Current Understanding and Pharmacological Management of Suicide Behavior in Clinical Setting

Amresh Shrivastava

The University of Western Ontario, amresh.srivastava@sjhc.london.on.ca

Follow this and additional works at: https://ir.lib.uwo.ca/psychiatrypres

Part of the Psychiatry and Psychology Commons

Citation of this paper:
https://ir.lib.uwo.ca/psychiatrypres/39
Current understanding and Pharmacological management of suicide behavior in clinical setting.

Amresh Shrivastava
The university of Western Ontario, London, ON

dr.amresh@gmail.com
‘Nearly half a century of routine clinical use of such treatments as, ADD, ECT, CBT, has not yielded evidence of reduction of long term suicidal risk ..., including from accidents, substance abuse, or stress-related cardiopulmonary distress’

_Tondo, JCP, 2000_
Learning objectives

- Nature of problem in clinical settings.
- Current Understanding about suicide behavior (neurobiology)
- What can be done to deal with suicide in clinical settings
- Pharmacological management
  - Diagnosis
  - Pharmacological agents
Suicide is a global public health problem, affecting more than a million people every year.
Suicide in clinical practice is NOT uncommon

- >50% - seen a physician in previous one month
- 50% of had experience in psychotherapy
- 1 of every 2 psychiatrists lose a patient to suicide across 20 years practice
Clinical issues and challenges

- Magnitude, Predictability
- Uncertain etiology
- Heterogeneous

- Unreliable Risk Assessment
- No specific treatment
- No evidence that it can be prevented

‘defeat depression’ program, UK.
US military using preventive program
Magnitude of death by suicide clinical settings:

- 5-6.5% in hospital;
- 3 to 5.5% in psychiatric hospital and
- 2% in general hospital Inpatient. Rate
- 1% of all suicides in UK occurs in inpatients facility

Risk of suicide and suicidal ideation in psychosis & At-Risk clients: Italian study

Prodromal (N=81, Significant F/H of suicide & SUD)
First Episode (N=87, P=short DUP)

- Attempted suicide before intake: 8.6 vs 6.9
- During First Year: 5.3 vs 0
- Conversion to psychosis: 7 vs 0

Schizophrenic Res. 2009 Sep;113(2-3):145-50. Epub 2009 Jul 1
Post discharge suicide

Before 1 month-post discharge, 43%
Before first F/U, 47%

SMR for suicide in first 28 days
SMR-male

Current understanding of suicide behavior
Paradigms in understanding of Suicidality

- Individuals At-risk
- Risk situation
- Risk factors

- ‘mental disorders’ >90% ¹
- >60-70% mentally ill experience Suicidality ²
- 20-35%-NO Mental Illness ³,⁴,⁵

Suicide behavior is not necessarily a correlate of mental illness:

Re-organizing Pathways to Suicide

1. Psychosocial Antecedents → Psychiatric Illness

2. Psychological Antecedents → Psychiatric Illness → Attempted Suicide

3. Psychosocial Antecedents → Psychiatric Illness

DSM-V, Axis II: David Shaffer

Amresh Shrivastava
Paradigm shift in understanding of suicide behavior

1. Biological Origins
2. Psychological symptoms
3. Diagnostic
4. Risk
5. Social and psychological experiences e.g. Abuse, Trauma
6. Biological Brain Changes
7. Vulnerability
Public Health Thinking Should Extend Beyond Traditional Policy Boundaries

If we really want to promote better health outcomes, then we must apply the science of early childhood and early brain development to a broader range of policies ... including child welfare services, adult mental health treatments, and workforce development programs for low income mothers, among others.

Adverse Childhood Experiences and Adult Cardiovascular Disease

Source: Deng et al., 2004
Childhood Experience & the Expression of Genetic Potential: What Childhood Neglect Tells Us About Nature and Nurture?

Suicide--Risk for Schizophrenia

- A cohort of 2759 of CSA
- Schizophrenia = 2.8% Vs. 1.4%

[Cutajar MC et al., Archives Gen psychiatry 2010 Nov]
Impulsivity- Link with childhood experience and trauma

- Childhood sex abuse
- Chronic exposure to trauma,
- Post traumatic stress disorder
- Neurobiology: Serotonin hypofunction, HPA Axis
- Childhood adversity
- Overlap between neurobiology of SB and impulsivity


CSA or Sexual Abuse
Mediated by affective response
Suicide intent and attempt

Sexual abuse/experience of ‘Trauma’ is a significant antecedent

Suicide as an independent psychopathological axis: The evidence: [a]

- Epidemiological,
- Phenomenological,
- Biological,
- Genetic,
- Biochemistry
Psychopathology
Impulsivity
Across diagnosis
No diagnosis
Severity of illness Vs Severity of attempt

Cluster B
Suicide:: subtype of schizophrenia
DSM-5

Implication: two treatment goal: 1. Treat mental illness, 2. Treat suicidality

(Meltzer & Okayli, 1995¹). (Hawton, et al., 2005)².
Research topics in suicide neurobiology

Neurochemical

5HT
ACH
GLU
GABA
DA
OPI
ADR

Neurobiology suicide

Stress
Glia
Systems study
Lipids
Signaling

WGAS
microRNA
Proteins modification

Future studies

twins
family
adoption
associations
epigenetic

Carl Ernst et al. ‘Suicide neurobiology, Progress in neurobiology 89 (2009) 315-333

DA-dopamine, ADR-adrenaline, 5HT-serotonin, OPI – opiates, GLU-glutamate, WGAS-whole genome association study
Neurochemical, 5Ht, ACH, GABA, GLU, ADR, DA, OPI

Genetics; Twins, family, Adoption, Association, Epigenetics

Neurobiology

system study; Glia, Stress, Lipids, Signaling

Future study, WAGS, micro RNA, Proteins study, Brain circuitry
Biological pathway; No simple method how to study neurobiology

- Uncovering markers
- Low sensitivity and predictability
- Environmental factors.
- No formal neurobiological consensus
- Indices of serotonergic NT and risk
- The 5 Ht association - ‘unspecific;
- mRNA proteins, - dismissed,
- GABAergic and glutaminergic dysfunction
- Etiological heterogeneity
- Endophenotypes
- White matter volume
Nature and nurture in suicidal behavior, HPA response & NA response

<table>
<thead>
<tr>
<th>Genetic investigation of suicide and suicide attempt (GISS)</th>
<th>Genes implicated in suicidality—Serotonin</th>
<th>Change in brain structures</th>
<th>Risk and protective gene variants</th>
</tr>
</thead>
</table>

Suicide behavior rate among First-degree relatives (%)

What is inherited?
- *Cluster B traits and impulsive behavior represent intermediate phenotypes of suicide*

Suicide behavior rate among First-degree relatives (%)

- Community comparison probands: 3.4%
- Nonsuicidal depressed probands: 6.5%
- Depressed probands who committed suicide: 10.8%

McGIRR ET AL, Am J Psychiatry 166:10, October 2009
Genetics

- Additive genetic factors
- Estimated: 30% to 50% for a broad phenotype of suicidality that includes ideation, plans, and attempts
- Largely independent of the inheritance of psychiatric disorder [1]
- Heritability estimates of 17% to 45% - Nonfatal suicide attempts, even after controlling for psychiatric disorder [2]

Overlapping endophenotypes

In Search of Endophenotypes for Suicidal Behavior

Low frustration tolerance
Impulsive behavior
Poor coping
Dyscontrol

“One candidate endophenotype for suicidal behavior is... ‘impulsive aggression.’”
Endophenotypes: criteria \([1]\)

1. Association with illness in population;
2. Heritable (20% or greater);
3. Primarily state-independent;
4. Illness and endophenotype co-segregate within families (linkage of trait to gene variant); and
5. Found in nonaffected family members more frequently than in the general population

Proposed endophenotypes for suicide behavior

- Impulsive-aggressive traits,
- Early onset of major depression,
- Neurocognitive function,
- Heightened cortisol response to social stress.
Pharmacogenomics
associations with polymorphisms in genes

- Transcription
- Neuroprotection
- Glutamatergic and noradrenergic NT
- Stress and inflammatory responses
- Synthesis of glycoproteins
- Phenotypes of response and medication side effects,
- Biological pathways

Brent D, Melhem N, Turecki G. Pharmacogenomics of suicidal events. Pharmacogenomics 2010 Jun;11(6):793-807
Neuroprotective Proteins: Abnormal BDNF

- Mood disorder, PTSD, SUD
- Suicide behavior [8], and Psychosocial stress [9]
- Elevated suicidality independently of psychiatric diagnoses.
- Biological marker [?] of suicidal
- Increased BDNF due to Tx can facilitate neural integrity and prevent suicidal behavior.

A neurobiological origin?

- PFC
- Serotonin transporter gene
- Behavioral traits correlated with 5-HT
- Role of dopamine: e.g. SUD
- Hopelessness & Impulsivity
Current understanding in clinical phenomenology of psychosis

- Behavioral traits
- Anxiety
- Depression
- Hostility
- Positive symptoms
- Affective domains
- Suicidality
Predictors

- Past attempt
- Family history
Pharmacological management
Approach to intervention and prevention

- Target Subgroups
- Comprehensive management,
- Risk assessment,
- Continues community care
- Monitoring
- Resources

Need for Community based experiments in prevention

Pharmacological agents
no specific ‘suicidocidal’ drugs

- Improved medication & social treatment
- Low symptoms
- Low risk
- Low suicidality
Antidepressants

- No evidence of therapeutic benefit
- ADD Treatment emergent SD-polymorphism of genes:
  - Transcription, Neuroprotection, NT-Glum, NA
  - Stress inflammatory response

Davis A, Gilhooley M, Agius M, Zaman R

Suicide risk and choice of antidepressant. Psychiatr Danub. 2010 Jun;22(2):358-9
Lithium

- Neuroprotection
- Lithium responsive endophenotype
- Genetic predisposition (basis) of lithium response
- Gene-by-environment
- Risk was lower. [1] by 80% in 18 months and sustained. [2]

---


### Effect of Lithium on Risk of Attempted or Completed Suicide

<table>
<thead>
<tr>
<th>No. of Studies</th>
<th>N</th>
<th>Risk w/Lithium*</th>
<th>Risk w/o Lithium*</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>17,294</td>
<td>0.27</td>
<td>3.39</td>
</tr>
</tbody>
</table>

- Apparent risk reduction: $9.20$ fold
  * $\%$/Year

- *Tondo et al Neurobiology of Suicide 1997*
Mood stabilizers

- Less effective than lithium
- Anticonvulsants and suicide behavior
The mode of action is not known

- Antidepressant action,
- Cognitive functioning,
- Compliance,
- Insight,
- Negative symptoms
- Substance abuse,

(Meltzer, et al., 2003).

Clozapine

- Normalization of central 5-HT activity, in the prefrontal cortex, through down-regulation of central 5-HT2A
- Increased availability of central 5-HT (Spivak, et al., 2003).
Clozapine versus other atypical antipsychotics for schizophrenia.

- A little more efficacious than zotepine and risperidone but (?)
- Differs more clearly in adverse effects from other SGA
- Most beneficial profile (Tiihonen et al., 2009)
- [A critical appraisal of the FIN-11 study] \(^2\)

Clozapine versus other atypical antipsychotics for schizophrenia.
Antipsychotic dosage and Suicidality

- Exacerbation of psychosis
- Neurological and other side effects
- Suicide behavior

- It could also be that antipsychotics do not help to prevent suicidal behaviour because suicide may be a partially independent illness.
Antipsychotics and suicide: FGA and SGA

- Possible hypothesis: Decrease, Increase, Do not influence
- Several controlled studies have rejected a negative influence
- Reduce the risk of suicide and suicide attempts in schizophrenia.
Pharmacological management Across diagnosis: outcome

- Good
  - Unipolar depression
  - Bipolar disorder,
- Moderate
  - Schizophrenia
  - Eating disorder
  - Dysthymia and common mental disorders

- Poor
  - Personality disorder
  - Substance abuse
  - Comorbid conditions
  - Organic mental disorder [case report]
  - PTSD

Electro Convulsive Therapy
Diagnosable psychiatric illness are found in 90% of all suicide based on ‘psychological autopsies’

- Affective disorder 30% to 80%
- Substance use disorder 19% to 60%
- Schizophrenia 2% to 14%

In Both major depression and BPD, suicide account for 20% of death
Rates of suicide in psychiatric population

<table>
<thead>
<tr>
<th></th>
<th>completed</th>
<th>attempters</th>
</tr>
</thead>
<tbody>
<tr>
<td>attempters</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>mood disorders</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>schizophrenia</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>alcoholism</td>
<td>2.5</td>
<td>8</td>
</tr>
<tr>
<td>distress/ CMD</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Personality disorder</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>comorbidity</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

(Individual values highlighted in red denote higher rates in attempters compared to completers.)
Suicide amongst psychiatric inpatient: a national clinical survey

- 50,352 cases in 10 years
- 34,891 confirmed suicide
- 13,331 in contact with mental health services
- 1,851 were currently inpatients

Clinical Audit: Hospitalization

Hospitalization, N=100

- First admission: 19
- > 1 past admission: 71
- With diagnosis: 72
- No definite diagnosis: 12
- Diagnostic dilemma: 10
- With suicide attempt: 36
- With suicidal crisis: 39
- Unrelated to suicide: 25

75%
Some Preventive measures for inpatient suicide $^{[1,2,3]}$

- Inpatient suicide reflects service quality $^1$
- Safe infrastructure, adequate monitoring,
- Regular risk assessment during recovery and prior to granting leave,
- Staff training programs in management of risk,

Preventive measures

- Improved staff communication
- Observe ward exits; Improved observation methods;
- Increased engagement and support, First few days are high risk
Mental health policy and its implementation

‘It is clearly challenging to achieve a balance between patient safety and patient autonomy, but the need to protect individuals from harm during a time when they are supposedly in a safe environment should be a principal objective of mental health services’. 
Dealing with inpatient suicide

- Assessment
- Setting the goals
- Level of monitoring
- Risk factors
- Physical environment
- Crisis intervention
- Psychological intervention
Dealing with inpatient suicide

- Pharmacotherapy
  - Aggressive management
  - Early introduction of Lithium or Clozapine
  - Optimizing the dosage

- Ward infrastructure
## Program based intervention

<table>
<thead>
<tr>
<th></th>
<th>Community with EI</th>
<th>Community without EI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rates of suicidal ideation &amp; attempt</td>
<td>56%</td>
<td>39%</td>
</tr>
<tr>
<td>Previous attempt</td>
<td>16%</td>
<td>5%</td>
</tr>
<tr>
<td>Decrease in Rates after first clinical contact</td>
<td>Similar</td>
<td>Similar</td>
</tr>
<tr>
<td>SUD</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Suicidal behaviors</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>
Prevention of Post-discharge Suicide:

- Discharge process
- Side effects
- Continuity of care
- Avoid typical antipsychotics
- Medication, dose, duration and compliance
- Identify risk & predictors
Conclusion

- Inpatient and post discharge suicide.
- Previous attempt and family history
- Psychopathological traits are inherited
- Not all suicide are due to mental illness
Suicide as independent pathological dimension
Epigenetics, neuroprotection, plasticity and serotonin are important
Lithium and clozapine are good for treatment
Treat both mental illness and suicidality
Need for paradigm shift in management of suicide behavior.

Thank you