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Contents

Original Article

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A Study of Attitude Towards Psychiatry Among Private Medical College Undergraduates

Abdul Rahman Baothman[1], Ramana Gattavalli[2], Vivek Kumar Rachakatla[3], Pramod KR Mallepalli[4]

Abstract

Introduction: The attitude of medical students towards psychiatry has been studied extensively in this developed world. The inability to attract medical students to specialize in psychiatry has always been a serious challenge to psychiatric recruitment in developing countries like India. *Aims andObjectives:* To study the attitude of undergraduate medical students toward psychiatry. *Materials and Methods:* This is a cross sectional study with sample size of 200 participants who are undergraduate medical students of Mamata Medical College, Khammam, Telangana. The samples were drawn using convenience sampling method. Attitude towards Psychiatry scale (ATP) was the tool used to collect data for this study. *Results:* The senior students have more favorable attitude towards psychiatry than the junior students (75% vs. 45%). Only 8% second year and 12% final year students affirmatively said they wanted to become a psychiatrist, while around 70% denied psychiatry as their career option. *Conclusions:* The final year students displayed a more positive attitude towards psychiatry when compared to second year students owing to the increased exposure during their clinical rotations.

Keywords: Medical College; Undergraduate; Attitude Towards Psychiatry.

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Introduction

Psychiatric disorders are becoming more protrusive and frequent over the years.

World Health Organization reports, neuropsychiatric disorders alone contribute to about 33% of the years lived with disability (YLD) and four of thefive leading causes are neuropsychiatric. (depression, alcohol use disorder, schizophrenia and bipolar disorder).[1]

Almost 10% adult are affected by psychiatric disorder at any given point of time. WHO estimates that unipolar depression will be the lead cause of disease burden succeeded by ischemic heart disease and road traffic accidents by the year 2030.[2]

The prevalence of serious mental illness, in India, is 6.5%, which translates to about 71 million people but the country still has deficit of health workers trained in mental-health to cater to such a huge population of the mentally ill.

Literature suggests the deficit to be roughly around 78% in contrast to ideal number of 1 per 100,000 populations.[3,4] As a result of this, mentally-ill patients are mostly ignored or are taken care primarily by the general practitioner.

Psychiatry remains subject known for its stigma.

Students seldom opt for the subject as a

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specialty. Medical students, being member of a large community, are also not immune to negative prejudice about mental illness.[5,6]

Meagre knowledge about the psychiatry as a science or rare interaction with the patient with mental illness may be the reason of irreparable stigma.

It is imperative that the students develop appropriate attitude toward psychiatry as a medical discipline,[7] because graduating as doctors with negative attitude toward psychiatry has far reaching consequences.

The integration of psychiatry in the curriculum has been found to have a significant Positive effect on the attitude of students toward psychiatry as a profession and the mentally ill patients.

Studies suggest that better clinical exposure in psychiatry is the key in changing the attitude of these students. Specific factors that are found to be crucial are the experience of direct involvement in care of patients, witnessing patients responding favorably to the treatment and the student having ample and satisfactory interaction with staff, both clinical and non-clinical, and patients at a psychiatric center.[8]

Aim

The aim is to comparatively study the attitude of 2nd year and Final year MBBS students toward psychiatry.

Materials and Methods

Study design

The study was conducted in the Department of Psychiatry, Mamata Medical College from 1st October 2019 to 31st December 2019. The sample comprised of 100 2nd year and 100 Final year students who were posted in the Department of Psychiatry for 2 weeks as part of their clinical rotations. A standardized questionnaire (Attitude Towards Psychiatry -30 ATP 30) and a socio-demographic profile was given to the students to fill up after taking written consent to participate in this study.

Inclusion Criteria

1. 2nd and Final MBBS year students who are willing to participate with written consent

Exclusion Criteria:

1. Students with major psychiatric illnesses/ substance use disorders
2. Students with prior exposure to psychiatry which might have influenced their attitude toward psychiatry (as patients/as patients' relatives/as relatives of psychiatrists)
3. Non-consenting Students

Size:

100 2nd year and 100 Final year students

Place:

Department of Psychiatry, Mamata Medical College

Duaration:

1st October 2019 to 31st December 2019

Type of Study:

Cross-sectional Prospective Study

Tools

1. The authors mapped out a questionnaire enquiring about socio-demographic details, which was used to obtain data, such as age and sex. It also enquired possible exposure to psychiatry in the past.
2. The attitudes of interns toward psychiatry (represented by psychiatric illness and alcohol/ drug dependence) was evaluated using standardized questionnaire (Attitude Towards Psychiatry-30 ATP30) which is basically a non-condition specific scale to capture biases, emotions, and expectations generated by medical condition descriptors. The ATP is based on 5-point Likert scale designed and validated in Canada by Burra et al.[9] It consists of thirty positive and negative phrases(items) that measure the strength of the participant's attitude to various aspects of psychiatry. A score of 1 denotes a highly positive attitude, 5 denote a highly negative attitude, and 3 denotes a neutral response. The score of each positively phrased item was converted by subtracting it from 6. The total global scores range from 30 to 150. A global score of <90 (scores of 1 and 2 combined) indicates a negative attitude to psychiatry, a score of >90 (scores of 4 and 5 combined) implies an overall positive attitude, while a global score of 90 (average score of 3) is representative of a neutral attitude. Each of the thirty questions were analyzed independently and thematically with groups of questions together. The study was conducted

after obtaining approval from the Institutional Review Board and permission was sought from the college authorities.

Statistical Analsis

Statistical analysis was done with Statistical Package for Social Sciences version 21 software. Descriptive statistics were used to analyze sociodemographic data. The change in attitude toward psychiatry as measured by 5-point Likert scale designed and validated in Canada by Burra et al.[9] 'P' value of less than 0.05 was considered to be statistically significant.

Prior approval for the study was taken from Institutional Ethics Committee, Mamata Medical College and Hospital. Prior written informed consent was taken from the participants of the study. Nearly 66% of second-year students and 68% interns completed the questionnaire and submitted to the investigator. For purposes of intergroup comparison of sociodemographic and attitudinal differences, Chi-square test was utilized.

Table 1: Sociodemographic characteristics of the participants.

Variable	Group of Medical Students (n)	Age (Mean ± SD)	P
Age	2nd year	20.10 ± 1.11	< 0.0001
	Final Year	23.65 ± 0.71	–

Characteristics	2nd Year	Final Year	P
Sex, n(%)			0.1594
Male	62	55	
Female	38	45	
Family type			0.0105
Joint	25	20	
Nuclear	30	45	
Nuclear extended	45	35	
Locality			0.1025
Urban	52	60	
Rural	48	40	
Monthly income			0.1192
< 10,000	4	3	
10,0000 - 20,000	66	57	
> 20,000	30	40	

Table 2: Attitude Toward Psychiatry-30 scores in terms of cutoff value 90 representing attitude toward psychiatry in both the groups.

Group	Positive ATP (ATP>90) (%)	Neutral ATP (ATP=90) (%)	Negative ATP (ATP<90) (%)	P
2nd Year	45	14	41	0.000058
Final Year	75	4	21	

Table 3: I would like to be a psychiatrist (Item 4 in attitude toward psychiatry 30).

Responses	2nd Year	Final Year
Strongly Agree	8	12
Agree	20	36
Neutral	24	16
Disagree	26	24
Strongly Disagree	22	12

Table 4: Means of scores on items measuring attitude toward psychiatric patients and illnesses.

Items	2nd Year (Mean ± SD)	Final Year (Mean ± SD)	P
Psychiatric illnesses need attention(12)	3.80 ± 1.22	4.29 ± 0.77	0.0008
Interesting to unravel cause(18)	3.91 ± 0.87	4.09 ± 0.95	0.1639
Psychiatric patients are human(27)	3.67 ± 1.35	4.08 ± 0.94	0.0135
Psychiatric patients are interesting(29)	3.42 ± 1.25	3.71 ± 1.12	0.0856

Table 5: Mean responses of items measuring attitude toward psychiatric knowledge and teaching.

Items	2nd Year (Mean ± SD)	Final Year (Mean ± SD)	P
Psychiatric teaching increases our understanding of medical and surgical patients (9)	3.45 ± 1.16	3.57 ± 1.04	0.4421
Students who report that their psychiatric undergraduate training has been valuable (10)	3.69 ± 1.06	3.54 ± 0.96	0.2955
Psychiatry has very little scientific information to go on (13)	3.26 ± 1.15	3.88 ± 1.00	<0.0001
These days psychiatry is the most important part of the curriculum in medical school (23)	3.18 ± 1.15	3.89 ± 1.20	<0.0001
Psychiatry is so unscientific that even the psychiatrists cannot agree to scientific basis (24)	3.37 ± 1.06	3.79 ± 1.01	0.0046
Most of the so called facts in psychiatry are vague speculations (26)	3.21 ± 0.97	3.68 ± 1.00	0.0009
Psychiatry is so amorphous that it cannot be taught effectively (30)	3.16 ± 1.25	3.14 ± 0.93	0.8980

Table 6: Mean responses of items measuring attitude toward psychiatric treatment and hospitals

Items	2nd Year (Mean ± SD)	Final Year (Mean ± SD)	P
Psychiatric hospitals little more than prison (3)	3.21 ± 1.21	3.37 ± 1.30	0.3687
Efficacy of psychotherapy (5)	3.32 ± 1.04	3.42 ± 1.20	0.5296
Psychotherapy is fraudulent (8)	3.84 ± 0.77	3.50 ± 1.33	0.0281
With therapy, patients improve (14)	3.77 ± 1.04	4.00 ± 0.78	0.0784
Psychiatric treatment cause patients to worry about symptoms (16)	3.33 ± 1.20	2.89 ± 1.11	0.0077
Little that psychiatrist can do for their patients (19)	4.01 ± 1.09	3.06 ± 1.18	<0.0001
Psychiatric hospitals have specific contribution to make to the treatment of mentally ill (20)	3.26 ± 1.18	4.01 ± 1.06	<0.0001
Psychiatric treatment has become effective (25)	3.70 ± 1.11	4.04 ± 1.08	0.0293

Table 7: Mean of scores on items measuring attitude towards psychiatrists and psychiatry

Items	2nd Year (Mean ± SD)	Final Year (Mean ± SD)	P
Psychiatry is unappealing because it makes little use of medical training (1)	3.20 ± 1.19	3.77 ± 1.22	0.0010
Psychiatrists talk a lot but do very little (2)	3.38 ± 1.26	3.70 ± 0.98	0.0464
I would like to be a psychiatrists (4)	2.75 ± 1.20	2.95 ± 1.21	0.2420
On the whole, people taking up psychiatric training are running away from participation in real medicine (6)	3.49 ± 1.01	3.15 ± 0.99	0.0171
Psychiatrists seem to talk nothing but sex (7)	4.00 ± 0.96	3.69 ±0.82	0.0149
Psychiatry is a respectable branch of medicine (11)	4.00 ± 0.82	4.14 ± 0.90	0.2516
Psychiatrist tend to be as stable as average doctors (15)	3.22 ± 1.11	3.41 ± 1.15	0.2360
Psychiatrists get less satisfaction from their work than other specialists (17)	3.04 ± 1.07	3.29 ± 1.19	0.1198
If I were asked what i considered to be the three most exciting specialities psychiatry would be excluded (21)	3.83 ± 1.22	3.25 ± 1.12	0.0006
At times it is hard to think of psychiatrists equal to other doctors (22)	3.50 ± 1.29	3.07 ± 1.18	0.0148
The practice of psychiatry allows the development of really rewarding relationship with people (28)	3.32 ± 1.20	3.78 ± 1.28	0.0094

The mean age of second-year and final year students was 20.10 years and 23.65 years, respectively (P < 0.0001) Table 1. There was no statistically significant difference in other sociodemographic characteristics Table 2. The senior students have more favorable attitude towards psychiatry than the junior students (75% vs. 45%). Mean score of ATP-30 was 96.5 and 99.8 for the second-year students and final year students, respectively (P = 0.001).

However, only 8% second year and 12% final year students affirmatively said they wanted to become a psychiatrist Table 3. However, Final year students had a firmer belief that psychiatric patients are human (2nd year = 3.67 ± 1.35, Final year = 4.08 ± 0.94, P = 0.0135) and that psychiatric illnesses

need attention (2nd year = 3.80 ± 1.22, Final year = 4.29 ± 0.77, P = 0.0008).

Meanwhile responses for item no. 12 and 27 Table 4 measures attitude of students towards psychiatric patients and illnesses. Scores were high for final year students (P = 0.0008, 0.0135 respectively).

Comparison of mean scores of items number 13, 23, 24, and 26 Table 5 between the two groups shows significantly higher scores of final years (P = <0.0001, <0.0001, 0.0046, 0.0009 respectively).

Responses to item numbers 8, 16 and 19 Table 6 show significantly higher scores of second year student (P = 0.0281, <0.0001, <0.0001).

Similarly, items numbers 6, 7, 21 and 22 Table 7 which is indicative of negative attitude towards psychiatry and psychiatrists had higher scores among 2nd year students (P = 0.0171, 0.0149, 0.0006, 0.0148 respectively).

Discussion

The current comparative study was designed to compute the attitude of medical students with different duration of exposure of medical education, toward psychiatry as a medical specialty and career choice. Final-year medical students have more positive attitude than the second-yearstudents. Yadav et al.[10] proved that interns had an overall favorable attitude toward psychiatric patients when compared with MBBS students.

Item no. 4 "I would like to be psychiatrist" has been given special concern because it provides an association between overall general attitude and career choice. Only 8% 2nd year students and 12% final year group decided to be a psychiatrist. Similar disparity between positive attitude and choosing psychiatry as a career choice was also found in study done in Kenya,[11]Pakistan,[12] and the USA.[13] One Israeli study found that those 32.8% of medical students who determined to do residency in psychiatry, only 6% opted psychiatry as their career option.[14]

In this study both the groups showed positive attitude toward psychiatric patients and psychiatric illnesses and they all agree that psychiatric patients are not only human but they are interesting also and require great deal of attention Table 4. Similar results were found in another study with somewhat different methodology and questionnaire conducted in medical colleges of Karachi and Abbottabad of Pakistan.[12]

This study found a significant improvement in final years' overall attitude toward psychiatry as assessed by ATP-30 (Burra et al) before and after exposure of students to clinical rotations in psychiatry. The results in the earlier studies have been conflicting with some studies showing significant changes in attitude toward psychiatry after clinical exposure and others concluding that there is no effect of a short exposure.

A study at Nigeria by Adebowale et al.[15] suggested that the 4 week clinical rotation in psychiatry resulted in significant increase in mean attitudinal score. Another study in Spain by Bulbena et al.[12] revealed improvement of attitude toward psychiatry after training in psychiatry.

On the contrary, the results obtained in our study are in contrast with some similar studies published earlier. A study in Bahrain by Al. Ansari and Alsadadi[16] did not support the hypothesis that the greater exposure to psychiatry changes the attitude of medical students toward psychiatry. Another study in Nigeria by Olotu and Osahon[17]indicated that there was no statistically significant change in the beliefs and attitudes of medical students toward psychiatry before the onset and after the end of a clinical posting in psychiatry.

There are limited data available on the impact of medical education and training on the attitude toward psychiatry in the Indian scenario. Gulati et al.[18] in their study concluded that 2 weeks' exposure to psychiatry as per the current curriculum seems to have a limited influence in bringing a positive change in attitudes toward psychiatry. This disparity in the findings could be attributed to various factors like the extent of engagement of interns in clinical care, orientation provided by the faculty, and the types of patients seen. Even the treatment response of the patients seen by the interns in the short duration of 2 weeks can have a bearing on the young impressionable minds.

Limitations

- Small sample size
- Medical students from single institution

Conclusion

In India Medical curriculum provides for a very short clinical rotation in the Department of Psychiatry as part of the compulsory rotational internship. This study indicated that even an exposure as short as 2 weeks had significant impact on the attitude of final year students towards psychiatry patients and the specialty as a whole. Future studies should aim at overcoming the

limitations of this study by improving the sample size and following them up in order to assess the sustenance of the favorable change in the long run. Also, the internship program in the Department of Psychiatry can be planned and structured, bearing in mind the engraving effect it may have on the future medical students and their attitude toward psychiatry.

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Original Article

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Depression and Anxiety Symptoms in Cardiac Patients

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Abstract

Background: Mental health and physical health are essentially intertwined. People living with severe psychiatric disorders are at significant risk of suffering from many physical disorders. The prevalence of depression and anxiety in patients with cardiac disease is little understood. *Aims & Objectives:* The objective of this study was to assess depression and anxiety in cardiac patients and to determine the relationship between them. *Materials and Methods:* The study sample comprised of 200 outpatients following up in the cardiology outpatient department (OPD) of the Mamata General Hospital, a tertiary care hospital in Khammam, Telangana, India over a period of 1 year from March 2019 to March 2020. The samples were drawn using a convenience sampling method. Mini International Neuropsychiatric Interview (MINI), Hamilton Anxiety Rating Scale (HAM-A) and Hamilton Depression Rating Scale (HAM-D) were the scales administered. *Results:* Anxiety and depression were present in 51% and 30% of the sample respectively. The mean scores of depression and anxiety were significantly high in females than males significantly. Correlation between depression and anxiety showed that depression and anxiety were positively correlated (r=0.738, P=<0.001). *Conclusions:* Depression and anxiety are associated with cardiac disorders. There is a need to keep in mind anxiety and depression as comorbidities in cardiac patients for adequate intervention that can be incorporated in the management plan.

Keywords: Depression; anxiety; cardiac patients.

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Introduction

Cardiovascular diseases (CVDs) and depression are one of the global disease causing burden.[1] Cardiovascular diseases are the most common cause of mortalityand are responsible for 17.9 million deaths across the globe, in 2015.[2] Depression affects more than 300 million people around the world,[3] and is predicted to become the main cause of disability worldwide, in 2030.[4] Likewise, in 2010, anxiety affected approximately 272 million people, globally.[5]

Mental health and physical health are essentially linked. People living with severe mental disorders are at higherrisk of suffering from many physical disorders.[6] Mentalor psychological disorders such as anxiety, depression, andsome personality types may lead to direct pathophysiological changes increasing the risk of developing CVD.[7] Problems with mental health have a direct physiological impact on the cardiovascular disease course and their adverse effect may be induced by non-compliant life style interventions, medicationor treatment.[8,9] Further more, these psychiatric disorders are add on to the impediments in cardiac diseases management, from the view point of

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emotional distress and treatment complexity. This is furtheramplified by the additional co-morbidities such as hypertension, diabetes and obesity.[10]

The American Heart Association (AHA) has advised screening for depression in cardiac patients. Nevertheless, health care services have not responded adequately and fewer than than 15% of cardiac patients are being diagnosed and treated for depression.[11]

Mental health problems are stigmatized in India. There is little information about the prevalence of depression and anxiety among cardiac patients.[12] Unaddressed mental care needs may be a significant obstacle to the effective management of cardiac patients, where CVD remains the leading cause of death.[13] The present study was planned to assess depression and anxiety in cardiac patients and to determine relationship between them.

Materials and Methods

The study sample comprised of 200 out patients following up in the cardiology out patient department (OPD) of the Mamata General Hospital, a tertiary care hospital in Khammam, Telangana, India over a period of 1 year from March 2019 to March 2020. A total of 212 patients were approached for participation in the study, of whom 7 did not meet the inclusion criteria and 5 refused to give consent. Patients aged between 40 and 75 years who had an episode of MI in the preceding 3 months and were clinically stable for an interview were included in the study.

Cardiology OPD identified patients meeting the inclusion criteria and were sought consent from them. Details were obtained from the patients and their relatives. The information was gathered using a structured questionnaire and information regarding the results of investigations was obtained from the medical records. Those patients fulfilling the criteria for a psychiatric diagnosis were referred to department of psychiatry for further management.

Mini International Neuropsychiatric Interview (MINI), Hamilton Anxiety Rating Scale (HAM-A) and Hamilton Depression Rating Scale (HAM-D) were the scales administered. The MINI is a brief structured diagnostic interview for psychiatric disorders, which gives diagnoses in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) and International Statistical Classification of Diseases, Tenth Revision (ICD-10).[14]

HAM-A and HAM-D are structured questionnaires to assess symptoms of anxiety and depression, respectively. HAM-A comprises 14 item questionnaire, each defined by a series of symptoms, and measures both psychological anxiety and somatic anxiety. The scale of each item is from 0 (not present) to 4 (severe).[15] The 17-item version of HAM-D was used in our study. A cutoff value of 8 on the scale is used to determine presence of depression, with higher scores reflecting severity of depression.[16]

Statistical Analysis

It was done using SPSS software for statistical analysis version 22. Descriptive statistics were used for the demographic and clinical variables. Student t test was done to verify differences between the categorical variables. Means for scales were calculated. Pearson correlation test was done to see the co-relations between different parameters. P-value was set at significance of <0.05.

Results

Table 1: Demographic and clinical variables

Sex	Male	150 (75%)
	Female	50 (25%)
Age	40-55	64 (32%)
	55-70	96 (48%)
	>70yrs	40 (20%)
Education	Up to 10th class	120 (60%)
	Above	80 (40%)
Occupation	Sedentary	105 (52.5%)
	Non sedentary	95 (47.5%)
History of smoking	Yes	128 (64%)
	No	72 (36%)
History of alcohol use	Yes	112 (56%)
	No	88 (44%)
History of hypertension	Yes	113 (56.5%)
	No	87 (43.5%)
History of diabetes	Yes	96 (48%)
	No	104 (52%)
History of previous MI	Yes	22 (11%)
	No	178 (79%)
History of angina	Yes	56 (28%)
	No	144 (72%)
HAM-A scores >5	Yes	102 (51%)
	No	98 (49%)
HAM-D scores >7	Yes	60 (30%)
	No	140 (70%)

Sociodemographic details

Males were the major proportion of sex constituting about 75% of the total sample. Patients in the age group of 55–70 years were the maximum constituting about 48% followed by those in the age group of 40-55 years (32%) and of above 70 years (20%). Majority of the proportion didn't finish high school (60%). Sedentary life style was predominant constituting about 52.5% of the total sample. (Table 1)

Risk factor profile

Hypertension and diabetes mellitus were the most common comorbidities associated constituting 56.5% and 48%, respectively. In patients with substance abuse, nicotine consumption in the form of smoking was seen in 64% and alcohol use was found in 56.5% of patients. [Table 1]

Depression and anxiety

On administering HAM-D & HAM-A, nearly 30% and 51% of the sample scored above the cutoff respectively. The mean scores of depression and anxiety were significantly high in females than males significantly. [Table 2]

Correlation between depression and anxiety showed that depression and anxiety were positively correlated (r=0.738, P=<0.001) which implies that higher depressive scores associated with higher scores for anxiety. [Table 3]

Table 2: Depression and anxiety among male and female cardiac patients

	MALES (n=150)		FEMALES (n=50)		T value	P value
	Mean	SD	Mean	SD		
Depression	5.48	3.782	7.75	5.225	3.3210	0.001
Anxiety	6.12	3.812	9.21	5.823	4.3043	<0.001

Table 3: Correlation between Depression and Anxiety among cardiac patients

	Anxiety	
Depression	R value	P value
	0.738	<0.001*

Discussion

The majority of the sample had men which reflects the health seeking methods in our country and also the patient's profile with cardiac diagnosis in an OP as cardiovascular diseases are more common and are prone to multiple risk factors such as alcohol use and smoking and deprivation of estrogen which acts as protective.[17]

The present study suggested that significant section of the sample had anxiety (51%) features which was measured by HAM-A as the features were similar to physical symptoms such as chest discomfort, sweating, palpitations.

Depression was found in 30% of the sample and it is important in cardiac patients as depression is associated with adverse consequences such as increased mortality, angina, arrhythmias.[18, 19]

H. Allabadi, A. Alkaiyat, A. Alkhayyat et al. found that high level of depression and anxiety in their sample of cardiac patients. 54% for severe depression and 19.2% for severe-to-very severe anxiety screened positive. Symptoms of depression and anxiety were more prevalent among females and less educated patients.[20]

Siddharth Sarkar, Rakesh K. Chadda, et al. reported significant anxiety and depressive symptoms were present in 48.5% and 25.2% in their study.HAM-A and HAM-D scores were highly correlated with each other suggesting that anxiety and depression symptoms coexist with each other in MI patients.[21]

D. Ramya Shruthi, S. Sunil Kumar et al. principal findings of their study were major depressive disorder (44%) and sanxiety disorders spectrum (18%) in acute coronary syndrome patients.[22]

Antidepressants along with cognitive behavioural therapy and physical activity such as aerobic exercise and cardiac rehabilitation are the cornerstone of treatment of depression in cardiac patients. The American Heart Association (AHA) along with the American Psychiatric Association (APA) in 2008 made proposal of the for the better sequalae of the patients: (i) Routine screening for depression should be done as effective treatment of depression improves the outcome, (ii) A Psychiatrist should assess patients with positive screening results, (iii) Cardiac patients with depression who are under treatment should be carefully monitored for adherence to their medical care, drug efficacy,

and safety with their cardiovascular as well as mental health concern, and (iv) Coordination of care among health-care providers is indispensable in patients with combined mental and medical health diagnoses.[9]

Study Limitations

It is a cross sectional single-center study of a small sample size. A large sample size needed with more women representation.

Conclusion

Looking for the existence of depression and anxiety are important because it may go unnoticed in the clinical population. Therefore, anxiety and depression as co-morbidities in cardiac patients need to be held in mind for effective intervention that can be integrated into management program. Long-term follow-up studies with large sample size are necessary to determine the role of anxiety and depression in cardiac patients.

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Original Article

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Postoperative Cognitive Dysfunction After General and Regional Anesthesia: A Prospective Randomized Controlled Trial

Bhushankumar Bhagwan Kinge[1], Shobhit Jain[2], Sharad Kumar Mathur[3], Mona Srivastava[4]

Abstract

Background: Postoperative cognitive dysfunction (POCD) is a well recognized complication following various operative procedures. The role of anesthetic agent in etiopathogenesis is still controversial. The present study aims to describe and compare effects of general and regional anesthesia on post-operative cognitive functions among patients undergoing orthopedics surgery. *Methods:* A total of 80 patients aged 20-60 years, belonging to either sex, scheduled for <120 minutes duration orthopaedic surgery of lower limb, with good physical status, and with ±20% ideal weight were included. Patients unwilling for consent, past anesthetic use, cognitive impairment, sub-normal intelligence, substance use disorder, psychiatric disorder, and chronic medical condition were excluded. Patients were randomized to receive either general anesthesia (n=40) or regional anesthesia (n=40) during surgery. After routine preanesthetic examination and laboratory investigations, Hindi version of mini-mental status examination scale was applied prior to surgery and at 24h, 2weeks, and 6weeks postoperatively. *Results:* The prevalence of POCD at 24 h, 2 weeks, and 6 weeks after the surgery was higher among general anesthesia group (80%, 52.5%, and 27.5% respectively) compared with regional anesthesia group (57.5%, 27.5%, and 15% respectively). When compared with regional anesthesia group, the cognitive domains related to orientation to time, place, registration, recall, and copying at 24 h and recall at 2 weeks postoperatively were significantly affected in general anesthesia group. *Conclusion:* Although POCD has multifactorial etiopathogenesis, the role of general anesthesia cannot be completely refuted. Besides preoperative and intraoperative precautions, postoperative cognitive remediation techniques may be recommended. Further studies investigating effect of individual anesthetic agent in causing POCD is required.

Keywords: Anesthesia; Postoperative Complications; Cognitive Dysfunction.

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Introduction

Use of anesthesia during surgery often leads to post-operative cognitive dysfunction (POCD)[(1)], which is characterized by impairment in attention, memory, language comprehension, abstract thinking, and reaction time, with preserved level of consciousness. Nearly all patients have one or more cognitive dysfunction during post-operative period, of which 19-80% persist at 1 week and 6-60% at 3months following surgery [(1,2)]. POCD is associated with poor rehabilitation outcomes and higher surgical mortality. [1,2] Several hypothesis have been suggested in development of POCD.[1,6] However, role of type of anesthetic

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agents in developing POCD is still controversial.[6] A few studies have recommended use of regional anesthesia to prevent risk of POCD due to general anesthesia[3,4]. Whereas, others did not reported significant difference in POCD with general and regional anesthesia[5]. There is a relative lack of longitudinal studies from India evaluating POCD induced by general and regional anesthesia.[7,8] Such studies will help in rational treatment decisions in selecting appropriate anesthesia for high risk patients. The present study aims to describe and compare effects of general and regional anesthesia on post-operative cognitive functions among patients undergoing orthopedics surgery.

Methods

A total of 80 patients scheduled for orthopaedic surgery of lower limb, of lesser than 120 minutes duration, aged 20-60years, belonging to either sex, with physical status I to II (American Society of Anesthesiology), and with body weight being 20% above or below ideal weight, were recruited in the study. The patients after consent were randomly assigned to one of the 2 groups, group 1(n=40) received general anesthesia and group 2 (n=40) received regional anesthesia during the surgery. Patients not willing for consent or with history of prior use of anesthesia, cognitive impairment, sub-normal intelligence, substance use disorder, psychiatric disorder, chronic medical disorder such as neurological disorder (eg. cerebrovascular accident, seizures, unconsciousness), cardiac disease (eg. hypertension, ischemic heart disease), respiratory disease (eg. asthma, recurrent infections), endocrinal disorder (eg. diabetes mellitus, hypothyroidism) and malignancy, were excluded. All patients underwent routine pre-anesthetic checkup including sociodemographic details, past and present history of medical and surgical illness, drug history, general and systemic physical examination including airway, vitals, and glassgow coma scale, routine laboratory investigations including hemogram, blood counts, renal fuction test, liver function test, fasting blood sugar, electrocardiography, chest x-ray. Sedatives were avoided on night before surgery. Hindi version of mini-mental status examination (HMSE) scale was applied 1 day prior to surgery and 24 hours, 2 weeks, and 6 weeks after the surgery. All patients were informed about the type of anesthesia to be given, however the observer applying HMSE was blinded. Patient's vitals were maintained within 20% of pre-operative values, oxygen saturation was kept above 90%. Peri-operative events of hypoxia, hypotension, thromboembolic episodes, and respiratory distress were documented. Post-operative pain was managed using 15mg/kg body weight paracetamol given 15 minutes prior to stopping anesthesia. The study was started after approval from institute ethics committee.

Tools and Technique

The modified Hindi Version of Mini-Mental Status Examination [9]

The Mini-Mental Status Examination is the most frequently used method to assess the cognition in post-operative period[1].The modified hindi version of the Mini-Mental Status Examination, also known as Hindi Mental Status Examination (HMSE), is a validated 22 items questionnaire which can be used even among illiterate Indian population. It tests cognitive domains such as orientation to time and place, attention and concentration, recognition of objects, language function, both comprehensive and expressive speech, motor function, and praxis. The score of ≤23 is used to screen the major neurocognitive disorders, with 88% sensitivity and 82% specificity.

General Anesthesia (GA; Group 1)

All patients in Group 1 were intravenously injected 0.03mg/kg body weight midazolam, followed by 2µg/kg body weight fentanyl and 0.01mg/kg body weight ondansetron, followed by 2 mg/kg propofol. After pre-oxygenation with 3 minutes of 100% oxygen, tracheal intubation was facilitated with intravenous administration of 0.01mg/kg body weight vecuronium. Maintenance was done using 40% oxygen – 60% nitrous oxide – isoflurane with 1.2 MAC. After surgery neuromuscular blockade was reversed with intravenous neostigmine 50µg/kg with glycopyrrolate 10 µg/kg.

Regional Anesthesia (RA; Group 2)

All patients in Group 2 were injected 10-12mg of hyperbaric bupovacaine in subarachnoid space at level of L3-L4 inter-vertebral space.

Analysis

Data were analysed using IBM SPSS version 20 software. Sociodemographic variables were described. Frequencies and percentages were used to describe the data. Due to small sample size and

skewed distribution, nonparametric tests were used. Categorical data were analyzed using Chi-square analysis, whereas, continuous variables were analysed by using Mann-Whitney Test for comparison in HMSE score between the two groups (i.e. GA vs RA) and Wilcoxon Signed Ranks Test for comparison of HMSE score obtained at 24h, 2weeks, and 6weeks w.r.t. preoperative score (baseline). A statistical significance level of 5% was used (p = 0.05) for all the comparisons.

Results

Socio-demographic profile

A total of 40 cases and 40 controls were recruited, mean age for group 1(GA) was 33.53y±12.74, whereas, for group 2(RA) was 42.05y±14.35 (Z=2.67, p=0.01), majority comprised of males (72.5% vs 67.5%; X2 =0.24, p=0.63), and rural residence (57.5% vs 50%; X2=0.45, p=0.50). There was no significant difference in socio-economic status (High: 50% vs 32.5%; Low: 50% vs 67.5%; X2 =2.53, p=0.11) and educational status among the two groups (Illiterate: 5.0% vs 17.5%; Primary(1-5 standards): 2.5% vs 5%; Middle(6-8 standards): 7.5% vs 7.5%; Secondary(8-10 standards): 20.0% vs 17.5%; Higher Secondary(10-12 standards): 22.5% vs 20.0%; Graduate and above: 42.5% vs 32.5%; X2=3.77, p=0.58).

HMSE Score

The prevalence of postoperative cognitive decline at 24h, 2weeks, and 6weeks after the surgery among patients who received General Anesthesia was 80%, 52.5%, and 27.5% respectively, whereas, among patients who received Regional Anesthesia was 57.5%, 27.5%, and 15% respectively. The mean HMSE score among group 1 (General Anesthesia) and Group 2 (Regional Anesthesia) prior to surgery (31.00 ± 0.00 and 30.95 ± 0.22 respectively; Z=-1.42, p=0.16) did not differed significantly (Table 1). Whereas, at 24 h (28.82 ± 1.44 and 30.00 ± 1.08 respectively; Z=-3.57, p<0.01) and 2 weeks after the surgery (30.38 ± 0.70 and 30.70 ± 0.51 respectively; Z=-2.20, p=0.03) differed significantly (Table 2, 3). However, the scores at 6 weeks after the surgery (30.68 ± 0.57 and 30.82 ± 0.44 respectively; Z=-1.08, p=0.28) did not differed significantly (Table 4).

The Wilcoxon Signed Rank Test revealed that among group 1 who received general anesthesia during surgery had significant decline in HMSE score at 24 h (Z=-4.98; p<0.01), 2 weeks (Z=-4.24; p<0.01), and 6 weeks (Z=-3.13; p<0.01) postoperatively when compared with preoperative(baseline) HMSE score (Table 5), whereas, among group 2 who received regional anesthesia during surgery had significant decline in HMSE score at 24 h (Z=-4.28; p<0.01) and 2 weeks (Z=-2.28; p=0.01), however the decline was not significant at 6 weeks (Z=-1.90; p=0.06) postoperatively when compared with preoperative (baseline) HMSE score (Table 6).

The cognitive domains related to orientation to time (Z=-4.69; p<0.01), place (Z=-4.24; p<0.01), registration (Z=-2.45; p=0.01), recall (Z=-4.90; p<0.01), repetition (Z=-2.00; p=0.04), and copying (Z=-3.46; p<0.01) was found significantly lower among group 1(GA) after 24 h postoperatively when compared with preoperative score (baseline), whereas, only recall score was significantly declined at 2 weeks (Z=-4.03; p<0.01) and 6 weeks (Z=-2.89; p<0.01) postoperatively. Among group 2(RA), when compared with preoperative score (baseline), there was significant decline in 24 h postoperative score of orientation to time (Z=-3.46; p<0.01), place (Z=-2.82; p=0.01), recall (Z=-3.46; p<0.01), and repetition (Z=-2.24; p=0.03), whereas, only recall score was significantly declined at 2weeks (Z=-2.83; p=0.01) and 6 weeks (Z=-2.24; p=0.03). There was significant difference between the two groups in the domains related of orientation to time (Z=-2.25; p=0.02), place (Z=-2.37; p=0.02), registration (Z=-1.97; p<0.05), recall (Z=-2.67; p<0.01), and copying (Z=-3.73; p<0.01) at 24h, whereas, only recall score significantly differed (Z=-2.33; p=0.02) at 2 weeks postoperatively. None of the domains differed significantly among the two groups at 6 weeks postoperatively

Discussion

Findings of the present study reveled that the prevalence of postoperative cognitive decline at 24 h, 2 weeks, and 6 weeks after the surgery was higher among patients who received general anesthesia (80%, 52.5%, and 27.5% respectively) when compared with those who received regional anesthesia (57.5%, 27.5%, and 15% respectively). When compared with regional anesthesia group, patients who received general anesthesia (group 1) had significantly greater decline in overall cognition at 24 h and 2 weeks after the surgery, particularly in domains related to orientation to time, place, registration, recall, and copying at 24 h, and only

Table 1: Comparison of preoperative HMSE score between two groups.

HMSE Preoperative	Group 1 General Anesthesia	Group 2 Regional Anesthesia	Z	P
Orientation to time	5.00 ± 0.00	5.00 ± 0.00	0.00	1.00
Orientation to place	5.00 ± 0.00	5.00 ± 0.00	0.00	1.00
Registration	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Attention	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Recall	3.00 ± 0.00	2.98 ± 0.15	0.00	1.00
Naming	1.00 ± 0.00	1.00 ± 0.00	1.00	0.32
Repetition	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Three step task	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Visual command	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Writing sentence	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Copying a figure	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Overall MMSE score	31.00 ± 0.00	30.95 ± 0.22	-1.42	0.16

Table 2: Comparison of 24 hour postoperative HMSE score between two groups.

HMSE 24h Postoperative	Group 1 General Anesthesia	Group 2 Regional Anesthesia	Z	p
Orientation to time	4.45 ± 0.50	4.70 ± 0.46	-2.25	0.02
Orientation to place	4.55 ± 0.50	4.80 ± 0.40	-2.37	0.02
Registration	2.85 ± 0.36	2.95 ± 0.22	-1.97	<0.05
Attention	2.95 ± 0.22	2.90 ± 0.30	-0.84	0.40
Recall	2.38 ± 0.49	2.70 ± 0.46	-2.67	<0.01
Naming	1.00 ± 0.00	1.00 ± 0.00	-1.00	0.32
Repetition	2.90 ± 0.30	2.88 ± 0.33	-0.35	0.73
Three step task	2.98 ± 0.15	3.00 ± 0.00	-1.00	0.32
Visual command	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Writing sentence	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Copying a figure	2.70 ± 0.46	3.00 ± 0.00	-3.73	<0.01
Overall MMSE score	28.82 ± 1.44	30.00 ± 1.08	-3.57	<0.01

Table 3: Comparison of 2 weeks postoperative HMSE score between two groups.

HMSE 2 wks Postoperative	Group 1 General Anesthesia	Group 2 Regional Anesthesia	Z	p
Orientation to time	5.00 ± 0.00	4.98 ± 0.15	-1.00	0.32
Orientation to place	5.00 ± 0.00	4.98 ± 0.15	-1.00	0.32
Registration	2.98 ± 0.15	3.00 ± 0.00	-1.00	0.32
Attention	3.00 ± 0.00	2.95 ± 0.22	-1.42	0.16
Recall	2.52 ± 0.50	2.78 ± 0.42	-2.33	0.02
Naming	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Repetition	2.95 ± 0.15	2.92 ± 0.26	-0.46	0.65
Three step task	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Visual command	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Writing sentence	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Copying a figure	2.92 ± 0.26	3.00 ± 0.00	-1.75	0.08
Overall MMSE score	30.38 ± 0.70	30.70 ± 0.51	-2.20	0.03

Table 4: Comparison of 6 weeks postoperative HMSE score between two groups.

HMSE 6 wks Postoperative	Group 1 General Anesthesia	Group 2 Regional Anesthesia	Z	p
Orientation to time	5.00 ± 0.00	5.00 ± 0.00	0.00	1.00
Orientation to place	5.00 ± 0.00	5.00 ± 0.00	0.00	1.00
Registration	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Attention	3.00 ± 0.00	2.98 ± 0.15	-1.00	0.32
Recall	2.72 ± 0.45	2.85 ± 0.36	-1.36	0.18
Naming	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Repetition	2.98 ± 0.15	2.98 ± 0.15	0.00	1.00
Three step task	3.00 ± 0.00	2.90 ± 0.44	-1.00	0.32
Visual command	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Writing sentence	1.00 ± 0.00	1.00 ± 0.00	0.00	1.00
Copying a figure	3.00 ± 0.00	3.00 ± 0.00	0.00	1.00
Overall MMSE score	30.68 ± 0.57	30.82 ± 0.44	-1.08	0.28

Table 5: Comparison of HMSE score at postoperative 24 hour, 2weeks, and 6weeks w.r.t. preoperative (baseline) among patients who received general anesthesia (group 1).

HMSE Group 1: General Anesthesia	Postoperative 24h Preoperative		Postoperative 2 week Preoperative		Postoperative 6 week Preoperative	
	Z	P	Z	p	Z	P
Orientation to time	-4.69	0.00	0.00	1.00	0.00	1.00
Orientation to place	-4.24	0.00	0.00	1.00	0.00	1.00
Registration	-2.45	0.01	-1.00	0.32	0.00	1.00
Attention	-1.41	0.16	0.00	1.00	0.00	1.00
Recall	-4.90	0.00	-4.03	0.00	-2.89	0.00
Naming	0.00	1.00	-1.00	0.32	-1.00	0.32
Repetition	-2.00	0.04	-1.41	0.16	-1.00	0.32
Three step task	-1.00	0.32	0.00	1.00	0.00	1.00
Visual command	0.00	1.00	0.00	1.00	0.00	1.00
Writing sentence	0.00	1.00	0.00	1.00	0.00	1.00
Copying a figure	-3.46	0.00	-1.73	0.08	0.00	1.00
Overall MMSE score	-4.98	0.00	-4.24	0.00	-3.13	0.00

Table 6: Comparison of HMSE score at postoperative 24h, 2weeks, and 6weeks w.r.t. preoperative (baseline) among patients who received regional anesthesia (group 2).

HMSE Group 2: Regional Anesthesia	Postoperative 24h Preoperative		Postoperative 2 week Preoperative		Postoperative 6 week Preoperative	
	Z	p	Z	p	Z	P
Orientation to time	-3.46	0.00	-1.00	0.32	0.00	1.00
Orientation to place	-2.82	0.01	-1.00	0.32	0.00	1.00
Registration	-1.00	0.32	0.00	1.00	0.00	1.00
Attention	-2.00	0.05	-1.41	0.16	-1.00	0.32
Recall	-3.46	0.00	-2.83	0.01	-2.24	0.03
Naming	0.00	1.00	0.00	1.00	0.00	1.00
Repetition	-2.24	0.03	-1.73	0.08	-1.00	0.32
Three step task	0.00	1.00	0.00	1.00	-1.00	0.32
Visual command	0.00	1.00	0.00	1.00	0.00	1.00
Writing sentence	0.00	1.00	0.00	1.00	0.00	1.00
Copying a figure	0.00	1.00	0.00	1.00	0.00	1.00
Overall MMSE score	-4.28	0.00	-2.84	0.01	-1.90	0.06

recall at 2 weeks postoperatively. However, neither of the two groups had cognitive decline to the extent of major neurocognitive disorder (MMSE Score < 24). Findings of our study is supported by previous study among elderly which reported significantly greater prevalence of POCD after general anesthesia compared to regional anesthesia after 1week postoperatively [4,7], whereas insignificantly after 3months postoperatively [4]. Also studies have reported statistically significant impairment of cognitive function after three days following general anesthesia, but not after use of local anesthesia (10–12). Anwer and colleagues (2006) reported similar findings among elderly, but not among young adults [13]. Whereas, Machado and colleagues (2000) reported significant 24 h POCD after general balanced anesthesia, but not with total intravenous anesthesia and regional anesthesia [14]. Whereas, contrary to our findings, a few studies have reported insignificant difference in POCD after general and regional anesthesia postoperatively [5].

Findings of our study suggest direct effect of general anesthesia that might have played in greater decline in cognition in group 1 [6,15,16], in addition to indirect effects[1,6] such anticholinergic effect on cognition, intraoperative poor cerebral oxygenation and cerebral micro-emboli that might have played in decline in cognition after regional anesthesia (group 2). Whereas, a few studies have refuted the role of anticholinergic [17], poor cerebral oxygenation [18], and cerebral micro-emboli [19,20] in POCD.

The use of regional anesthesia to the control group and the use of well defined selection criteria have provided a methodological strength to the present study in minimizing several confounding bias observed by previous studies such as elderly age, low education, pre-existing medical illness eg. hypothyroidism and metabolic syndrome, cerebro-vascular accidents, neuropsychiatric illness eg. depression and cognitive dysfunction, type of surgery (cardiac and hip), longer duration of surgery, respiratory complications, infections, re-operation, post-operative pain and inflammation, and delirium [1,4,6,21].

Conclusion

To conclude the present study highlights the role of general anesthestic agent in causing postoperative cognitive decline. Although magnitude of this decline was small, however, it was observed in both the groups. When compared to regional anesthesia, cognitive decline after general anesthesia was significantly greater in domains related to orientation to time and place, registration, recall, and copying at 24 h, and only recall at 2 weeks postoperatively. Compared to previous studies on elderly population, present study extends findings over to young and middle aged adults. Hence, findings suggest besides preoperative and intraoperative precautions, postoperative cognitive remediation techniques such as reorienting, attention, recent memory, verbal fluency, and visuo-spatial task may be recommended during early postoperative period, whereas recent memory task may be continued till later. Future studies investigating the effect of individual anesthetic agent in causing POCD is required.

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Original Article

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A Prospective Study on Monitoring and Reporting of Adverse Drug Reactions Associated with Psycholeptic and Psychoanaleptic Drugs in a Tertiary Care Teaching Hospital

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Abstract

Background: Psycholeptic and psychoanaleptic drugs are associated with adverse effects which can affect the patient compliance and course of treatment. Psychiatrist awareness about this can facilitate rational and safe use of these medicines. Pharmacovigilance studies for psychiatric drugs are found to be very low in our country. *Objectives:* To assess the types, severity, causality, preventability, predictability and management of Adverse Drug Reactions (ADRs) among Psycholeptics and Psychoanaleptics. *Method:* A Prospective spontaneous reporting study was carried out for 6 months in the patients of psychiatry department. The study includes the ADRs among the Psycholeptics and Psychoanaleptics in any age of either sex from in-patients. The medication charts of patients were analysed for ADRs. *Results:* Among the 141 admitted psychiatric patients, 35 ADRs were reported during the course of study. Risperidone and Olanzapine were the frequently used drugs having the highest number of ADRs and tremor was the commonest ADR. Number of ADRs was found to affect the neurological system. Type A reactions were found to be more in males than in females. The causality assessment was done using Naranjo scale and majority of the reports were rated as possible (85.71%). Mild and moderate reactions accounted for 31.43% and 62.86% respectively as per Hartwig scale and only 5.71% of the reactions were found to be severe. Preventability assessment using Schumock and Thornton scale showed that most of the ADRs were definitely preventable (48.57%). *Conclusion:* Continuously monitoring the safety profile of psychiatric drugs fosters the rational and safe use of the medicines.

Keywords: Adverse Drug Reactions; Psycholeptics; Psychoanaleptics; Antipsychotics.

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Introduction

The WHO defines an adverse drug reaction (ADR) as any response to a drug that is noxious and unintended and occurs at doses normally used in humans for the prophylaxis, diagnosis, and treatment of disease, or for modification of physiological function.[1] The detection of an ADR is crucial to the management of any patient since failure to recognise an AD Rmay result in continuing patient morbidity.

Psycholeptic drugs like antipsychotics, anxiolytics and mood stabilizers; psychoanaleptic drugs like antidepressants, psychostimulants and antidementia are associated with adverse effects which can affect the medication adherenceand treatment outcome in mental disorders. Many of these adverse effects are preventable. Clinician's awareness about the adverse effects of psychotropic drugs can establish rationality and safety profile of these medicines.[2] There are many case reports involving ADRs among psychiatric drugs but there

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is a lack of Indian studies on pharmacovigilance activities in a mental health setting.[3]

Antipsychotic medications are widely prescribed and have a tendency to cause weight gain and subsequently hyperglycaemia, hypertension and hyperlipidemia. These metabolic risk, along with poor life style habits and smoking, are known to occur around two to five times more often in patients suffering from psychosis as compared to the general population. Judicious tailoring of the usage of antipsychotic medications and early detection and intervention for cardio-metabolic risks, may help in improving the long term outcomes in these patients.[4] Several reports are published regarding causation of myocarditis or cardiomyopathy by the antipsychotic drug, Clozapine. Other drugs in the same therapeutic class may share similar toxicity.[5] Taking all this in to consideration, this study was undertaken as there were very few studies in this part of the region.

Materials and Methods

Study design:

This is a prospective, spontaneous reporting study.

Study location:

This study was conducted at the Psychiatry department of S.N. Medical College and HSK Hospital, Bagalkot.

Study population:

Study was based only on those patients who experienced an adverse reaction to medicine use during their stay at the psychiatry department of HSK Hospital and ultimately reported to student clinical pharmacist.

Inclusion criteria:

ADRs of drugs like psycholeptic and psychoanaleptic in any age of either sex from in-patients.

Exclusion criteria:

The ADR that is due to

1) Medication errors, over prescribing, over dosing/ excess consumption.
2) Drug-Drug interaction, Drug-Food interaction, Drug interaction with the use ofalternative system of medicine.
3) ADR from out-patients.
4) ADRs of drugs other than psycholeptic and psychoanaleptic.

Recording of data:

The data collected in the six months period was analyzed for the following parameters.

- The total number of ADRs that are reported.
- Reports received from different departments of the H.S.K. Hospital & research centre.
- Age groups and gender of the patients.
- Different organ systems affected by reactions.
- Classification of drugs that causing reaction.
- Assessment of causality based on Naranjo scale.(ANNEXURE III)
- Severity of the reaction based on Hartwig scale. (ANNEXURE IV)
- Assessment of causality based on WHO. (ANNEXURE V)
- Assessment of preventability based on Schumock and Thorntonscale.(ANNEXURE VI)

Results

During the 6 months of study, 35 ADRs were found from 23 patients. The total number of patients during this study period was 147 from which the 35 ADRs were reported. The overall incidence of ADRs during hospitalization in this patient group was 15.65%.

We observed more ADRs in females 20 (57.14%) than in males 15 (42.86%)during their hospital stay. The rate of ADRs in elderly patients was not considerably higher than in adult patients (Fig a).In present study majority of the reactions were Type A (97.15%), while Type B accounted (2.85%) very less in the observed patients (Table 1).Most of the reported ADRswere from psycholeptics (typical antipsychotics, atypical antipsychotics & anxiolytics) which accounted for 88.57% and psychoanaleptics (antidepressants) 11.43%. Psycholeptics such as Risperidone and Olanzapine were the most commonly involved drugs causing ADRs, whereas Escitalopram among psychoanaleptics (Fig. b).Antipsychotics with greater D2 receptor blockade potency showed 56.67% of ADRs while with lesser potency accounted 43.33% of ADRs (Table 2).During the time period of our study, the incidence of ADRs was found to be more in patients diagnosed with depression with psychotic symptoms (34.28%)

followed by paranoid schizophrenia (17.4%) as depicted in table 3.

We studied organ system affected with ADRs amongst which the neurological system ranked first with 54.29% followed by gastrointestinal (34.28%), endocrine (5.71%), haematology and CVS(Fig c).

Upon causality assessment using Naranjo scale, majority of the reports were rated as possible (85.71%) followed by probable (14.29%). According to Hartwig and Siegel scale, mild, moderate and severe reactions accounted for 31.43%, 62.86%and 5.71% respectively.Preventability assessment was done usingSchumock and Thornton scale showed that most of the ADRs were definitely preventable (48.57%) and 25.71% were probably and not preventable ADRs (table 4). Upon assessment of the type of prescription causing ADRs, the majority of the reports showed that the polypharmacy acts as the predisposing factor of ADR in both adults and elderly. Polypharmacy showed statistically significant difference between adults and elderly in causing ADRs (table 5).

In the majority of reported ADRs, the drug was not withdrawn for 71.43% of cases and managed by altering the dose for 31.43% of cases. The ADRs were also managed by instituting additional treatment for 62.86% of cases (Fig d).An improvement in the patients with ADRs was observed majorly (74.29%), because of the drug withdrawal, dose alteration and institution of additional treatment (Fig e).

Table 1: Types and incidence of reported ADRs.

Type	% of ADRs reported	Incidence rate (%)	Number of ADRs	ADRs %
Type A	97.15 %	>10%	15	44.11
		1-10 %	16	47.05
		<1 %	3	8.82
Type B	2.85 %	>10%	00	00
		1-10 %	00	00
		<1 %	01	100

Table 2: ADRs based on D2 receptor blockade potency.

Name of drug	Dopamine D2neuroreceptor potency	No. of ADRs	Total %
Haloperidol	High	05	56.67
Risperidone	High	12	–
TOTAL		17	
Olanzapine	Low	11	43.33
Quetiapine	Low	02	–
TOTAL		13	

Table 3: Distribution of ADRs based on the disorders diagnosed.

Disorders	No. of patients with ADR	No. of ADRs	% of ADR
Paranoid schizophrenia	05	06	17.14
Depression without psychotic symptoms	05	12	34.28
Catatonia	01	01	2.86
OCD	01	01	2.86
Depression with psychotic symptoms	03	03	8.57
Adjustment disorder	01	01	2.86
Dementia	01	01	2.86
Psychosis	01	04	11.43
Somatoform disorder	01	01	2.86
BPAD	04	05	14.28

Table 4: Analysis of ADRs for selected parameters.

Parameter	Number of ADRs	ADRs %
Causality Definite	00	00
Probable	05	14.29
Possible	30	85.71
Severity	–	–
Mild	11	31.43
Moderate	22	62.86
Severe	02	05.71
Preventability	–	–

Table 5: Influence of polypharmacy in adults and elderly.

Age	Type of prescription			Chi-square test	P- value
	Number of drugs(>5)	Number of drugs (≤5)	Total		
Adults	03	24	27	9.243	0.0024 Statistically significant
Elderly	05	03	08		
Total	08	27	35		

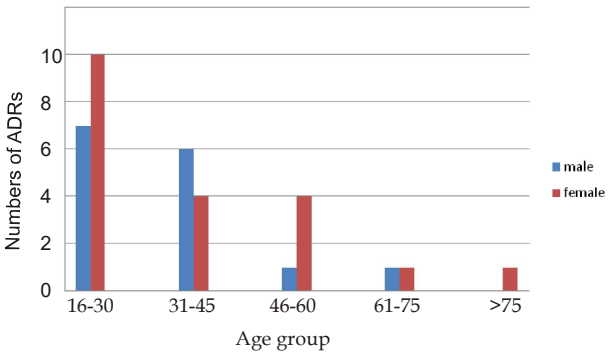


Fig. a: Percentage of the patients and patient characteristics.

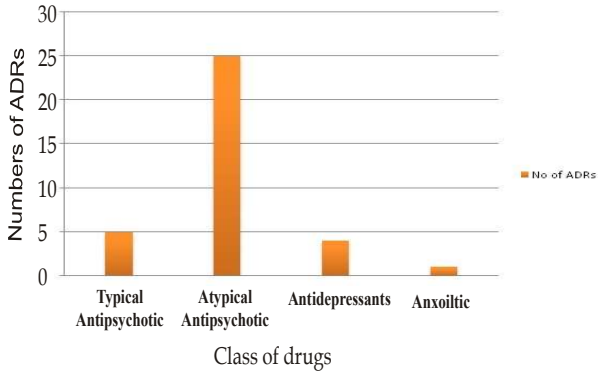


Fig. e: Percentage outcome of ADRs.

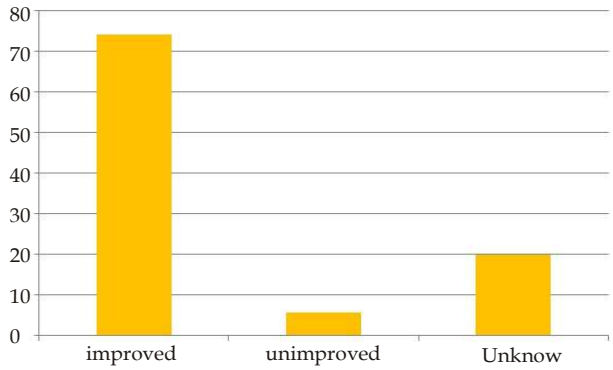


Fig. e: Percentage outcome of ADRs.

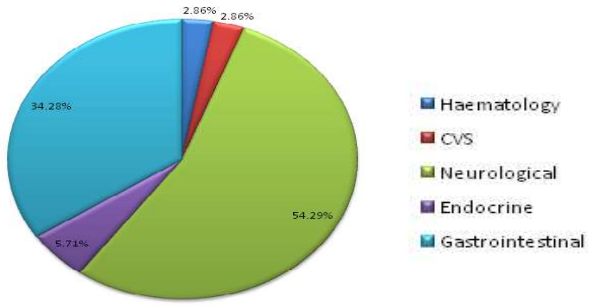
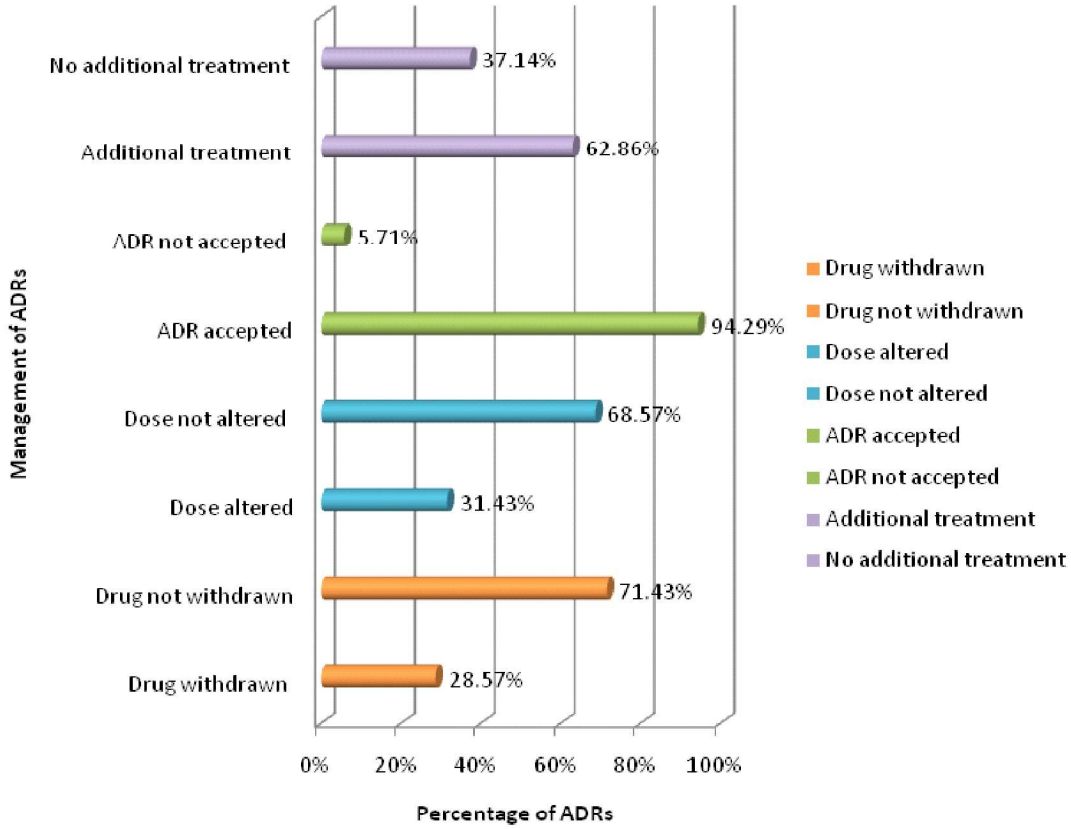


Fig. c: Organ system affected with ADRs.

Discussion

Adverse Drug Reactions and Drug-drug interactions to psychotropic agents are common and can lead to noncompliance and at times discontinuation of therapy.In our study, we found number of ADRs was more in females than in males and majority of patients were found to be in the median age 35 years. However this finding is in contrast with the study done byLashmi Pet.al, which reported ADRs were noted more in males than females and the median age was 31.5 years.[6]

Depression without psychotic symptoms and paranoid schizophrenia were found to be the



commonest clinical diagnosis. Among them, more ADRs were with depression than with paranoid schizophrenia. This finding is similar to the study by Venkatesh K et.al, which reported paranoid schizophrenia as the commonest clinical diagnosis.[6]

Class of drugs responsible for ADRs included atypical antipsychotics, typical antipsychotics, antidepressants and anxiolytics. Among these, the ADRs caused by atypical antipsychotics and typical antipsychotics were preventable. Previous studies done by Courtney et.al, showed more ADRs among mood stabilizers followed by typical antipsychotics, atypical antipsychotics and antidepressants. Out of these mood stabilizers, atypical antipsychotics and typical antipsychotics were commonly associated with preventable ADRs.[7]

In previous studies, the causality assessment of suspected ADRs done by using Naranjo Scale and WHO Scale revealed that majority of the ADRs were possible than probable. We also accounted the similar result.

The severity assessment of ADRs was done by using Hartwig and Siegel Scale in which 58.93% were found to be moderate and 41.43% mild. This is similar to our study where we found ADRs of moderate severity.6

We studied organ system affected with ADRs amongst which the neurological system (tremor) ranked first followed by gastro intestinal, endocrine, haematology and CVS. Sengupta et.al, had also found that neurological ADRs (tremor) were the commonest followed by metabolic (weight gain) and gastro intestinal effects (constipation).8In this study most of the reactions were type A (97.15%), while type B (2.85%) accounted very less in the observed patients.

In our study, we found an incidence of ADRs as 32.91%. The highest number of ADRs was shown by Risperidone and Olanzapine, tremor the most recurrent one. Pritom Ket.al also found an incidence of ADRs as 9.19% in their study. Olanzapine was the commonly used drug having the highest number of ADRs and tremor the frequent ADR.[9]

The preventability of the ADRs was assessed using Schmock and Thornton Scale, in which definitely preventable ADRs came as the highest one. But in another study not preventable ADRs like agranulocytosis, increased blood sugar level etc were noted more than probably preventable ADRs like tremor, akathisia, dystonia.[9]

No ADR found turned out to be fatal, life-threatening or required hospitalization for management. Some of the events, such as tremor were temporarily disabling but were managed by clinicians with appropriate medicines (such as trihexyphenidyl for EPS) or dose modification (for example, the doses of antipsychotics can be decreased for the management of sedation and drowsiness cases).

Conclusion

By this study, it is evident that ADRs with psycholeptics and psychoanaleptics are common in the psychiatric population of HSK hospital,Bagalkot. But the involvement of the clinical pharmacist in monitoring and reporting ADRs will help the patients for medication adherence and the psychiatrists to provide better treatment outcome.

Acknowledgement

The authors thank Principal,H.S.K. College of Pharmacyand Dean, SN Medical College and HSK Hospital, Bagalkot, Karnataka, India, for providing necessary facilities and support during the course of this study.

Conflict Of Interest

Authors declareno conflict of interest

Abbreviations Used

ADR	:Adverse Drug Reaction
WHO	:World Health Organisation
D2 Receptor	:Dopamine 2 Receptor
CVS	:Cardio Vascular System
EPS	:Extra Pyramidal Symptoms
OCD	:Obsessive Compulsive Disorder
BPAD	:Bipolar Affective Disorder

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Review Article

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Comorbid Anxiety Disorders in Schizophrenia

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Abstract

Anxiety disorders commonly co-occur in patients of schizophrenia and have significant influence on course and prognosis of schizophrenia. However, probably due to diagnostic and treatment hierarchical reductionism anxiety disorders have been overlooked in schizophrenia. Review of the literature reveal great differences in prevalence estimates as a result of variations in symptom descriptions and different diagnostic instruments. There are significant differences in psychopathology of individuals with Schizophrenia with and without anxiety disorders. With regard to treatment response it is seen that subjects with Schizophrenia and anxiety disorders respond poorly to only antipsychotics but respond better to antipsychotics plus the SSRIs. Further, the duration of illness of schizophrenia subjects with anxiety disorder is comparatively briefer. The presence of comorbid anxiety disorder in schizophrenia patients may indicate a better prognosis. It is essential that schizophrenia patients undergo proper psychiatric screening and detailed evaluation to detect and treat comorbid anxiety disorders, since this may improve their quality of life and future prospects.

Keywords: Schizophrenia; anxiety disorders; prevalence; management.

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Introduction

In general medicine, Feinstein has defined comorbidity as, any separate and supplementary disorder that has coexisted or that may occur while the patient is suffering from the index disease under study.[1] In recent times this expression is frequently used in clinical psychiatry to describe patients who receive a medical diagnosis in addition to their psychiatric disorder (e.g. major depression and hypertension), but much more frequently patients who are diagnosed with two or more psychiatric disorders.[2] Dual diagnosis are associated with a number of undesirable sequels comprising higher dose and/or number of medicines, non-compliance, psychosocial problems, depression, deliberate self-harm, relapse, increased load on family and vagrancy . In addition, they often have a poorer treatment outcome than those with a single diagnosis of a mental disorder.[3]

In the past two decades a number of studies have concluded that the co-occurrence of psychiatric disorders along with schizophrenia is frequent especially depression, substance abuse, anxiety disorders and obsessive-compulsive disorder (OCD).[4-5] Despite these findings, there is paucity of well-planned studies in order to determine the prevalence and correlates of these co-morbid disorders. Furthermore, conclusive studies have not been done on the treatability of such conditions, although it is widely recognized that without comorbid schizophrenia these disorders are eminently treatable. Apart from all this, these co-morbid conditions may increase the infirmity of such patients as well. [6]

In classical phenomenology, certain unusual

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mental experiences are objectified as psychiatric symptoms which in turn form the components of classification. However mental experiences may also be seen as stages in a psychopathological process. The role of affect in schizophrenia has recently been a focus of psychological accounts of positive symptoms like hallucinations and delusions. Birchwood and Iqbal [7], have concentrated on depression, while Garety et al.[8] believed in the centrality of anxiety, at the minimum in some patients. This group has studied the cognitive concomitants of anxiety : attentional biases; metacognitive processes like worry and views about the controllability of thoughts; Safety behaviors i.e. avoidance.[9-11] Their findings imply that the intellectual procedures that accompany anxiety play a role in maintaining the symptoms of psychosis.[9-11] Anxiety at the inception of insanity is fundamental to the neuropsychological explanation put forward by Gray et al., who implicated arousal in the development of delusions.[12]

It has been postulated that anxiety is a vital forerunner of schizophrenia. If this were true then a high prevalence of co-morbid anxiety disorders is expected in schizophrenia. The relationship can be established by studies either at the symptom level or at the level of diagnostic classes- both are potentially illuminating but unfortunately the psychiatric literature provides few references to a link between the symptoms of anxiety and schizophrenia as discussed earlier. This is despite the fact that various phenomenologists have been aware of the link. From early in the 20th century Eugen Bleuler described non psychotic abnormalities precede the commencement of schizophrenia. These were reported by him as well as others as anxiety, panic, depression, vague somatic complaints, obsessions and compulsions. [13]

Fish also accepted that anxiety exists in individuals with schizophrenia. He believed that anxiety generally accompanied hallucinations and delusions of persecution during the acute phase of the illness. Conspicuous anxiety and depression was produced due to the abrupt inception of hallucinations . The patient with self-reference hallucinosis is usually very anxious and frightened. He therefore clearly saw anxiety arising secondary to the symptoms of the illness, though he also recognized that severe anxiety states might precede the inception of schizophrenic symptoms.[14] Leonhard wrote about anxiety in relation to his concept of the cycloid psychoses. He named one variety the anxiety elation psychosis. He stated the basic disorder is a mood change of either anxiety or ecstasy. Anxiety is associated with typical ideas of reference and sometimes with illusions and hallucinations. These paranoid symptoms are understood as arising from the mood. The pre psychotic personality is often anxious or hypomanic. He also has written about anxiety and other affective disorders sometimes occurring as accessory symptoms in the acute stage or systematic peripheries.[15] In paranoid schizophrenia there is a morbid distortion of subject's beliefs or attitudes concerning relationship between themselves and other people. In chronic schizophrenia social withdrawal and emotional apathy are prominent features. Anxiety might therefore be specifically attached to other people in a way similar to the social anxiety syndromes. If this were so, one would certainly expect these disorders to be more prevalent in schizophrenia. On the other hand, non-social anxiety might lead to relatively more specific distortions in the capacity to evaluate the evidence in an objective way providing another potential route to distorted thinking.

Anxiety as a sign or as a disorder is common. Therefore its occurrence in subjects with schizophrenia is expected. The association could be no more than chance. However, anxiety may have been already present in the individual who later developed schizophrenia. The cause of anxiety could be the same neurodevelopmental abnormality that results in schizophrenia. It might also be secondary to distressing psychotic symptoms.[16] In clinical practice however, the occurrence of anxiety disorders in schizophrenia is not very common. The reasons may be numerous. Clinicians often discount the presence of anxiety disorders in schizophrenia due to hierarchical considerations. The symptoms of anxiety disorders are attributed only to schizophrenia. Patients often conceal the syndromes due to shame. Symptoms of psychosis are intense and demand urgent action. In the presence of these symptoms minor signs of anxiety tend to be neglected. Additionally impaired cognitions and negative symptoms may interfere with the assessment of anxiety disorders in schizophrenia patients. Sometimes effects of antipsychotic medications may impede the identification of anxiety disorders in schizophrenia. Lastly few second generation antipsychotic drugs are reported to have precipitated symptoms of panic disorder (PD) [17] and social anxiety disorder. [18] Despite the clinical confounders, numerous recent studies have reported growing frequency of anxiety disorders in schizophrenia.[4- 6, 19-25] Thus to illuminate the problems in recognizing anxiety disorders in schizophrenia, the recent and past

literature was reviewed. First of all addressing the prevalence of anxiety disorders in schizophrenia, and then concentrating on the various correlates of such an association and lastly on those few treatment studies available for such conditions.

Comorbid anxiety and schizophrenia: earlier views:

Early observations on the co-occurrence of anxiety in patients with schizophrenia is found in some of the first observational studies. Eugen Bleuler's[13] monograph and Kraeplin's [26] Dementia Praecox and Paraphrenia, both describe commonly occurring and profound levels of anxiety in schizophrenia. Both discuss in particular, how often individuals with schizophrenia experience intense worry, over concern and panic, fearfully avoid others and are beset by a myriad of obsessions and compulsions. Particularly in the work of Bleuler, symptoms of anxiety are best described as commonly intervened with other more central schizophrenic symptoms and were noted to complicate the course of the disorder. In Bleuler's work, anxiety symptoms are associated with even greater withdrawal from social situations. Thus examination of Bleuler and Kraeplin's early works make it apparent that anxiety disorders have been identified in individuals with schizophrenia for nearly a century. In addition it has been posited that comorbid anxiety disorders may worsen the outcome of schizophrenia.

Prevalence of various anxiety disorders in schizophrenia

Boyd et al. conducted an epidemiological study in five US cities. All subjects were diagnosed using the NIMD- Diagnostic Interview Schedule (DIS). The prevalence of panic attacks was 37.9%. [27] Different studies with clinical samples tried to evaluate the presence of comorbidities, principally concentrating on the different anxiety disorders. But due to the peculiarities inherent to the clinical samples and to the small sample size included in the studies, the results are highly variable and sometimes difficult to pool together.

Garvey et al., assessed ninety-five psychiatric inpatients for the coexisting anxiety disorders, out of which eighteen met the DSM-III criteria for schizophrenia. They reported that 44% of the individuals had comorbid anxiety disorder of which 17% had a current PD and 22% with generalized anxiety disorder. They also hypothesized that individuals with comorbid anxiety disorder possibly had a better prognosis.[28] Strakowski et al. studied one hundred and two acutely psychotic, hospitalized first episode patients with ten having disorders in schizophrenia spectrum and found a rate of 6% for PD. They also said that comorbidity in schizophrenia was associated with longer hospitalization.[29] Sixty schizophrenia or schizoaffective disorder outpatients were randomly selected by Zarate et al. Out of which twenty-eight were with a comorbidity and thirty-two without a comorbidity. Of the patients having a comorbidity, 56.7% had a lifetime anxiety disorder, and 19.4% had PD. Also the individuals with comorbidity had poorer overall functioning.[30] Cassano et al. evaluated ninety-six consecutively hospitalized currently psychotic patients out of which ten had a diagnosis of schizophrenia as per the DSM-IV criteria and found a prevalence of 19.4% for PD in these patients. [19]

Cosoff and Hafner, in sixty schizophrenia inpatients diagnosed using SCID DSM-III-R, identified 33% to have a comorbid anxiety disorder . The prevalence of the specific anxiety disorder was PD 5%, social phobia 17% and generalized anxiety disorder 12%. Although symptoms of psychiatric disorders were significantly higher in those with anxiety disorders on self-rating scales, hospital admissions rate were not. They also said that patients regularly admitted to hospital have elevated prevalence of anxiety disorders compared to those treated primarily in the community.[20] But this was in contrast to what was found by Soni et al. who found higher levels of anxiety in patients who were managed in the community. [31]
Bermanzohn et al. too found a prevalence rate of 40% of comorbid anxiety disorder in thirty-seven schizophrenic day care patients using the SCID-DSM-IV to find a prevalence of 29.7% for OCD and 10.8% for PD.[21] Goodwin et al. while assessing 184 schizophrenic inpatients using DIGS, DSM-III-R found a prevalence of 42.5% for the anxiety disorder which constituted 5.4% of OCD patients, 7.1% with PD, 8.2% for agoraphobia as well as social phobia, 13.6% for the specific phobias.[22]

While assessing thirty schizophrenic outpatients using MINI-DSM-IV, Tibbo et al. observed a rate of 26.7% (N=8) for generalized anxiety disorder, 23.3% (N=7) for social phobia, 6.6% (N=2) for PD with or without agoraphobia, 26.7% (N=8) for agoraphobia. These rates decreased when anxiety signs associated with symptoms of psychosis were excluded. Further they concluded that the comorbid anxiety disorders did not alter the outcome of schizophrenia in their study.[23] Pallanti et al. found a much higher prevalence rate of 60.2% using SCID DSM-IV in a group of eighty schizophrenic

outpatients. Out of which 36.3% were detected with social phobia, 22.5% with OCD, 13.8% with PD and a lower percentage of 3.8% with agoraphobia, 2.5% with specific phobia and generalized anxiety disorder each and a rate of 1.3% with PTSD. [6]

While following a group of twenty-three schizophrenic out patients, Ciapparelli et al. found a prevalence of 47% for the comorbid anxiety disorders, which was quite similar to the most of the studies. It consisted of 40% of social phobia as well as PD and a rate of 20% for OCD and almost 33% of the patients received multiple anxiety diagnosis. Moreover patients with panic disorder and OCD showed greater severity of illness at baseline whereas patients with social anxiety disorder showed greater illness severity in remission.[25]

Apart from the above studies there are several others which have frequently reported a high level of anxiety as a common symptom and a cause of disability in schizophrenic patients. It is frequently related to the positive symptoms of schizophrenia. So it is not taken into account as it has been established as a common symptom associated with schizophrenia. There are other studies which have concentrated on a single anxiety disorder comorbid with schizophrenic illness rather than focusing on the entire anxiety disorder spectrum. Of which most of them have concentrated on the epidemiology of PD and the rest of the disorders have obtained less attention. The following paragraphs will discuss about these studies.

Panic disorder in schizophrenia

Boyd reviewed the ECA data that included five large community samples (N=18,572). He observed the prevalence of panic attacks in individuals with schizophrenia varied from 28% to 63% in different communities. He specified panic attacks, not PD, and so the problem was more prevalent. Due to differences amongst DIS diagnosis and clinical diagnosis, he clearly mentioned that diagnoses were made as per DIS criteria and not DSM-III criteria.[32] Tien and Eaton reexamined the ECA data and observed that individuals with panic attacks had increased odds (relative risk=2.28) of subsequently suffering from schizophrenia. This relation however, was not statistically significant (p=0.062). [33]

A Canadian community-based study also utilized the DIS instrument, also found that schizophrenia patients had an increased occurrence of PD. They also reported that onset of PD was prior to the onset of schizophrenia. [34] Argyle reported that 7 (35%) of twenty consecutive outpatients on maintenance treatment of schizophrenia complained of panic attacks that was occurring regularly. Four of the seven patients (18%) met the DSM III R criteria for PD, while three (15%) met the criteria for agoraphobia with panic attacks and one (5%) had agoraphobia without panic attacks.[35] After this Cutler and Siris interviewed a series of forty-five outpatients with schizophrenia and schizoaffective disorder with post psychotic depression and found panic attacks in eleven (25%) patients. [36]

Bermanzohn et al. evaluating 37 chronic schizophrenia or schizo-affective disorder outpatients and found twelve (32.4%) had panic attacks, while eight (21.6%) had PD, five of whom also had agoraphobia. [37] Another study included 60 schizophrenia or schizo-affective disorder patients. The authors reported PD in 8 (13%) patients, out of whom 5 (8%) had agoraphobia while 3 (5%) did not have agoraphobia. [30]

A prevalence rate of 43% (n=21) for PD was found by Labbate et al. in thirty outpatients of schizophrenia using the SCID DSM-IV diagnostic instrument. Out of which 33% had (n=16) PD currently of in the past. [38] On the other hand Bayle et al. in forty schizophrenia in and outpatients reported PD in 36.8%. Twelve of which were related to paranoid ideations.[39] Craig et al. found a low prevalence of 5% of PD using SCID DSM-III-R in two hundred twenty five of his patients suffering from schizophrenia and schizoaffective disorder, 14% of the patients had symptoms of PD.[40] Ulas et al. evaluated 49 schizophrenia patients and observed that fifteen patients had suffered panic attacks during their illness, seven of which had a lifetime history of PD. [41]

Social anxiety disorder in schizophrenia

Pilkonis et al. initially reported that schizophrenia patients had high social anxiety compared to controls.[42] Penn et al. evaluated social anxiety in thirty eight schizophrenic patients by means of a battery of self-report measures of anxiety, a modified stroop task and an unstructured role play and found that the intensity of social anxiety was within the clinical range reported by pretreatment social phobic patients.[43] The full diagnosis of social phobia was first assessed in the Argyle study. They found social phobia in four (20%) of twenty consecutive schizophrenia patients on maintenance treatment.[35]

Pallanti et al. evaluated eighty schizophrenia outpatients using SCID-DSM-IV-TR and found

Table 1. Frequency of Comorbid Anxiety Disorders in Schizophrenia.

First Author (Year)	Sample (size)	Diagnostic Instrument	PD	SP	GAD	Agora-phobia	Specific Phobia	AD NOS
Kessler (1994) [46]	National Co-morbidity survey	CIDI DSM-III-R	2.3%	7.9%	3.1%	2.8%	8.8%	-
Cosoff (1998) [20]	In-patients (60)	SCID DSM-III-R	5%	17%	12%	5%	5%	-
Bijl (1998) [47]	Netherlands Mental Health Survey and Incidence Study	CIDI DSM-III-R	2.2%	4.8%	1.2%	1.6%	7.1%	-
Labbate (1999) [38]	Out-patients (30)	SCID DSM-IV	43%	-	-	-	-	-
Henderson (2000) [48]	Australian adult population survey	CIDI ICD -10	1.3%	2.7%	9.7%	1.1%	-	-
Bermanzohn (2000) [21]	Day hospital (37)	SCID DSM-IV	10.8%	-	-	-	-	-
McConnell (2002) [49]	Out-patients (100)	SCAN ICD-10	2.4%	-	0.15%	0.7%	0.2%	-
Tibbo (2003) [23]	Out-patients (32)	MINI DSM-IV	3.3%	13.3%	16.7%	16.7%	-	-
Goodwin (2003) [22]	In-patients (184)	DIGS (SMIIIR)	7.1%†	8.2%	-	8.2%	13.6%	-
Pallanti (2004) [6]	Out-patients (80)	SCID DSM-IV	13.8%	36.3%	2.5%	3.8%	2.5%	-
Huppert (2005) [50]	Outpatients (32)	ADIS IV DSM IV	18.8%	37.5%	12.5%	-	-	-
Seedat (2007) [51]	Inpatients (70)	MINI DSM-IV	-	5.7%	8.6%	-	-	-
Nebioglu (2009) [52]	Out-patients (82)	SCID DSM-IV	8.5%	13.4%	8.5%	2.4%	9.7%	1.2%
Belene (2010) [53]	Out-patients (105)	SCID DSM-IV	4.76%	4.76%	NA	0.95%	14.28%	2.85%
Rapp (2012) [54]	Out-patients (255)	DIGS DSM IIIR	27.5%	-	-	-	-	-
Young (2013) [55]	Out-patients (174)	SCID DSMIV	6.9%	-	-	-	-	-
Aguocha (2015) [56]	Out-patients (367)	PSE 10ICD 10	NA	NA	6.3%	2.7%	NA	-
Nagargoje (2015) [57]	In & out-patients (60)	SCID DSM-IV	24.13%	31.3%	13.79%	NA	NA	NA
Lowengrub (2015) [58]	Outpatients (50)	SCID DSM-IV	NA	38%	-	-	-	-
Kiran (2016) [45]	Inpatients (93)	MINIICD 10	18.28%	9.68%	1.08%	6.45%	-	-
Vrbova (2017) [59]	Out-patients (61)	MINI ICD10	-	-	-	-	-	-
Bener (2018) [60]	Outpatients (396)	SCID5 DSM5	-	-	-	-	-	-
Aikawa (2018) [61]	Out-patients (207)	MINI DSM-IV	-	14.5%	-	-	-	-
Achim (2011) [88]	Meta-analysis	_	9.8%	14.9%	10.9%	5.4%	7.9%	

Abbreviations: PD: panic disorder; SP: social phobia; GAD: generalized anxiety disorder; ADNOS Anxiety disorder not otherwise specified; CIDI: Composite International Diagnostic interview; SCID: Structured Clinical Interview for Diagnosis; MINI: Mini International Neuropsychiatric Interview; DIGS: Diagnostic Interview for Genetic Studies; ADIS-IV: Anxiety Disorders Interview Schedule for DSM-IV

outpatients using SCID-DSM-IV-TR and found twenty-nine (36.3%) patients suffered from social anxiety disorder.[6] Mazeh et al. evaluated 117 patients with schizophrenia using DSM-IV SCID-P-Hebrew version and found that thirteen of them had a comorbid social phobia (11%). Higher severity PANSS total sore was associated with comorbid social phobia. Significant correlation was found between the scores of Leibowitz social anxiety scale fear and PANSS positive subscale.[44]

Studies from India

Using a prospective, purposive sampling technique 93 inpatients of a tertiary care psychiatric hospital diagnosed as schizophrenia by ICD-10 DCR criteria and equal number of age and sex matched normal controls were evaluated for comorbid anxiety disorders. The prevalence of anxiety disorders in schizophrenia patients (35.48%) was significantly higher than in normal control subjects (16.12%).[45]

Treatment of comorbid anxiety disorders in schizophrenia:

There is a lack of controlled studies evaluating

Table 2. Management of anxiety symptoms and comorbid anxiety disorders in schizophrenia

First author (Year)	**Design, (sample size)**	**Diagnosis**	**Management**	**Outcomes**
Blin et al. (1996) [63]	Randomized trial (N = 62)	Schizophrenia with anxiety symptoms	Risperidone vs. haloperidol vs. methotrimeprazine	Significantly greater reductions in Psychotic Anxiety Scale in risperidone vs. methotrimeprazine group
Kasper et al. (2004) [64]	Open-label extension of randomized trial (N = 415)	Schizophrenia with anxiety symptoms	Quetiapine	Significant reduction in BPRS anxiety/depression factor maintained over long-term tx
Stern et al. (2009) [65]	Non-randomized, prospective trial (N = 16)	Schizophrenia, schizoaffective disorder with social anxiety symptoms	Aripiprazole (switched from existing antipsychotic to aripiprazole)	Significant reduction in LSAS, SDS
Tollefson et al. (1999) [66]	Randomized trial, secondary analysis (N = 335)	Schizophrenia with anxiety symptoms	Olanzapine vs. PL; haloperidol vs. PL	Significantly greater reduction in BPRS anxiety depression factor in olanzapine (7.5–20 mg/day) vs. PL. No significant difference for haloperidol vs. PL groups
Kanh (1988) [67]	Open trial (N=7)	Schizophrenia with panic disorder	Alprazolam	Clinical improvement on panic symptoms
Argyle (1990) [35]	Case series (N=3)	Schizophrenia with panic attacks	Diazepam/alprazolam	Symptoms reduced
Pallanti et al. (1999) [18]	Non-randomized, prospective trial (N = 12)	Schizophrenia with tx emergent social anxiety	Fluoxetine add-on to clozapine	Significant improvement in fear and anxiety subscore of LSAS
Kiran (2018) [68]	Open label prospective study (N=33)	Schizophrenia with anxiety disorders	Fluoxetine add-on to antipsychotics	–
Arlow (1997) [69]	Open trial (N=11)	Schizophrenia with panic disorder	CBT	Panic symptoms reduced in 7. Three patients decompensated
Halperin (2000) [70]	Single blind, randomized study (N=20)	Schizophrenia with Social phobia	Group CBT for 8 weeks	Improvement of social anxiety and quality of life
Kingsep (2003) [71]	Single blind, randomized study (N=30)	Schizophrenia with Social phobia	Group CBT for 12 weeks	Improvement of social anxiety and quality of life

BPRS Brief Psychiatric Rating Scale, LSAS Liebowitz Social Anxiety Scale, OCD obsessive–compulsive disorder, OCS obsessive compulsive symptoms, PANSS Positive and Negative Syndrome Scale, PL placebo, pts patients, SDS Sheehan Disability Scale, SSRIs selective serotonin reuptake inhibitors, tx treatment, Y-BOCS Yale-Brown Obsessive–Compulsive Scale

twenty-nine (36.3%) patients suffered from social anxiety disorder.[6] Mazeh et al. evaluated 117 patients with schizophrenia using DSM-IV SCID-P-Hebrew version and found that thirteen of them had a comorbid social phobia (11%). Higher severity PANSS total sore was associated with comorbid social phobia. Significant correlation was found between the scores of Leibowitz social anxiety scale fear and PANSS positive subscale.[44]

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Using a prospective, purposive sampling technique 93 inpatients of a tertiary care psychiatric hospital diagnosed as schizophrenia by ICD-10 DCR criteria and equal number of age and sex matched normal controls were evaluated for comorbid anxiety disorders. The prevalence of anxiety disorders in schizophrenia patients (35.48%) was significantly higher than in normal control subjects (16.12%).[45]

Treatment of comorbid anxiety disorders in schizophrenia:

There is a lack of controlled studies evaluating the management of panic symptoms in patients with schizophrenia. Anecdotal reports point to the fact that PD may be treated as usual in the presence of schizophrenia. One open prospective case series with alprazolam and case reports with alprazolam, diazepam, and imipramine consistently report improvement in panic symptoms.[35,72] A case report has reported improvement in panic symptoms with the switch from haloperidol, bromperidol

and risperidone to quetiapine, which hadn't shown any improvement on fluoxamine,[73] and another had reported improvement with switch from haloperidol to risperidone.[74] Fer reports indicate that panic symptoms may worsen with long term use or increasing the dosages of antipsychotics. [75] Eight patients with schizophrenia and comorbid PD underwent a 16 week clinical trial of cognitive behavioral group therapy. Results suggest that cognitive behavioral group therapy may be helpful in lessening symptoms. [76] This was again confirmed by a study of four patients utilizing a cognitive behavioural intervention (panic control treatment) in 15-17 sessions with considerable improvement in both panic attacks and psychotic symptoms.[77]

There is paucity of information regarding management of social phobia in schizophrenia. Two studies from Australia used cognitive behavioral group therapy for management of comorbid social anxiety in patients with schizophrenia.[70-71] In one of them conducted by Halperin et al. patients were randomized to the treatment group or a waiting list group including 20 patients. The treatment which included exposure situation, cognitive restructuring and homework assignment in both groups was effective in improving measures of general psychopathology, social anxiety and quality of life after group CBT for a duration of 8weeks.[70] In the other group the sessions took place for a duration of 12 weeks including 33 individuals. [71] Good evaluated the effect of CBT on psychotic symptoms in a schizophrenic patient suffering from social anxiety but no attempts were made to treat the psychotic symptoms per se, the scores for social phobia had decreased to a subclinical level over the course of treatment and also the psychotic symptoms rapidly abated. [78]

The schizophrenia patients were evaluated for psychopathology and the presence of anxiety disorder at baseline. After being prescribed with antipsychotic medication in a suitable dose for 8 weeks, they were followed up at monthly intervals for the course of both schizophrenia and anxiety disorders. Thereafter, an selective serotonin reuptake inhibitor (SSRI) was also prescribed to the schizophrenia patients with comorbid anxiety disorder, and the patients were again followed up for a period of 8 weeks to assess the progress of schizophrenia and anxiety disorder Schizophrenia patients with anxiety disorder had a significantly higher positive score of the Positive and Negative Symptom Scale for Schizophrenia (PANSS) and a significantly lower score on the negative scale and the general psychopathology scale of the PANSS, as compared to the scores of the schizophrenia group without anxiety disorders. Schizophrenia patients with anxiety disorders responded well to the combination of SSRIs and antipsychotics but not antipsychotics alone. These anxiety disorders are quite responsive to the SSRIs but not to antipsychotics alone. Further, there is a shorter duration of illness in schizophrenia patients with anxiety disorders as compared to schizophrenia patients without anxiety disorders assigning a prognostic significance to the presence of comorbid anxiety disorders in schizophrenia.[68]

Conclusion

The current review thus leads to the conclusion that patients with schizophrenia commonly have comorbid anxiety disorders. There is no significant association of these anxiety disorders and the basic psychopathology of schizophrenia. Schizophrenia patients with and without anxiety disorders show major differences in their symptomatology. The absolute reason for this is not known but the phenomenon most likely exists because of a common pathologic process or a common etiology. There is some evidence that subjects with schizophrenia and anxiety disorders have a shorter duration of illness compared to those without anxiety disorders. Comorbid anxiety disorders in schizophrenia respond well to treatment with SSRIs. Further the search for the causes of such an association might help in a better and more robust classification system for the proper placement of these disorders as well as the others.

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A Case Report on Risperidone Induced Prolactinoma

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Abstract

Risperidone is a second generation antipsychotic reported to cause hyperprolactinemia due to its D2 receptor antagonism, which may induce amenorrhea, altered menstrual cycle, loss of libido and increase the long-term risk of osteoporosis. However, to our knowledge, all previous reports have focused on risperidone induced hyperprolactinemia.Here we are presenting a rare case report on prolactinoma caused by risperidone.

Keywords: Risperifone; Adverse Drug reaction; prolactinoma.

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Introduction

Prolactinomas are prolactin secreting pituitary tumors that account for 40% of the pituitary adenomas.[1] Anobserved elevation in serum prolactin level is often due to a drug-induced benign pituitary tumour (prolactinoma), with risperidone utilization apart from other antipsychotic medications in causing pituitary tumors, especially in women.[2] Risperidone being an atypical antipsychotic cause hyperprolactinemia by blocking D2 dopamine receptors and therefore dopamine action. Because dopamine inhibits prolactin release from the pituitary gland, the drugs which decrease dopaminergic tone results in elevated prolactin levels 3. Hence risperidone by blocking dopamine 2 receptor can induce certain types of pituitary hyperplasia.[2]

Case Report

A 35 year old woman with significant psychiatric history of paranoid schizophrenia presented with complaints of suspiciousness, talking and smiling to self, unable to do work, disturbed sleep, auditory hallucination, fearfulness and feeling angry since 7 years. She took multiple consultations from different psychiatrists and was taking Tablet Risperidone 4 mg and Tablet Carbamazepine 200 mg since 2009.

She came to our tertiary care teaching hospital and was advised with many laboratory investigations. Her reports were normal except thyroid function test (Hypothyroidism) and serum prolactin level (Hyperprolactinemia; >200ng/ml). For further clarification she underwent a scanning which revealed features subjective of pituitary microadenoma (prolactinoma) involving right posterior-lateral aspect of anterior pituitary. Physician assessed that risperidone was the cause of increased prolactin levels and prolactinoma. Her medication was then switched on to olanzapine 20mg for paranoid schizophrenia but, it did not show significant decrease in prolactin levels and

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hence tablet bromocriptine 1.25 mg was added to alleviate the increased prolactin levels and to revert prolactinoma.

Discussion

Risperidone exerts an acute and persistent effect on serum prolactin to a greater extent than the other atypical antipsychotics by blocking dopamine D2 receptors in the anterior pituitary.Prolactin levels are strongly correlated withrisperidone dose. Risperidone has been shown to occupy the D2 receptor by 82% at 6mg and 72% at 3mg.[4]

According to the pharmacovigilance study done by Szarfman et.al, pituitary tumors were higher among patients treated with risperidone than with other antipsychotics. He interpreted that a causal relationship exists between risperidone and pituitary adenoma based on the reports of adverse events due to antipsychotics. The reported ratios implied that pituitary tumors were 8-fold higher in patients treated with risperidone than in olanzapine, 31-fold higher than in quetiapine treated patients, 6-fold higher than in ziprasidone treated patient and 3-fold higher than in haloperidol treated patients.[5]

Dopamine agonists have been in clinical use for many years and remain the fundamental therapy for prolactinomas. Most commonly used dopamine agonists are bromocriptine and cabergoline.[6]

In this case report, there is a clinical significant relationship between long-term risperidone administration and pituitary adenoma. The patient also shows increased serum prolactin levels (hyperprolactinemia). Although there is a causal relationship between the administration of amisulpride and increased prolactin levels; in this patient hyperprolactinemia and resultant prolactinoma are featured only due to risperidone. In order to reduce the further elevation in prolactin levels, olanzapine was added as a substitute to risperidone. For the resolution of prolactinoma, dopamine agonist bromocriptine was added.

Conclusion

Findings from this study suggest that the long term use of risperidone is associated with the occurrence of pituitary adenoma and concurrently hyperprolactinemia. For the patientswith schizophrenia and a prolactinoma, the endocrinologist, psychiatrist and clinical pharmacist should work in concert with one another and with the patient to monitor tumour size, serum prolactin level and adherence to antipsychotic medication. Hence it is recommended to evaluate serum prolactin levels annually in patients taking risperidone to see if there is any indication of a medication-induced pituitary prolactinoma which could suggest the need to stop primary drug treatment and /or switch to an alternative drug.

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Conflicts of Interest

Authors declareno conflict of interest

Abbreviation used

D2 receptor: Dopamine2 receptor

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Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. Extra or supplementary materials and technical details can be placed in an appendix where it will be accessible but will not interrupt the flow of the text; alternatively, it can be published only in the electronic version of the journal.

Discussion

Include summary of key findings (primary outcome measures, secondary outcome measures, results as they relate to a prior hypothesis); Strengths and limitations of the study (study question, study design, data collection, analysis and interpretation); Interpretation and implications in the context of the totality of evidence (is there a systematic review to refer to, if not, could one be reasonably done here and now?, What this study adds to the available evidence, effects on patient care and health policy, possible mechanisms)? Controversies raised by this study; and Future research directions (for this particular research collaboration, underlying mechanisms, clinical research). Do not repeat in detail data or other material given in the Introduction or the Results section.

References

List references in alphabetical order. Each listed reference should be cited in text (not in alphabetic order), and each text citation should be listed in the References section. Identify references in text, tables, and legends by Arabic numerals in square bracket (e.g. [10]). Please refer to ICMJE Guidelines (http://www.nlm.nih.gov/bsd/uniform_ requirements.html) for more examples.

Standard journal article

[1] Flink H, Tegelberg Å, Thörn M, Lagerlöf F. Effect of oral iron supplementation on unstimulated salivary flow rate: A randomized, double-blind, placebo-controlled trial. J Oral Pathol Med 2006; 35: 540–7.

[2] Twetman S, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, et al. Caries-preventive effect of fluoride toothpaste: A systematic review. Acta Odontol Scand 2003; 61: 347–55.

Article in supplement or special issue

[3] Fleischer W, Reimer K. Povidone-iodine antisepsis. State of the art. Dermatology 1997; 195 Suppl 2: 3–9.

Corporate (collective) author

[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000; 71: 1792–801.

Unpublished article

[5] Garoushi S, Lassila LV, Tezvergil A, Vallittu PK. Static and fatigue compression test for particulate filler composite resin with fiber-reinforced composite substructure. Dent Mater 2006.

Personal author(s)

[6] Hosmer D, Lemeshow S. Applied logistic regression, 2nd edn. New York: Wiley-Interscience; 2000.

Chapter in book

[7] Nauntofte B, Tenovuo J, Lagerlöf F. Secretion and composition of saliva. In: Fejerskov O,

Kidd EAM, editors. Dental caries: The disease and its clinical management. Oxford: Blackwell Munksgaard; 2003. pp 7–27.

No author given

[8] World Health Organization. Oral health surveys - basic methods, 4th edn. Geneva: World Health Organization; 1997.

Reference from electronic media

[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979–2001. www.statistics.gov.uk/downloads/theme_health/HSQ20.pdf (accessed Jan 24, 2005): 7–18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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