The Use of Long-term Antipsychotics and its Effects on Prolactin and Bone Mineral Density

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INTRODUCTION

- Antipsychotics are the mainstay of treatment for patients suffering from Schizophrenia and Bipolar disorder.
- Studies have shown that by blocking D2 brain mesolimbic receptors, antipsychotics reduce or control psychotic experiences, but also lead to adverse effects such as reduced bone mineral density (BMD), leading to increased fracture incidence after prolonged use.
- Low dietary calcium intake, smoking, polydipsia, and antipsychotic-related hyperprolactinemia have been implicated.

Objectives

In this study, we explore the specific side effect – high prolactin levels due to chronic use of the anti psychotic medications leading to decrease in BMD using literature review.

- Educated Psychiatry residents, nurses and staff:
  1. Factors leading to falls
  2. Importance of Checking Prolactin Levels
  3. Fall Precautions

METHODS

A multistep approach was utilized:

Retrospective Study:

Literature Review: This study reviews current literature surrounding the use of long-term (for more than 6 months) antipsychotics and their effects on bone homeostasis. (Tables 1-3 and Fig 1-4). The primary medical search engine used for the study is PubMed (1950-2020) database.

We provided lecture on:

- Anti-Psychotics and side-effects specific to hyperprolactemia to Psychiatry residents on factors leading to falls, and importance of checking prolactin levels.
- Falls precautions and extensive education was provided to the nurses, and staff about care of specific patients.

We compared

- The rate of falls pre and post intervention (lecture; excluding patients with orthostatic hypotension) (Table 4 and Fig 4-6)

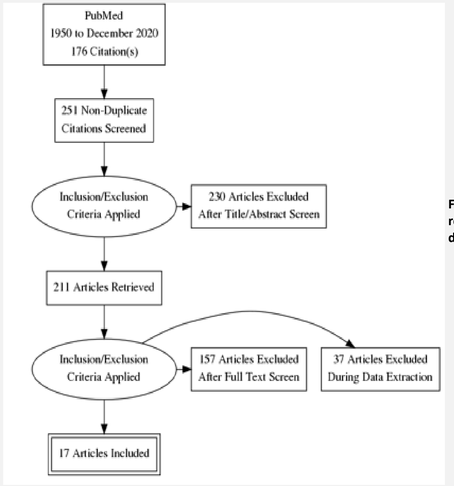


Figure 1: Flowchart of the article selection process in a systematic review of associations between serum prolactin and bone mineral density in psychotic disorders.

RESULTS

- High prolactin levels have been associated with elevated markers of bone turnover (Fig 2-3)
- Prolactin Raising Antipsychotics have shown to have more adverse events due to decrease in BMD, including more incidences of falls and fractures in comparison to Prolactin Sparing Antipsychotics (Table 2 and 3)
- Inverse relation is noted to have in patients with Prolactin and BMD, as well as with years of use of antipsychotics and BMD (Fig 2-3).
- After the lecture, there was an increase in checking the levels of prolactin for patients receiving anti-psychotics for a long time (>6 Months)
- In addition, nurses, staff and residents were noted to provide more education to the patients regarding the adverse effects to anti-psychotics
- Fall precautions orders increased to 80% (Fig 5). Overall, the study helped to decrease amount of fall episodes from 64% to 30%. (Fig 6)

Table 1: Characteristics of included studies (PRL= Prolactin)

Study	Mean Age (years)	Duration of illness (years)	Serum Prolactin (mIU/L)
Abraham et al 2003	43 ± 11.6	22.2 ± 10.4	845.9 ± 801.4
Becker et al., 2003	-	-	Risperidone: 2,068 ± 3,052 Olanzapine: 549.1 ± 544.8
Bergemann et al, 2008	33.8 ± 6.5	8.1 ± 6.3	1,628.0 ± 1,212.0
Bulut et al, 2016	37.9 ± 10.5	9.19 ± 8.3	448.2 ± 369.3
Howes et al., 2005	46.0 ± 13.1	-	698.7 ± 915.9
Hummer et al, 2005	34.8 ± 6.2	9.8 ± 7.4	730.2
Jung et al, 2006	39 ± 5.3	-	883.5 ± 598.1
Kishimoto et al, 2008	58.9 ± 12.2	34.6 ± 13.0	587.8 ± 255.3
Lee et. Al, 2010	49.5±11.1	24.7±9.3	517.3 ± 383.3
Liang et al, 2016	60.4±7.0	30.0±10.0	682.3 ± 443.6
Lin et al, 2015	42.9±9.7	20.0±9.4	835.3 ± 829.1
Renn et al, 2010	47.5±18.7	-	939.0±124.5
Rey-Sánchez et al, 2009	61.2±14.3	-	244.0±191.1
Sugawara et al, 2011	42.6±12.8	-	875.6±839.5
Wang et al, 2014	34.5±10.7	0.65±0.45	913.5±503.7
Lin et al, 2020	41.1	20.5	11.3
Xiangdong Du et al, 2020	Elevated PRL Group 45 Non Elevated PRL Group 47	Elevated PRL Group 24 Non Elevated PRL Group 26	Elevated PRL Group 33.21 Non Elevated PRL Group 33.21

Table 2: Prolactin Sparing Antipsychotics

Antipsychotic	Prolactin Level (ng/ml)
Ziprasidone	<5
Quetiapine	<5
Clozapine	<5
Aripiprazole	<1
Asenapine	<5

Table 3: Prolactin Raising Antipsychotics

Antipsychotic	Prolactin Level (ng/ml)
Haloperidol	34-75
Risperidone	45-87
Paliperidone	34-75
Olanzapine	30-47
Iloperidone	26

Figure 2 – Increase in Prolactin leads to decrease in bone turnover.

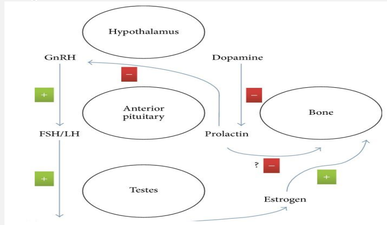


Figure 3: Scatter Plot showing Inverse Correlation of BMD with years of use of antipsychotics

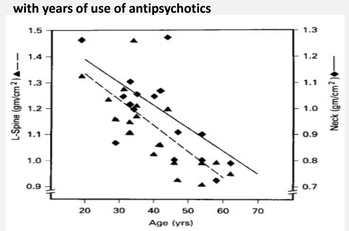


Table 4: Demographics of patients in both pre and post interventional groups

	Pre-intervention group	Post-intervention group	Total
Mean Age	44.4	41.2	42.8
Female (%)	22 (44%)	24 (61.5%)	46 (51.7%)
Male	28 (56%)	15 (38.5%)	43 (48.3%)
n-value	50	39	89

Figure 4 Fall Precautions orders shown in RUMC EMR

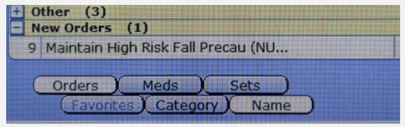


Figure 5. Pre and post intervention of adding fall precaution orders in the EMR

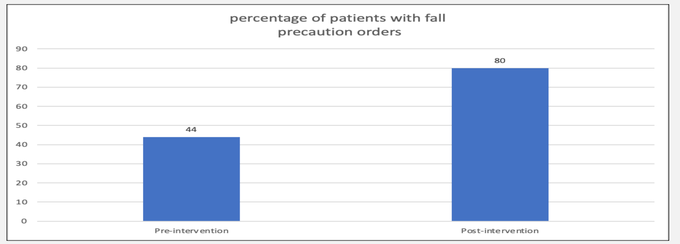
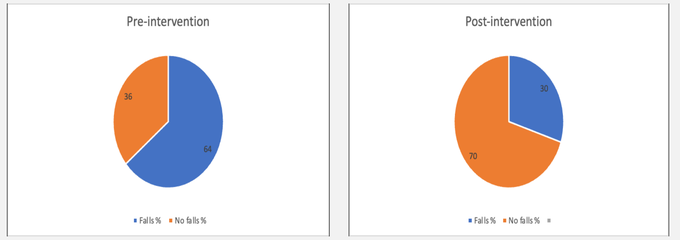


Figure 6. Comparing adverse side effect (falls) in pre and post interventional groups



CONCLUSION

Increasing awareness of the side effect profile of antipsychotic medications on bone metabolism may prompt clinicians to screen patients at high risk of antipsychotic-induced osteoporosis and provide treatment and education, which may reduce the incidence of potentially avoidable fractures.

ACKNOWLEDGEMENTS

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- References:

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