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RESEARCH ARTICLE

Suicide Curative Treatment Study and Drug Development

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ABSTRACT

Aims: Suicide is still a biologically mystery event that leads to a great number of human mortality globally. However, human suicide cases and mortality have not been declining over the past century despite the flourishing of biomedical and technical progression. There is no existing therapeutic architecture that can greatly convert suicide ideation and mortality worldwide. A multidisciplinary system is proposed to improve suicide diagnostic and therapeutic studies. **Methods:** Influenced by a great diversity and complex risk factors, clinical suicide prevention and management were poorly provided. Correspondingly, the integration of neurobiological and psychoanalysis concepts (multiple diagnostic parameters) may impact clinical suicide management and biomedical progress. **Results:** Neuropsychiatric evidence suggests that the new landscape of suicide study (biological exploitation) may have great potential in the future. Overlapping symptomatic and molecular biology data among different suicide patients may form a tangible bioscience concept in the clinic. Today, drug treatment against human suicide is commonly chemical agents that need drug utility life-long. Thus, other types of central nerve systems drugs (mainly biotherapy) may assist current ones for curability treatment. By this new integration, a faster pace of clinical diagnostic and treatment study will dawn. **Discussion:** Nonetheless, understanding the complex nature of human suicide is no easy task. A great deal of clinical neurobiological evidence and multidisciplinary diagnosis may create new hope for clinical paradigms against human suicide. After the promotion of biotherapy, a variety of new therapeutics, such as curative treatments for suicide may emerge and wide clinical application can be achieved. **Conclusion:** By multidisciplinary diagnosis and drug development, the next generation of clinical suicide prediction, pharmacology, and therapeutics can be constructed for the purpose of safety and curability for refractory suicide.

Keywords: Biomarkers, CNS drugs, Human suicide, Molecular targets, Neuropsychiatry, Psychoanalysis, Psycho-morphology

INTRODUCTION

Epidemics for suicidal events

Suicide has a high ratio of human mortality (approximately 2% globally).[1] In male adolescents or youngsters (14–28 years old) in Western countries, suicide is the first leading cause of human mortality.[2] In addition, elderly (> 80 years males) who have less economic and family support show doubled rates of human suicide evidence and mortality compared with normal people in other age groups among Western society.[3]

Unfortunately, human suicides are difficult to predict. Human suicide cases and mortality have hardly changed over the past century. Therapeutic systems, such as psychoanalysis approaches were

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not well enough to make any difference in mortality reduction.[4-7] Given incomplete knowledge of suicide behavior and biology, highly effective drug development is still a modern challenge.

To attain the goal of suicide reduction, multidisciplinary evaluative architecture, especially molecular biology systems should be accelerated. After all, drug targets, development and marketing against human suicide should be promoted, especially biotherapy and evaluative system updating.

Major landscapes

To promote suicide study, we shall face different risk factors (molecular diagnostics and comorbidities) and general translation from past progress into a new landscape or diagnostic system.[8,9] This article outlines a general therapeutic mindset and crusade on novel biological theory. To begin with, historical reports of human suicide should be highlighted.

Historic reviews and general limitation

There was a long historical recording of human suicide in literature and legendary. However, the medical significance of historic recordings is very low from current viewpoints. Several ideas and arguments were mostly held before AC 1800;[10-13]

- Moral corruption (stigma)
- Deficiency of special matter
- Personality deficiency (coward or sheep spirit)
- Social inequality.

There is a great shortage of molecular evidence and therapeutic targets, that is, associated with treatment response for human suicide until now. To reduce the evidence and rate of human suicide as great as possible, potential molecular clues and targets should be discovered. After further efforts, effective therapeutic paradigms can be formed in the clinic.

POSSIBLE CAUSATIONS

Association between suicide and other diseases

In most people's mind, human suicide behavior is an impulsive act. It is not a disease-related behavior. After a double decade of hard work and persistence, new associations and evidence began to be unveiled. The complex nature of human suicide began to be known in molecular biology. However, this kind of medical knowledge should be based on more genetic or molecular discoveries and their association with clinical evidence of human suicides.

A wide variety of risk factors are associated with human suicides. It needs to be stratified, especially biomedical ones. Among these risk factors, mental diseases and physical disability are mostly correlated.[8,9] Based on the comorbidity study, molecular clues and drug targets were investigated. New therapies will be gradually developed after research scope expansion and druggable molecular discoveries.

Therapeutic evaluations

Anti-psychiatric drugs alleviate psychiatric symptoms. They are the main part of drugs for suicide prevention and treatment.[14-27] This is not enough now. Other drug categories should be investigated. Apart from a small number of anti-psychiatric drugs, we can do nothing for human suicide at present. Morphological or molecular pathogenesis pathways should be translated for drug targeting and pharmacological mechanisms. Overall, medical correlations between psychiatric-induced pathogenesis and pharmacological mechanisms should be elucidated.[7] After all, new drugs should be evaluated and clinically investigated.

Psychiatry and neurobiology

Apart from mental symptoms and behaviors, seeking targets from molecular and neurobiology is a modern trend.[28-32] Broadening drug types and targeting for therapeutic purposes was gradually accepted. To further reveal neural-pathologic principles, literature survey, symptom categorization, brain anatomy, and molecular biology data should be well integrated. Patho-therapeutic knowledge accumulation and distribution can determine the benefits of suicide

treatment. Novel drug evaluative architecture should be utilized for the promotion of suicide management in the future.

The fundamental principle of human suicide lies in endless networks of molecular biology risk factors and psychoanalysis in a greater amount of the human population. In addition, environmental variables may lead to gradual changes in genetic predisposition, molecular dysfunctions, neural circuitry, and cerebral morphological alterations. By upholding biomedical principles and knowledge, a wider range of clinical therapeutic paradigms could be embraced.

DISEASE OVERLAPPING

Risk factor analysis

At present, we cannot pinpoint the causalities of human suicide easily. Comorbidity treatment is currently the best way for suicide prediction and treatment in the clinic. Similarly, diagnosis of neuropsychiatric diseases is difficult due to devoid of neurobiological knowledge. Of course, major anti-psychiatric drugs are the first choice for mitigating psychiatric symptoms and possibly reducing suicide rates correspondingly [Table 1].

Human psychiatric diseases (A major part of comorbidities of human suicide) have multiple dimensions and categories. Luckily, clinical psychiatric diagnosis (psychoanalysis) is a guiding principle for suicide prediction and management. In the past medical evidence, suicide always happened no matter what kind of financial condition of the patient. Correspondingly, outside variables should not be underestimated. Etio-pathological relations and study play key roles in drug targeting and development. At present, comorbidities and psychiatric symptoms are common pathways for clinical therapeutics. It is increasingly acceptable that comorbidity treatment may be an effective diagnosis for reducing suicide behaviors and mortalities and increasing druggable targets in clinical trials.

Central nerve systems (CNS)

As shown in Table 1, several comorbidities are noted for understanding human suicides and its management.[8,9] Until now, psychiatric disorders are associated with suicidal behaviors by comorbidities.[22,23] However, it is intrinsic mechanisms need to be understood. Major psychiatric-suicide associations and pathogenesis were categorized below: [15-17]

Neuropsychiatric pathways and network

- Different types of human mental illness
- A history of past physical or psychiatric traumas
- Neural transmitter production changes in the human brain (signaling transduction pathways, network, and axis)
- Chemical or drug-induced brain damages
- Chronic traumatic encephalopathy (CTE)
- Physiological deteriorating and personal isolation in elderly

Table 1: The linkage between suicide events and comorbidity

Originality	Future diagnostics	Therapeutics	References
Mental disorders	Genetics/molecular/image	Drug or brain surgery	10
Personality	Temperament	Social work	19
Repeat self-harm/injure	Past episodes and symptoms	Psychiatric intervene	14
Socioeconomic deprivation	Financial evaluation	Social/legal support	3
Chemical exposure	Brain damage	Exposure control	15
Viral infection	Brain inflammation	Vaccine or drugs	27
Physical state change	Cognitive impairment	Keep calm	20
Long physical handicaps	Constance suffering	Pain-killers or others	25–26
Alcohol/drug addictive	Paracetamol overdose	Physical exercise	17
Cognitive impair	Decision-making deficit	Logic reasoning	27
Adolescents	Dependent in living	Family/peer	28

- Human genetic polymorphisms, deletion, copy-number, and translocation
- Malfunction of CNS and neural plexus.

Every bad experience may trigger events or behavior of suicide or self-harm. Based on the hypothesis of psychiatric or physical trauma, therapeutic drugs or counteractive measures against two causalities will be developed – single or combinatorial drug treatment. To make such biomedical progression, suicide origins, evidence, and targeting studies should be boosted;[29-32]

Diversity of mental disease dimensions

Suicide is proposed to involve different types of psychiatric diseases, especially schizophrenia. These comorbidities with suicides are a fast-growing area in modern medicine.[15-17] What kind of biological relation is there? Is there any change between different psychiatric diseases? Mounting medical evidence implies the necessity of novel suicide diagnosis and management within the scope of neural science.

There are many dimensions of psychiatric diseases in the clinic. Different psychiatric diseases have different symptoms and molecular characteristics. Psychiatric diagnosis and drug selection require psychiatrists who have a deep understanding of the varied symptoms of different human mental diseases (at least 2 years of psychiatric practice in hospitals). Disease diagnosis in both psychiatric symptoms and underlying molecular mechanisms may increase the quality of therapeutic selection, responses, and outcomes, yet more straightforward than psychoanalysis alone. In addition, molecular diagnosis may promote mental disease diagnoses and treatment.

MENTAL DISORDER CHARACTERS

Chronic diseases

Mental health problem was growing in popularity worldwide – at least one suicidal event in the lifetime of every psychiatric patient – mostly triggered by the feeling of either depression or mania. Most intrinsic relations and underlying mechanisms remain to be elucidated.

Different from other high-mortality diseases, neuropsychiatric diseases are often chronic diseases that need drug intake life-long.[33-35] Thus, the cost of regular disease treatment is a big burden for patients and society. As a result, this public health and economic burden needs to be reduced as early as possible. To counteract this limitation, curable treatments are the only way. It is imperative to know how molecular targeting and activation are involved in suicide therapeutics and management.

Different diagnosis

The variability of therapeutic responses and benefits depends on the quality of disease diagnoses. Since most dimensions of mental diseases are long-lasting and incurably at present, drug development for curative treatment is a daunting challenge.[33-40] Facing this medical challenge, molecular diagnostics and treatment have great potential and space to move forward.

Generally speaking, psychoanalysis and molecular diagnosis are mutual benefits. Psychiatrists review and treat patients by rating patient's cognitive, behavioral, and emotional scores. This pattern of clinical tradition might be improved with a more complex nature of molecular biology (genome, epigenome, proteome, transcriptome, and metabolome). A growing number of doctors and psychiatrists are aware that diagnostic and therapeutic transitions might be made in the near future. Proposal for diagnostic transition spoke lauder and lauder.[29-32] Yet, diagnostics in multiple parameters should go from the bench to the bedside.[33-39]

A comparison between psychoanalysis and molecular diagnostics is useful. The diagnosis between psychiatric review and molecular biology is different. Two systems are mutually beneficial. Overlapping and integration of two diagnostic systems will introduce new calibers and parameters. Correspondingly, these diagnostic overlapping and integration may promote the infrastructure of suicide diagnostics and drug selection in clinical trials.

Advanced knowledge about suicide machinery on a molecular basis is a spotlight of modern medicine. Neurobiology investigation is the focal point to bridge two systems (psychoanalysis and molecular diagnosis). System variation between psychiatric features and molecular mechanisms paves the way for therapeutic progress and drug selection. Mapping the relationship between diagnostic datasets, molecular networks, and therapeutic responses could help suicide prediction, prevention, and management in the future [Tables 2 and 3]. Many biomedical discoveries for human suicide are highlighted below.

At present, "suicide risk" is managed from the surface (ideation, events, and cognitive impairment). Nonetheless, the major difference between psychiatric rating and molecular biology is the gradual undergoing diagnostic and therapeutic transition. Biological parameters and state-of-the-art technology are still growing and breakthroughs are foreseeable. New suggestions and clinical evidence for suicide diagnosis and management are enumerated.

NEUROBIOLOGY

Pathological knowledge

Today, pathological features for suicides are largely investigated. Without fundamental knowledge breakthroughs in molecular biology and targeted therapy for suicide are accumulating and widely distributed. Yet, suicide diagnosis and prediction are still advancing and fruitful.[41] Correspondingly, advanced pathogenic knowledge of suicide is of great medical significance. Knowledge exchange worldwide is increasing. In the past, this world was devoid of existing and mature theories.

Broadening suicide diagnostic systems is the key to moving forward. In different neuropsychiatric models, brain image (cerebral ventricle examination)[37,38] can be successful and popularized in global hospitals soon. They can be official data without any technical barriers now. Deepening brain image evaluation and comparison between patients and normal persons will help both psychiatric and molecular diagnosis. As a result,

Table 2: Outlook of suicide-related pathologic progress and drug development

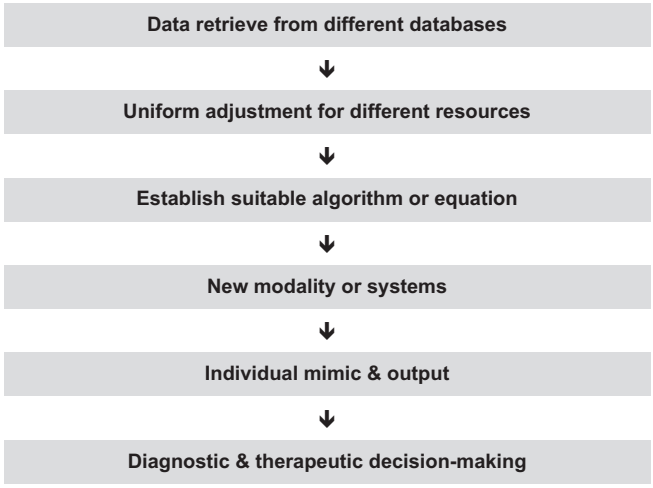
Total causations						
Biological related			Chemical and viral		Non-biological related	
Complex biochemical information						
Genome	Transcriptome	Proteome	Epigenome	Methylome	Metabolome	Glycomes
Anatomic and chemical study						
Location			Neural transmitters		Cellular types	
Suicide behaviors						
Ideation		Events		Repeats		Victims
Drug targets						
Schizophrenia		Mood disorders		Neural-degenerative		Depressive-related
Pharmaceutical						
Doses	Intervals		Delivery		Nano-drugs	Toxicity
Clinical applications						
Molecular diagnosis		Curable treatment		Personalized medicine		Artificial intelligence

Table 3: Diagnostic comparisons from symptoms to biochemical parameters

Psychiatric symptoms	Morphology	Biochemical parameters
Low mood	Somatic variability	Genomic changes
Diurnal mood variation	Brain compartment	Bioinformatics
Insomnia and early awaking	Neural plexus	Inflammatory cytokine
Lack of interest and energy	Ratio (gray/white matter)	Immune-components
Poor concentration	Brain anatomy	Signal transduction
Weight loss	Neurodegeneration	Neurotransmitters

a large quantity of neurobiology information and molecular datasets could be more useful.

Knowledge progress and system establishment need multiple steps and transition. Figure 1 offers part of these processes.



Neural transmitters

A neural transmitter is a series of pharmaceutical targets for psychiatric diseases and human suicide.[40,41] In the past, a number of neural transmitters have been recognized to play key roles in many mental disease diagnoses such as depression and neurodegenerative diseases.

At this stage, several chemical neural transmitters are utilized for drug targets against psychiatric diseases.[40-42] Dopamine modulators are the widest drug target, activation, and regulators for mental disorders. Of course, their releases, receptors, and regulators are associated with different types of neurons and neural fibers in the human brain, spinal, and other sites of nerve plexus.

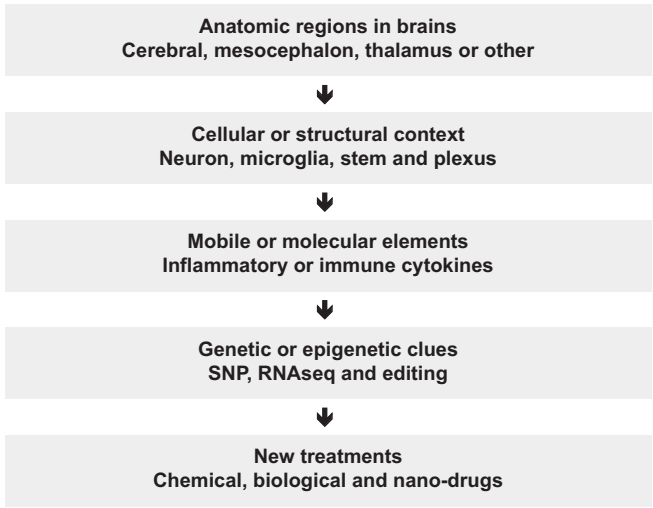


Figure 1: Neuropsychiatric domains for human suicide

Genetic factors

The human gene is the fundamental issue of many human diseases. The proposed pathway and technology for complex genetic alterations in mental diseases are shown in Table 4.[42-46] Totally, the association between complex features of mental disorders and genetic variations has been gradually found. With these discoveries, more suitable clinical molecular diagnosis will be formulated.

From different genetic technologies, genetic variations are shown among different mental disorders [Table 4]. Genome-wide association studies will be more popular in clinical evaluation and diagnosis. Statistically significant variations could be more easily identified by advanced genetic techniques (microarray, RNAseq, qPCR, and others), and relevant algorithms (massive calculation).

Genomic mapping of different mental disorders can broaden our vision of suicide biology.[46] Different genetic alleles or polymorphisms can contribute to a variety of mental health problems. If we continue to map suicide-vulnerable genomic deficiency, more genetic and molecular markers will be found and translated into clinical diagnosis and therapeutic paradigms. The genomic draft explosion nowadays shows promising signs of suicide study breakthroughs.

Brain image updating

The human CNS is divided into several anatomic entities and structures, majorly cerebrum diencephalon, mesencephalon, cerebellum, medulla, thalamus, and so on. The image changes (relative volume, density, and macromolecules) in different sizes of brain ventricles can help us pinpoint specific brain damage, such as CTE and post-traumatic stress disorder (PTSD).[47,48] In CTE and PTSD, both suicide and image changes have been found. This evidence supports the argument for multidisciplinary diagnosis promotion and

Table 4: Genetic technology for different mental disorders

Genome-wide association study (approved)				
Schizophrenia		Bipolar	Autisms	
Copy-number variation				
Schizophrenia	Intellectual disability	Autisms	Language impairment	Reduced cognitive
SNP				
MDD-bipolar disorders		MDD-Schizophrenia	MDD-ASD-ADHD	
Whole-exome sequencing				
ASD		Cognitive function		

ASD: Autism spectrum disorders

drug-targeting selection in the clinic. Image diagnostic systems may become more useful for suicide studies and clinical applications. Its diagnosis has been matured already in world-leading laboratories and hospitals. More clinical data will be accumulated.

Brain image technology has been advancing rapidly.[49] Previously, different mental disabilities were localized in special areas of human brains (cerebral location, neural circuitry, cell types, and inflammatory molecules). High-resolution brain image data associated with suicidality should be established, including technical, mathematical, or computational efforts. New breakthroughs can be achieved in clinical trials by adding clinical evidence and data from high-resolution brain images [Figure 1].

MULTIDISCIPLINARY SYSTEMS

Evaluative systems

Until now, three different types of diagnostic architectures (psychoanalysis, neurobiology, and molecular biology) are parallel yet integral parts of suicide prediction and treatment [Table 5].[50,51] By systematic comparison, new knowledge and insights into the combination of suicide risk factors and causations may be recalculated and utilized in therapeutic decision-making.

Advantageous and disadvantageous factors of different diagnostic systems can be optimized by technical integration (multiple parameters in patients). Diagnostic information from psychoanalysis, neural biology, and molecular biology may mutual support. Genetic- or molecular-based diagnosis not only supplements psychoanalysis but also promotes drug selection using more relevant biomarkers [Figure 2].

Table 5: Different techniques for suicide-related diagnosis

Psychoanalysis	Clinical diagnosis	Animal models
Cognitive	NMRi	Biomarkers
Behavior	Genetic biomarkers	Genomics
Emotional	Molecular Characterization	Proteomics
Risky-decision	Different neural types	Metabolomics
Social processing ability	Chromatography	Whole-exome-seq
Language problem	Brain anatomy	Glycoconjugates
Intelligent disability	Electroencephalogram	Microarray

Negative feelings in patients are very similar between suicide risk factors and symptoms of mental disorders. These differences cannot be easily separated.[6,7] The Diagnostic and Statistical Manual (DSM) of mental disorders – from DSM-I to DSM-V of mood problems and the Hamilton depression rating scale (HAM-D) for suicide risks should be in-depth evaluated and compared with each other. Neurobiology and molecular biology data and discoveries can be the bridges that link knowledge between different systems.

Figure 2 shows comparisons between three diagnostic systems.

Biological linkage

The medical knowledge about diagnostic-therapeutic relations is escalated by advanced technology. To do such a diagnostic transition, molecular biology infrastructure is the key to moving forward. Currently, collecting wealth data of genetic or molecular information is a modern avenue for shedding new light. A lot of work and discoveries can be made according to this flow chart [Figure 3].

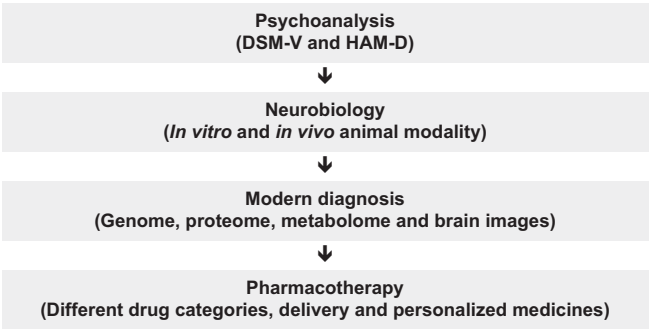


Figure 2: Diagnostic and therapeutic progress for suicide management

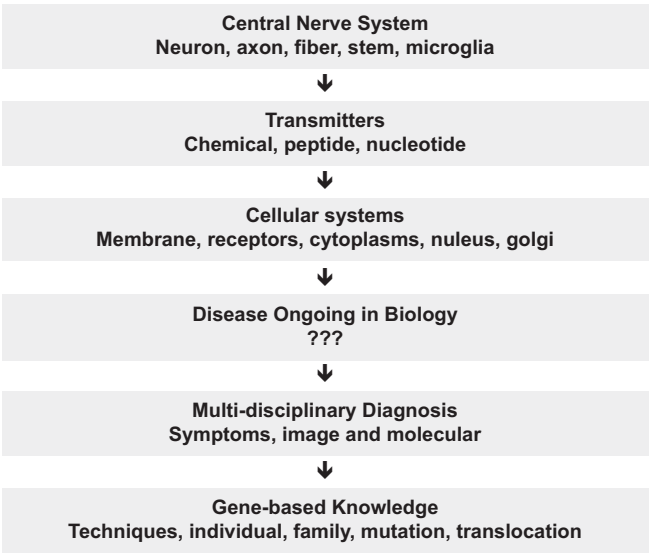


Figure 3: Biological linkage between neural malfunctions and suicide behaviors

THERAPEUTIC INNOVATION

Clinical conventions

Above, we discussed the possibility of high-quality "pathogenesis" diagnosis for suicide in the clinic. For prospective diagnostics, new drug targets and delivery systems may be also associated [Table 6].[50-53] With increasing popularity for neuropsychiatric study, the new drug licensing number for CNS ranks 4th place in the US.[52] However, it is far from successful in suicide management and drug development. New types of "anti-suicide" drugs are still at a hypothetical stage. Since chemotherapeutic drugs were not well chosen for different individuals, personalized medicine, or precision medicine (PM) would be promoted in the future.[54-59] After all, the doctor's experience, interests, and familiarity with PM was the key factor for drug selection and therapeutic optimism in the clinic. Slow-releasing and curative drug development should be pharmaceutical priority because these categories of drugs are easy to utilize in the clinic. This trend is majorly focused on drug safety, cost-effectiveness, and pharmaceutical availability.

Table 6: Different types of anti-psychiatric drugs and pharmacological properties

Common drug targets			
Neural transmitter			
Neurons	Genes	Nutrition	Microglia
Current drug types			
Tricyclic antidepressants	SSRIs	Monoamine oxidase	Noradrenalin reuptake
Herbal medicine			
Ayurveda	Chinese	Greeks	Others
Pharmacological and toxicology			
ADME	Toxicity	Doses	Derivatives
Biotherapy and technology			
Bioagents	Genomic editing	Gene therapy	Death cell clearance
Environmental pressures			
Social problem solving	Financial crisis alleviation	Comorbidity treatment	

Drug selections

At present, psychoanalysis comparison between psychiatric disorder and suicide is difficult due to symptom similarity and overlapping. A lot of normal people also felt helpless while facing economic or social shocks. Drug doses and concentration in a patient's blood are also valuable parameters for clinical application and therapeutic responses.[54-59] Molecular biology diagnosis is relatively straightforward for drug selection. Due to the highly complex features of CNS, it needs a great foundation and projects in money and personnel.
Apart from drugs, several types of instruments, such as light therapy can also reduce deaths or economic loss for suicide patients. To conclude, therapeutic instruments may assist suicide treatment and reduce death in the clinic.

Drug types and categories

At present, therapeutic drugs against mood disorders or other mental disorders are mainly chemotherapeutic drugs [Table 6]. Chemotherapeutic

drugs are temporally and relatively more toxic because they are not human biological components. They need drug treatment life-long. To the best of our knowledge, the safety issue is still an important area for the next generation of therapeutic drugs. To change this scenario, biological therapy might be more useful in the future.

NEW AVENUES

Technology

Cutting-edge techniques can change the outlook and convention of suicide prediction and treatment. Pharmacological and technical study for drug selection opens a new era for suicide and self-injure management. Creating a new generation of cutting-edge biological techniques in drug development is imperative. Gene therapy or gene editing proves promising for most bio-agent availability and therapeutic promotions in suicidal persons and relevant mortality [Table 6].

Bio-agent development

At present, neuropsychiatric disease is incurable by chemotherapeutic drugs. Biological management for mental diseases has different pathways and strategies.[6,7,59-63] These kinds of clinical approaches can trigger curative therapeutics in the future. However, these kinds of different biology therapies are currently immature. To develop curable treatment, long-term clinical evaluation should be embraced. After all, new biology treatment breakthroughs are awaiting. As a result, a new evaluative system must be supported by multidisciplinary parameters and systems.

Mathematics, computation, and artificial intelligence

To promote drug treatment, high-quality diagnostic and therapeutic data sharing, integration and mathematical analysis play key roles.[64-70] It suggests that new computational algorithms and techniques could further promote human suicide diagnostics and therapeutics. A lot of pioneer mathematical work has been carried out on different incurable diseases, including neuropsychiatric diseases.

Pharmaceutical modification

For CNS drugs, chemical properties, biocompatibility, and delivery systems play critical roles because of the presence of blood–brain barriers. Only 1/10 of chemical compounds can freely enter into human brains. In drug development, liposomes, glycol- or lipid-conjugates, nanoparticles, vector-binding, or others can help drug delivery into the CNS or herbal medicine.[71-74] Such agent delivery to human brains can promote chemical- or bio-agent distribution, responses, and favorable outcomes for suicide patients.

Suicide management in the future

Many drug targets are pursued, which consist of neural transmitter agonists, reuptake inhibitors and receptor blockers, genomic editing, signal-receptor disruption, neural circuitry, natural chemotherapeutic drugs, bio-agents, herbal medicine, and others.[75,76] Transitioning from psychiatric symptoms to molecular targets has a lot of therapeutic benefits. New evaluative architectures are depicted in Figure 4.

Breakthroughs in molecular biology

Knowledge accumulation, exchanges, integration, and distribution help a lot for drug targets, delivery, and therapy. That can eventually

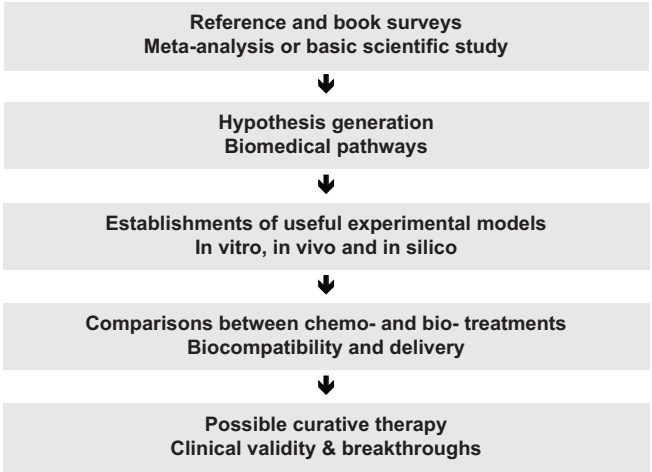


Figure 4: Schematic program for curative suicide treatment

reduce or even eradicate human suicide in broad ranges. For creating curative treatments in the future, knowledge breakthrough is imperative. Only through molecular biology breakthroughs, significant therapeutic promotion and curative treatments can be achieved.

CONCLUSION

New evaluative architectures can provide novel suicide prediction and therapeutics in the clinic. The relationships between chemical, genetic, molecular, morphologic, and neurologic properties should go individually and curatively. In the search for suicide-related causations as much as possible, multidisciplinary diagnosis is the key. We look forward to discovering more curable treatments finally.

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CONFLICTS OF INTERESTS

Authors declare there is no conflict of interest with other institutes and academies.

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