (J.-T. Xie et al., 2005) Mice homozygous for the obesity spontaneous mutation Lep ob (also called ob or ob/ob) have low amounts of leptin in their bloodstream. They have increased plasma insulin, obesity, hyperphagia, transitory hyperglycemia, and glucose intolerance. They is also subfertile, hypometabolic, and hypothermic. The ob/ob mice had significant hyperglycemia and pancreatic islet degeneration, which are indicative of pronounced diabetes mellitus and early mortality. (J. T. Xie et al., 2002)The main goal of the ob/ob mouse paradigm is to assess the efficacy of novel anti-stoutness drugs in mitigating a strong hyperphagia-induced obesity phenotype.Between 10 and 14 days, the db/db mice have high plasma insulin levels and leptin deficit., and obesity development between 4 and 5 weeks. Despite having a significant loss of pancreatic β cells in the islet, they show signs of Hyperinsulinemia, polyphagia, proteinuria, glycosuria, polyuria, and polydipsia. and lack the leptin receptor. (La Russa et al., 2019)

MATERNAL-OVERFEEDING AND EXPOSURE TO HIGH FAT DIETS:

It is thought that a mother's obesity poses a significant risk for her kids to also become obese. Obesity and impaired glucose tolerance in adult offspring may result from matornal obesity combined with increased nutrient or food intake before to and during pregnancy. Neonatal tal rat pups show evidence of extended and enhanced leptin spike as a result of maternal overfeeding. (Wong et al., 2016) The model aids in containing the obesity pandemic. The model may be used to investigate how particular developmental phases are impacted

by prenatal environment and genetic variables. The primary drawback of this approach is that emphasizing maternal obesity and food in adult disease prevention programs may exacerbate the obesity epidemic in coming generations. (Wong et al., 2016)

CONCULSION:

In this review recapitulate about different models of stoutness considering the ordinary models of animal, animal models where stoutness due to manner of living. The selection of animal models according to need is very important depending upon the target and availability of all the parameters which is required during the induction of models.Other use animal models such as numerous surgical models are used to induce stoutness such as castration and ovariectomy which is much more applicable for very late onset of diabetes. Other than this "VMH Lesion" can also be a factor for production of stoutness because pathway that ultimate for production of stoutness in food.

ACKNOWLEDGEMENTS:

I would like to express my special thanks of gratitude to my principal sir "Dr. G S Chakraborty" for their able guidance and support and providing me with all facility that was required in completing my Review Articles.

I would also like to thanks my Research Scholar "Rohit Agrahari" for their support and help.

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