Human Obesity, Pathological and Therapeutic Advances

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Abstract

Obesity is a prevalence metabolic phenotype caused by host-environmental interactions. Heavy financial burden is translate to obese people. Many types of preventive and therapeutic options have been widely sought after. However, most of these medications are temporal and expensive. In order to improve this special type of energy disturbance, glucose homeostasis and adipose dysfunction, further pathological and therapeutic investigations are desperately needed. To fully adapt human body in a good-shape, genetic, molecular, physiological, behavior, environmental and clinical approaches are in full swing now.

Keywords: Obesity; Endocrinology; Human Genome; Inflammatory Factors; Neural Disorder; Mental Disorder; Obese Treatment; Life-Style Adjustment; Metabolic Disease

Backgrounds

Current scenario

Obesity is a prevalence metabolic and physiological disorder caused by host-environmental interactions. Obese people commonly face a lot of personal trouble in the society and a number of patho-physiologic damages. Heavy financial burden is translate to obese people. Many types of preventive and therapeutic options have been widely sought after. However, most of these medications are temporal and expensive. In order to improve this situation, a series of preventive and therapeutic measures have been explored against this special item of metabolic phenotype-energy imbalance and glucose homeostasis disorder [1-4]. Since different patterns of therapeutic interventions are often temporary and commonly bounce back due to pharmaceutical limitation and setback. The great cost of obese control requires 20% of all medical expenditure in US [5]. More seriously, it has been increasingly prevalent in both industrial and agricultural-based countries. People with obesity commonly face a number of personal image troubles, social status downwards and a number of patho-physiological consequences.

Therapeutic limitations

It has been difficult and costly to fully manage human obesity by existing knowledge and therapeutic advances. After discontinuation of medical intervention (life-style and drug intakes), obese people regain their body-weight. To face with this grim therapeutic limitation, new ideas and perspectives must be created.

Pathologic and social issues

Pathologic consequences

Obese persons have a higher risk or rate of metabolic, cardiovascular or mental illnesses, such as depression, type 2 diabetes, cardiovascular symptoms and many others [2-10]. These clinical symptoms are difficulty to cure, which need to take medicine very long and overseen by specialists and doctors. It is overall costly. In addition, obese youngsters often meet with some forms of social embarrassment-difficult to be accepted by new acquaintance and match-makers.

Economic burdens

Obese managements encompass wide-spectra of medical/pharmacologic issues that exhibit a seriously economic burden-including diet control, life-style adjustments, high-quality exercises, surgery, drug utility and clinical therapeutics [2-12]. All these management systems require 190 billion USD (2010 - 2012) that attribute 20% all healthcare expenditure in the US [5]. Formal pharmaceutical therapeutics and putative drug target candidates need growing sum of money worldwide. Only by wide-ranges of scientific efforts and clinical validity, better therapeutic options and healthy social environments can be reliant against human overweight and obesity [13-22].

Therapeutic outcomes in general

Generally speaking, purposed weight loss is very difficult to achieve no matter what types of personal practice versus formal medications are seek in general hospitals and healthcare centers. Only a small proportion of obese people can get satisfactory therapeutic outcomes in the clinic worldwide. Many obese people, especially without receiving doctor's advice regain their body weight after intervention discontinuations [1-4]. As a result, most obese people struggle with this problem in a long period of times. These negative feelings further impact obese people for life quality reductions and pathological consequences.

Etiopathology

Obstacles

There are three major limitations for obese counteractive up to now:

1. Different types of counteractive measures are suitable for different individual with obese conditions and therapeutics;
2. Large proportion of obese people may bounce back after the therapeutic discontinuation; The scenario for therapeutic reversal needs to be notified.
3. It is necessary to seek doctor's/expert's advice because general people do not have essential medical and pharmacological knowledge [10,11]. This character is also costly.

To overcome these obstacles, cellular and molecular etiologic/pathological mechanism and study may improve potential therapeutics against human obesity.

Genetic predisposition

Similarly to many other chronic diseases, genetic predispositions play key roles for human obesity, metabolic disturbance and glucose homeostasis [18-30]. This element of biological/pathological issue in obese people may generally receive less therapeutic progresses by food limitations or cathartic therapeutics.

In the early stage of obese study, human genomic exploration and hypothesis-driven approaches are common avenues for finding curable medications in the clinic. In search for excellent therapeutic options, obese people are more suitable for combinations of life-style adjustments and drug treatments due to diverse obese originality and therapeutic resistance by current licensed drugs. More counteractive actions are required for meet with high-quality of drug discovery, licensing and marketing.

In the future, curable therapeutics must be look for. In order to attain this goal, patho-therapeutic relation must be built.

Multiple causes

Human obesity is caused by multitude and diverse factors:

- Overfeed (high proportion of obese population)
- Pathologic factorials (endocrinological factors)-leptin, thyroxine, insulin and many other hormonal dysfunction
- Sedentary (less physical activity and working)
- Gastro-intestinal abnormal (functional increase and overdone)
- Brain-visual-appetite axis (hypothalamic)
- Adipose dysfunctions (hypoxia or other stressing factors)
- Energy disturbance and glucose homeostasis
- Psychiatric burden and disorder
- Behavior (alcoholic and laziness)
- Drug-induced (hormonal drugs, antibiotics or other drugs associated with human liver dysfunction)
- Inflammatory factors (TNF secretion)
- Tumor-induced (pituitary tumors and others)
- Physiological change (adipose cells or tissues)
- Genetic alleles (loss-of-function or copy number changes of key genes and molecules)
- Inheritance and epigenetic switch
- Hormonal or blood glucose level escalations

Cellular and genetic mechanisms

To make any dramatically therapeutic breakthroughs, genetic/molecular approaches are fundamental. Until now, several mechanisms of obese etiology and pathologic pathways are discovered:

1. Until now, human brain can trigger appetite feeling through different neural axis or circuits. These processes include many neural-related pathways; hypothalamic-pituitary-somatotropic system (HPS); hypothalamic-pituitary-adrenal system (HPA) and hypothalamic-automic-gastroduodenal system (HAG) have been proposed [14].

2. Damaged metabolic tissues and organs require greater part of foods and glucose in human bloodstream for compensating. These compensatory processes may trigger weight-gain and metabolic syndromes [24].

3. Epigenetic ON/OFF switch is recently observed and clinically targeted in animal and human bodies. One of those genetic pathways is via TRIM28/TRIM28 [19,20].

4. Adipose-hypoxia can increase inflammatory-related pathways and further result in human obesity, metabolic imbalance and an increase of lipid ratio in adipose tissues [15].

5. Inflammatory pathways; Human inflammation commonly triggers a number of cellular/tissue damage machinery that may change normal/abnormal functionality in cells and tissues. Furthermore, damaged metabolic tissues or cells will lead to dysfunction of metabolic system [25].

6. Energy imbalance and glucose homeostasis disturbance; Energy imbalance may determine body weight-gains.

Life style and behavior activity

Life style and behavior adjustment is a useful counteractive measures against phenotypic characters of a great number of obese people. Many types of life-style/behavior adjustments are usually as effective as drug therapy. There are multiple selections, such as food restrain, vegetable and seafood consumption, regular exercises, bad habit avoidance (long-term sedentary activity), spiritual focusing and other types of life-style adjustments for fighting weight gains [3]. Equal effective as drug therapy, many details and style of non-drug therapeutics need to be classified for different types of weight-problems in human beings in the clinic.

Human exercises

Human exercise is very important factor for fighting weight-gain. There are different patterns of body exercises until now. However, their therapeutic outcomes vary in intensity, duration and regularity of exercises [5-6]. Different human exercises may be suitable for different individuals from human desires and physiological conditions.

Healthy food consumption

Food types and components are very relevant to human body-mass. Vegetable, fruits, cereal, seed and nut consumption can help to build desirable body shapes [30]. Based on past knowledge, many traditional beverages, such as tea, coffee [14,15] and so on are effective in body-mass reductions. This type of beverage is introduced to more people. Nonetheless, most of beverage, such as beer, sweet beverage may increase human body-mass.

Co-morbidity and complications

Metabolic phenotypes

Currently, little is known for sure about co-morbidity between obesity and other pathogenesis. Several factors of pathogenesis have been correlated in the clinic [15-18,21-26]. We list them into the following categorizing:

- Cardiovascular risks (heart-attack, brain stroke and so on)
- Type 2 diabetes, atherosclerosis, hypercholesteremia and so on
- Immune impairment and system abnormality
- Higher incidence of viral-induced human mortality
- Human inflammation, infection (foots) and related processes
- Mental illness (depression, suicide, intimidate and so on).

Counteractive measure categories

The counteractive measures against human obesity are important and therapeutic variable in categories [14-22] (Table 1). Main types of obesity managements include surgery, drugs and life-style. However, most of these counteractive measures are not perfect until now. Molecular mechanisms and genetic/epigenetic approaches are indispensable (Table 1).

Therapeutic categories	Specific options
Surgery	Gastric bariatric surgery
	Brain surgery (if available)
	And so on
Dietary	Higher-content of fibers in foods
	Fresh vegetable
	Reduce sweet and dessert consumptions
	Beverage selections
	Sea food consumptions
	And so on
Drug developments	Chemical drugs
	Bio-agents
	Herbal therapy
	And so on
Clinical therapy	Drug utility
	Gene therapy
	Drug combination
	Personalized medicine
	Precision medicines
	And so on
Others	Life-style/behavior adjustment
	Biotherapy (genomic editing, genetic circuits and others)
	Community supports
	Modern diagnostics
	Psychoanalysis and interventions
	And so on

Table 1: Major patterns of clinical therapeutics.

Drug development study

Multiple drug mechanisms and types target against variant pathologic elements and phenotypes. Like green tea, it can decrease body weight by energy expenditure and fat-oxidation reductions [22-24].

Chemical, biological and herbal drugs are the commonest therapeutic options in the obese treatments. In therapeutic mechanisms (pathways and components, human hormonal factors such as adipocytokine, leptin and adiponectin) are important to develop more active drugs and therapies.

The suggestion for overall therapeutics against different categories of obese and diabetic conditions is classified in table 2 [31-36]. These therapeutic selection principles may help clinical anti-obese trials in serious conditions [34].

Body mass index	Blood glucose level (mM/L)	Therapeutic options (proposed)
28 < BMI < 30	NORMAL	Less sedentary work
> 30	NORMAL	Food and life-style adjustment
35 > BMI > 30	6.2- 8.0	First-line chemical drug + life-style
35 > BMI > 30	8.0 - 12.0	Drug (chemical or insulin) + life-style
> 35	> 8.0	Gastric surgery + Drugs

Table 2: *Suggestion for therapeutics against different categories of obese and diabetic conditions.*

Mathematical network study

Mathematical modeling is an emerging possibility to find new relations-including risk origin, modern diagnostics, patho-therapeutic relation, drug mechanisms and treatment selections. These kinds of mathematical approaches are not mandatory, but indispensable for quality medications, cost reduction and new ideology from vast sources of experimental and clinical data and information on pharmaco-therapeutics. Equation 1 and 2 represent our vision towards this topic [37-39]:

$T (P1, \cdots, P_n) = \theta (P_n)$ (Eq 1)

T: Incidence of obesity in random human population.

Associations between pathogenesis simulation and events of human obesity may be established and better utilized as equation 2 and others.

$B = f(x; \alpha) + f(y; \text{ß}) + f(z; \gamma) + E$ (Eq 2)

B = Body mass index

x = Food related variables

y = Drug related variables

z = Genetic related variables

E = A common constant

A lot of mathematical methodologies and computational network, such as algebra, iterative, matrix, Monte Carlo and others may be applied for this area of biomedical campaign. In addition, artificial intelligence (AI) for obese diagnosis and treatments may be gradually established (Table 3).

System buildup stages	Mathematical methodology
Descriptive statistics	Data collection
Inferential statistics and description	Iterative, matrix
Mode building	Methodological selections
New equation and computations	Theorem establish
Workable AI	Association with computers

***Table 3**: Layout for computational network and AI system in the future.*

In the future, more competitive and cost-effective mathematical simulation and AI systems may assist clinical anti-obese therapeutics and teach medical students and junior doctors in the hospitals.

Future Trends

Effective anti-obese therapeutics should be targeted against disease origins, unique pathogenesis pathways and novel drug targets. Without targeted therapeutics and primary health-care progresses, clinical anti-obese therapy will remain unchanged and progress slowly.

Therapeutic combinations (drugs plus life-style) are widely recommended for obese patients over the past two decades. These kinds of therapeutic paradigms are very useful for many other chronic diseases, such as HIV/AIDS and neoplasm metastasis. Further work is inevitable. Maybe any other therapeutic breakthroughs may be created from other disease categories, like HIV [40,41] and cancer treatments [42,43]. These therapeutic paradigms of other diseases (drug combination, personalized medicine and herbal medicine) may be lend into anti-obese therapeutics in the world. Nonetheless, these therapeutic systems are usually based on doctor's experience rather than scientific-supportive formats [44,45]. Further scientific work is needed.

Herbal medicine is an effective measure against a lot of diseases, including obese phenotype due to higher therapeutic index for many common diseases [46-48]. Different spectra of plant ingredients must be validated for drug developments in this medical area.

Conclusion

Though there is no direct association between obesity and death, obesity is a strong risk for human morbidity and mortality. New insights into human obese causality and therapeutics may help human beings with overweight problem. We need to promote these researches in the near future.

Conflict of Interests

None.

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