Attitudes of patients and family members towards implantable psychiatric medication

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Abstract

Introduction: Medication is a necessary part of treatment for severe psychiatric illnesses such as schizophrenia and nonadherence to prescribed medication is one of the most important public health issues in psychiatry today. The devastating consequences of nonadherence have motivated the development of novel therapeutic strategies, including a new long-term implantable medication delivery system.
Methods: The current study assesses attitudes towards implantable medication in psychiatric patients and their family members. Patients included in the study had diagnoses of Schizophrenia, Schizoaffective Disorder, Mood or Anxiety related disorders.
Results: 49.62% of patients and 74.47% of family members endorse support for implantable medication.
Conclusions: This study demonstrates that implants may be an acceptable alternative to oral and injectable medication for a subset of psychiatric patients and their families.
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Keywords: Medication; Psychiatry; Attitude; Schizophrenia; Adherence; Family; Drug implant

1. Introduction

Poor medication adherence leads to poor function, relapse, and rehospitalization (Adams and Howe, 1993; Casper and Regan, 1993; Weiden and Olfson, 1995; Viguera et al., 1997; Bergen et al., 1998; Cramer and Rosenheck, 1998; Valenstein et al., 2001; Rittmannsberger et al., 2004). Factors associated with nonadherence included poor insight, negative attitude, substance abuse, inadequate discharge planning/therapeutic alliance (Lacro et al., 2002). Methods of long-term medication delivery being introduced include transdermal patches for contraception and cancer pain, depot injections and implants for prostate cancer (Grond et al., 1997; Moul and Civitelli, 2001; Archer et al., 2002). Use of extended formulations in psychiatry has been variable. Although psychiatry has seen a shift toward newer oral antipsychotics, a recent study showed 74% of patients discontinued their initial oral medication within 18 months, suggesting that newer agents do not meet the entire need for improved treatment (Lieberman et al., 2005).

In response to low adherence with oral medications, we developed an implantable long-term delivery system for treatment of psychiatric illness (Siegel et al., 2002, 2006; Metzger et al., 2007; Rabin et al., 2008). Implants are the size of several rice grains, would be inserted under the skin and could deliver medication for one year. This technology could alleviate the need to take daily medication and significantly decrease nonadherence. A major question regarding implantable medication is its acceptance. Therefore, we asked psychiatric patients and family members about the acceptability of implantable medication. This manuscript presents results from a survey of patients family members in 19 countries and throughout the United States.

2. Methods

Surveys were formatted at an eighth grade reading level and based on recommendations for questionnaire development (McLaughlin, 1969; Hogan et al., 1983; Morisky et al., 1986; Fox, 1996). Patient and Family surveys had similar questions and measures (Appendix A and B). The primary outcome was whether the respondent would accept/support implantable medication. Surveys included demographic variables, respondents' behavior and beliefs towards medication and illness, comprehension of the procedure.

All procedures and surveys were approved by IRBs at all sites. Patient inclusion criterion was a diagnosis of schizophrenia, schizoaffective disorder, mood or anxiety (Diagnostic and Statistical Manual of Mental Disorders, 2000). Family members of individuals with schizophrenia, schizoaffective disorder, mood or

Table 1
Recruitment venues used for patient and family member survey distribution

Recruitment venue for patient surveys	% of sample
University of Pennsylvania research program and clinic	8.96
Conferences, NAMI, Internet, other	13.75
Collaborators	77.29

Location of collaborator by country	% of sample
Bulgaria	4.07
China	4.38
Costa Rica	6.26
France	2.19
Germany	9.08
Indonesia	3.13
Iran	3.13
Israel	3.13
Japan	3.24
Korea	3.13
Pakistan	3.13
Philippines	3.03
Poland	3.13
Romania	3.13
Scotland	3.13
Spain	2.82
Sweden	3.13
UK	2.30
United States	34.45

Recruitment venue for family member surveys	% of sample
Research facility	40.47
NAMI	49.42
Conferences, internet, other	10.12

anxiety disorders were included in the family survey. Patients were recruited at the University of Pennsylvania, educational conferences and collaborators from 27 sites in 19 countries. Neither patients nor investigators received financial support or incentives to participate. Family survey venues included The University of Pennsylvania, educational conferences and NAMI Family-to-Family classes (Table 1) (Dixon et al., 2001). Neither respondents nor Family-to-Family facilitators received financial support to participate. A standard protocol for distributing surveys was followed including an explanation of the technology. The survey was anonymous to protect respondent privacy and promote candid responses.

Surveys were translated/back translated for distribution in Bulgaria, China, Costa Rica, France, Germany, Indonesia, Iran, Israel, Japan, Korea, Pakistan, Philippines, Poland, Romania, Spain and Sweden. Scottish and British surveys were adapted to reflect UK educational categories. Data were entered into separate databases. Discrepancies resulted in consultation of source material and correction.

Pearson Chi-square or Fisher's exact tests were used for the association between categorical variables and

Table 2
Logistic regression analysis models

Final multivariable logistic regression model for patient acceptance of implantable medication

Parameter	Estimate*	Wald Chi-square	Pr> Chi-square
Diagnosis of bipolar disorder	0.56	8.49	0.004
Taking antipsychotic medication	−0.63	11.21	<0.001
Selects "runs out of medicine" as a main reason for nonadherence	0.69	7.85	0.005
Indicates need for continued medication once he/she feels better	0.80	12.31	<0.001
Indicates he/she will get sick if he/she stops taking medicine	0.61	6.79	0.009
Answers all 5 comprehension questions correctly	0.86	11.96	<0.001
Fit of logistic regression model		$C = 0.714$	

Final multivariable logistic regression model for family member acceptance of implantable medication

Parameter	Estimate*	Wald Chi-square	Pr> Chi-square
Family member diagnosis of depression	−0.62	9.06	0.003
Indication that family member is moderately ill	−0.30	0.92	0.339
Indication that family member is mildly ill	−0.86	7.92	0.005
Indication that family member is not ill	−0.68	3.80	0.051
Indication that respondent is unsure of severity of family member's illness	−1.06	6.23	0.013
Selects "runs out of medicine" as a main reason for family member's nonadherence	0.55	4.64	0.031
Answers one or more comprehension questions incorrectly	−1.46	19.75	<0.001
Indicates need for continued medication once his/her family member feels better	1.05	17.00	<0.001
Fit of logistic regression model		$C = 0.687$	

* Positive estimate values indicate that the respondent is more likely to consider implants and negative estimate values imply that respondent is less likely to consider implants. For example, all illness severity responses noted in the model show negative estimates relative to "very ill", indicating that they were less likely to support implants than those with very ill relatives.

Table 3
Demographics information for respondents to the patient survey

Patient demographics	%
Age(mean±sd)	41.37±12.73
Gender	
Male	53.72
Female	46.28
Ethnicity	
White	52.36
Non-white	47.64
Education	
Did not finish high school	33.02
Finished high school	25.71
At least some college	41.27
Diagnosis	
Schizophrenia	34.10
Schizoaffective disorder	9.79
Bipolar disorder	24.67
Depression	31.08
Anxiety disorder	12.94
Other	7.74
Duration of illness	
0–10 years	51.12
Over 10 years	48.88

Table 4
Types of medications in each population surveyed

Patient identified medication type	%
Any antipsychotic	70.12
Mood stabilizers	34.95
Antidepressants	36.64
Anxiolytics	20.97
Other	43.52
Unsure	3.83
None	2.48

Total number of psychiatric medications	%
0	2.48
1	38.11
2	30.10
3 or more	29.31

Family member identified medication type	%
Typical antipsychotics	16.79
Atypical antipsychotic	58.34
Mood stabilizers	35.74
Antidepressants	35.20
Anxiolytics	16.68
Other	33.37
Unsure	9.10
None	6.24

Total number of psychiatric medications	%
0	6.70
1	31.70
2	25.77
3 or more	35.82

whether the respondent would consider implants. Cochran–Mantel–Haenszel test for trend was used for ordinal variables. Forward selection logistic regression models were performed using a *p*-value to enter of 0.05 to assess which factors were most important in consideration of implants. Factors having bivariate *p*-value<0.10 were considered for inclusion in the model. Models were repeated using backward selection with a *p*-value for removal of 0.05l (SAS version 9.1, SAS Institute, Cary, NC).

Table 5
Behaviors, beliefs, and attitudes towards illness and medication among survey respondents

Patient behaviors, beliefs, and attitudes towards illness and medication	%
Do you have a psychiatric illness?	
Yes	88.95
No	11.05
How Ill are you right now?	
Very Ill	9.28
Moderately Ill	25.84
Mildly Ill	38.08
Not Ill	26.79
Over the past two months how often did you miss a dose of medicine?	
Never/rarely missed	85.52
Often/always missed	14.48
Once you feel better, do you need medicine for your psychiatric illness?	72.06 (yes)
Will you get sick if you stop taking medicine for your psychiatric illness?	72.64 (yes)
Do you prefer not to take medicine for any medical problems (for example an infection, pain, high blood pressure, diabetes etc.)?	33.30 (yes)

Well family member's behaviors and beliefs	%
How often do you have contact with your family member?	
Daily	59.72
Less often than daily	40.28
How ill is your family member right now?	
Very	11.67
Moderately ill	35.21
Mildly	31.99
Not ill	14.29
Unsure	6.84
Over the past two months how often did your family member miss a dose of medicine?	
Never/rarely missed	65.88
Often/always missed	17.93
Unsure	16.19
Once he/she feels better, does your family member need medicine for his/her psychiatric illness?	90.12 (yes)
Will your family member get sick if he/she stops taking his/her medicine?	91.07 (yes)
Do you prefer not to take medicine for any medical problems (for example an infection, pain, high blood pressure, diabetes etc.)?	23.89 (yes)

Table 6
Comprehension of implant procedure by patients and family members (correct answer was "yes" to all questions)

Comprehension of implant procedure	% correct by patients	% correct by family members
Would a surgical implant be placed under the skin?	90.42	97.25
Would putting in the implants require a 15 min surgery with a local anesthetic?	91.69	99.04
Could the implant be taken out by a doctor?	93.87	99.28
Would the medicine be released by the implant for many months?	91.46	98.56
Do the risks of the surgery include minor infections or irritations of the skin and a small scar?	91.70	98.20
Number of comprehension questions answered correctly by family members	%	%
One or more wrong	17.59	3.74
5 correct	82.41	96.26

Questions with low response rates were excluded from the analyses. Many respondents did not indicate the number of family members with psychiatric illness in the appropriate format and few respondents selected the option "voices tell him/her not to take the medication." Among respondents that selected that option, none recommend their family member receive an implant. Therefore, there was insufficient power to include this response in the model. Questions 13 and 14 of the patient and family member surveys asked participants why they would/would not accept/recommend implants. These questions were deemed too closely related to the final question and were excluded from the analyses. To explore cultural contributions towards attitudes about implants, we performed exploratory analyses of response rates between participants in Asia, Europe and North America in both studies.

3. Results

3.1. Patients

We distributed 1481 surveys and 967 were completed (65%). This response rate is consistent with the average rates for surveys in medical journals of $62 \pm 21\%$ and is slightly higher than the average of 52% for anonymous surveys (Asch et al., 1997). Because a subset of questions was excluded from the analysis, results represent the evaluable sample of 583 patients.

The logistic regression analysis identified several variables that were predictive of implant acceptance (Table 2). Respondents with bipolar disorder were most likely to accept implants. Respondents taking antipsychotic medication were least likely to endorse implants. Those who identified running out of medicine as a

Table 7
Patient and family member attitudes towards implants

Reasons to accept/not accept implant for patients	%
What are some reasons you WOULD want to get medicine for your psychiatric illness from an implant?	
You don't like what happens when you miss your medicine.	32.04
You do not like to take medicine everyday by mouth.	31.57
You forget to take your medicine everyday.	20.42
To help you stay well.	45.66
There would be less problems for your family if you got an implant.	20.07
Other	17.02
There are no reasons.	26.41
What are some reasons that you would not want to get medicine for your psychiatric illness from an implant?	
You don't want to try something new.	24.34
You like taking your medicine by mouth.	24.22
You don't want to feel controlled.	18.22
You would never have surgery for anything, even if you needed it.	11.76
You are worried about side effects of surgery.	34.60
Other	18.69
There are no reasons.	23.53
Would you consider getting medicine for your psychiatric illness from an implant?	49.12

Reasons to accept/not accept implant for family members	%
Some reasons why you think the implant is a good idea for your family member's psychiatric illness are	
You don't like what happens when your family member misses his/her medicine.	53.98
You would prefer that your family member not have to take medicine everyday by mouth.	41.54
Your family member has difficulty taking his/her medicine every day.	28.23
It would help your family member stay well.	60.07
There would be less burden on the family if he/she got an implant.	40.17
Other	18.03
There are no reasons.	12.44
Some reasons why you think the implant is a bad idea for your family member's psychiatric illness are	
You don't want him/her to try something new.	9.89
Your family member prefers taking his/her medicine by mouth.	15.17
Your family member might feel controlled.	29.55
You would never have or recommend surgery for anything, even if it was needed.	4.09
You are concerned about the side effects of surgery.	22.96
Other	27.44
There are no reasons.	26.39
Would you support a surgical implant as a way of providing psychiatric medicine for your family member?	73.76

reason for nonadherence and those who answered "Yes" to the questions "Once you feel better, do you need medicine for your psychiatric illness?" and "Will you get sick if you stop taking medicine for your psychiatric illness" were more likely to accept implants. Respondents that answered all comprehension questions correctly were more likely to endorse implants that those who answered one or more incorrectly. The model had a very good fit with a c-value of 0.714. Descriptive statistics for responses are presented in Tables 3, 4–7.

Table 8
Demographics of respondents to family survey and their ill family member

Family member respondent demographic variables	%
Age(mean±sd)	53.76±13.02
Gender	
Male	25.58
Female	74.42
Education	
No education to finished high school	27.27
Some college	23.89
Finished college	21.91
Graduate or professional degree finished	26.92
Respondent's relationship to patient	
Parent	59.25
Spouse	14.96
Child, sibling, or grandparent	19.20
Other	6.60
Total number of family members affected by psychiatric illness*	
1	43.84
2	24.35
3	13.70
4	7.91
5 or more	10.20

Patient demographic variables	%
Age(mean±sd)	37.44±14.84
Gender	
Male	61.17
Female	38.83
Education	
No education to finished high school	50.18
Some college	28.67
Finished college or more	21.15
Diagnosis	
Schizophrenia	35.11
Schizoaffective disorder	15.90
Bipolar disorder	32.98
Depression	17.67
Anxiety disorder	7.71
Unsure	3.32
Other	7.47
Duration of illness	
0–10 years	48.69
Over 10 years	46.90
Unsure	4.40

50% of patients reported they would accept implantable medication. Patients in Asia (30%) had lower support for implants than those in Europe (57%) or North America (56%) (Chi-square<0.001).

3.2. Family members

2241 family surveys were distributed and 1028 were completed (46%) with an evaluable sample of 705. The logistic regression analysis found several variables that were predictive of implant acceptance by family members (Table 2). Respondents who identified a family member with depression were less likely to support implants. Respondents who reported family member to be very ill were more likely to accept implants. Respondents who identified "running out of medicine" as one of the reasons for nonadherence and those who answered "Yes" to the question "Once he/she feels better, does your family member need medicine for his/her psychiatric illness?" were more likely to accept implants. Respondents that answered all comprehensions correctly were more likely to endorse implants than those who answered one or more incorrectly. The model had a very good fit with a c-value of 0.687. Descriptive statistics are presented in Tables 4–8. 74% of family members reported they would support implants. Family members in Asia (49%) had lower support for implants than those in Europe (73%) or North America (80%) (Chi-square<0.001).

4. Discussion

The translational value of implants depends on support among stake holders in health care delivery. Results indicate that implants may be acceptable for a subset of patients and their families. One key finding of this study was the relationship between a patient's insight into the need for continued medication and acceptance of implants. These findings suggest that respondents based their decisions on the need for continued care during periods of remission and that implants may be best suited for patients with good insight (Bosveld-van Haandel et al., 2001). Diagnosis influenced support for implants such that patients with bipolar disorder were most likely to accept implants. Individuals with schizophrenia reported less need for continued treatment than those with bipolar disorder, which may have contributed to differences in attitudes towards implants. Illness severity influenced acceptance of implants by family members. However, severity of a patient's illness did not predict their own acceptance of implants. This difference may have reflected that family

members tended to judge affected family member's illness as more severe than patients judged their own illnesses (Table 6).

We found that answering all comprehension questions correctly was predictive of implant acceptance in both groups. Thus, the most likely condition for acceptance of implants occurred when both family and patient understood the procedure. Conversely, these data suggest that both populations appropriately declined something they did not understand.

One limitation was that data were obtained through patient self report and family members' knowledge about the affected individual. While this may have affected the accuracy of factual information, it was less relevant to subjective issues such as the need for continued treatment and consequences of nonadherence. An additional limitation may have arisen from the degree of patients' willingness to disclose their behavior. In order to encourage candid responses, surveys were anonymous and could not be traced to specific respondents.

74% of family members and 50% of patients supported implants as treatment. This latter number is consistent with a pilot survey in which 47% of 206 patients in the Northeastern United States supported implants (Irani et al., 2004). Although many factors will influence the future of this novel treatment, the surveyed populations showed moderate to strong support for implants. Thus, implantable medication may have promise to improve adherence and outcomes for a subset of patients.

Contributors

Author SJ Siegel was responsible for the overall conception, design, and execution of the study. Author ME Dankert was responsible for the daily activities, management and execution of the study, maintaining relationships with collaborators, data entry and database management, and primary writing of the manuscript. Authors CE Brensinger and WB Bilker were primarily responsible for the statistical analysis. Author KL Metzger was responsible for data entry and management. All other authors were collaborators who contributed to the collection of surveys at sites outside of the University of Pennsylvania. All authors contributed to and have approved the final manuscript.

Conflict of interest statement

As principal investigator and corresponding author, Dr. Steven J. Siegel had full access to all the data in the study and had final responsibility for the decision to submit for publication. Intellectual property related to implantable delivery systems developed at the University of Pennsylvania is owned by the University. Steven J. Siegel is a consultant to NuPathe Inc., and received research funding from NuPathe to develop delivery systems for Parkinson's Disease. No other authors have disclosures relevant to the content of this manuscript.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j. schres.2008.05.008.

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