The Pharma Innovation Journal 2017; 6(2): 121-123

www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2017; 6(2): 121-123

www.thepharmajournal.com
Received: 20-12-2016
Accepted: 21-01-2017

Rahul Bhalsinge
Assistant Professor, Department of Pharmacology, Dr. D. Y. Patil Medical College, Pimpri, Pune, Maharashtra, India

Kalbhairav Shinde
Assistant Professor, Department of Pharmacology, Dr. D. Y. Patil Medical College, Pimpri, Pune, Maharashtra, India

Sanjeevani Chawre
Assistant Professor, Department of Pharmacology, Dr. D. Y. Patil Medical College, Pimpri, Pune, Maharashtra, India

Shrikrishna Shende
Junior Resident, Department of Pharmacology, Dr. D. Y. Patil Medical College, Pimpri, Pune, Maharashtra, India

Makarand Jadhav
Junior Resident, Department of Pharmacology, Dr. D. Y. Patil Medical College, Pimpri, Pune, Maharashtra, India

Abhijeet Tilak
Professor and Head, Department of Pharmacology, Dr. D. Y. Patil Medical College, Pimpri, Pune, Maharashtra, India

Correspondence
Larysa Sydorchuk
Assistant Professor, Department of Pharmacology, Dr. D. Y. Patil Medical College, Pimpri, Pune, Maharashtra, India

Original Research Article

To elucidate mechanism of action of nicotine in depression

Rahul Bhalsinge, Kalbhairav Shinde, Sanjeevani Chawre, Shrikrishna Shende, Makarand Jadhav and Abhijeet Tilak

Abstract
Aims & Objectives: The present study was planned:

- To study role of nicotine in depression by using serotonergic mechanism- Lithium induced head twitches.
- To compare mechanism of action of nicotine given subcutaneously and by inhalation.

Materials and Methods: Serotonergic mechanism of nicotine was studied in Lithium induced head twitches model in rats.
3 groups of 10 rats each were taken. Following drug treatments were administered: Control (vehicle) in a dose of 1 ml/kg administered subcutaneously, nicotine given subcutaneously (s.c.) (0.4 mg/kg) and inhalational route (0.2 mg/kg).
Results: In this model, nicotine has shown serotonin induced behavioural changes producing 'head twitches' in rats using lithium.

1) In vehicle treated group, rats showed less number of head twitches.
2) In nicotine (s. c.) treated group, rats showed 'lithium induced head twitches 'which started from 10 mins-90 mins. Result was highly significant compared with vehicle treated rats.
3) Inhalational administration of nicotine showed significant induction of head twitches at 10 mins -90 mins compared with vehicle treated rats.
4) When comparison of number of head twitches induced by nicotine (s. c.) with that of nicotine (inhalational) has shown that nicotine (s. c.) produced induction of head twitches for long lasting till 90 mins. While with that of nicotine (inhalational) produced short lasting action till 70 mins.

Conclusion: 1) Serotonin mediated lithium induced head twitches was seen with both nicotine (s.c) and nicotine (inhalational) compared with that of vehicle treated group.
2) Nicotine administered by inhalational route showed short lasting action than nicotine administered subcutaneously.

Keywords: Elucidate mechanism, lithium induced head twitches

Introduction

Hippocrates in 17th and 18th century described symptoms of the disease 'Melancholia' which are the presenting diagnostic symptoms of depression today [1]. Depression is one of the most common psychiatric disorders. It is characterized by feelings of intense sadness, helplessness, worthlessness, and impaired functioning [2, 3] Clinical depression differs from normal grief, sadness, and disappointment. However, dysphoria or demoralization are often associated with depression [4].

Mood and anxiety disorders are the most common mental illnesses in the general population with incidence of about 10%. According to W.H.O. 26% of population will suffer from depression by the year 2020 [4].

Depression is a multifaceted disorder, where neurotransmitters play an important role in depression. Decreased serotonin is said to be one of the major contributory factor in depression [4].

The efficacy of lithium in the treatment of mania and prophylaxis of manic depressive disorder is now accepted. Head twitches can be used to study serotonin (5-HT) neuron activity. Several drugs are used to induce head twitches in rats i.e. 5 hydroxytryptophan (5-HTP) by increasing the free concentration of serotonin at its receptor site and 5 methoxytriptamine by directly mimicking endogenous 5-HT at its receptor sites. Head twitches also occur in rats treated with lithium chloride (LiCl) [5].

Majority of human studies have reported an antidepressant like effect of nicotine. In chronic smokers, smoking cessation leads to exacerbation of depressive symptoms [6].

So smoking maybe used by smokers to attenuate depression. Chronic smoking has been shown to inhibit MAO, thus producing antidepressive effects [3, 7]. Central nicotinic actions of other nicotinic acetylcholine receptor activators are mediated through modulation of neurotransmitter systems [8].
Tobacco smoke contains nicotine which is inculcated in antidepressive effects. It has been reported to have stimulant and depressant action of nicotine. Preclinical and clinical data regarding this issue are ambiguous.
Therefore, present study is to estimate the mechanism of action of nicotine in depression by using lithium induced head twitches model.

Aim & Objectives
The present study was planned:
- To study role of nicotine in depression by using serotonergic mechanism- Lithium induced head twitches.
- To compare mechanism of action of nicotine given subcutaneously and by inhalation.

Materials and Methods
Animals: The experimental procedures and protocol for the study were reviewed and approved by the Institutional Animal Ethics Committee (IAEC). Wistar rats weighing between 150-250gm of either sex were selected for the study. The rats were maintained under standard conditions of temperature (25ºC ± 5ºC) and relative humidity (55 ± 10%) and a 12/12 hr light/dark cycle.

Drugs
Following drugs were used for the study:
1. Nicotine Hydrogen Tartrate- Sigma-Aldrich, Poland
2. Lithium – Thomas Baker, Mumbai, India
3. Serotonin - Sigma-Aldrich, Poland

Serotonergic mechanism of nicotine was studied in *Lithium induced head twitches* model in rats. 3 groups of 10 rats each were taken.
Following drug treatments were administered:
Group 1: Control (vehicle) 1 ml/kg s.c.
Group 2: Nicotine (0.4 mg/kg) s.c.
Group 3: Nicotine (0.2 mg/kg) inhalational.

Instrument used: Perpex Chamber with two compartment and Electric Dhoopdani. Electric Dhoopdani was placed in one compartment and rat was placed in second compartment of perpex chamber. For nicotine administration by inhalation, weighing quantity of nicotine was put into the Electric Dhoopdani. Nicotine was smoked and inhaled by the rat in the other compartment.

To elucidate the mechanism of action: The following model were used to study mechanism of action of the nicotine. Serotonergic activity - Lithium induced head twitches [5].

Serotonergic activity- Lithium induced head twitches [5]
Effect of study treatment on serotonergic activity was studied in "Lithium induced head twitches" model in rat. The study treatment was administered before lithium injection. The number of head twitches induced by injecting lithium chloride (200 mg/kg, i. p) were counted at intervals of 10 min, starting immediately from the time of injecting lithium chloride up to a period of 90 min.

Procedure: Vehicle (s.c.), nicotine (s.c.), nicotine (inhal.) was administered in a dose of 1ml/kg,0.4mg/kg and 0.2mg/kg respectively 30 min before lithium administration. Rats received lithium chloride (200mg/kg) after study treatment. Numbers of head twitches were observed for 1min at every 10min interval upto 90min after lithium chloride injection. Number of head twitches in vehicle treated rats were considered as a baseline and compared with that of study treatment groups.

Observation: The results were expressed in number of head twitches.

Statistical analysis: The statistical significance was determined by one-way analysis of variance (ANOVA) followed by Tukey test, using Primer of Biostatistics' $p<0.05$ was considered to be statistically significant [9].

Role of serotonergic activity in antidepressant action of nicotine: Lithium induced head twitches [5]

Table 1: Number of Head twitches

Time (min)	Vehicle (Mean ± SD)	Nicotine (s.c.) (Mean ± SD)	Nicotine (inhalational) (Mean ± SD)
10	1±0.82	6.2±1.55 *	8.1±1.20 *
20	4.2 ±1.62	10.2±1.62 *	12.7±1.49 *
30	5.3±1.64	12±1.89*	15.1±2.96*
40	8.4±2.17	18.6±4.58 *	20.3±1.89 *
50	10±2.67	27.4±3.10 *	33.1±2.85 *
60	8.9±2.33	33±3.77 *	28.8±3.65 *
70	7.9±2.18	29.7±4.47 *	23.2±3.91 *
80	6.9±1.75	24±5.81 *	14.6±1.78*
90	4.9±1.75	12.1±4.86*	10.1±2.96#

* = Comparison with vehicle group ($p<0.001$)
# = Comparison with vehicle group ($p<0.01$)

Results were expressed as number of head twitches per min at every 10 min interval till 90 min. (Table)
In the vehicle treated group, lithium induced head twitches up to 90 min. However, both groups receiving nicotine by subcutaneous route as well as by inhalational route, number of head twitches were significantly more from '10'min to '90'min. This increase in head twitches was highly significant as compared to vehicle treated group.
The results are depicted in fig.1

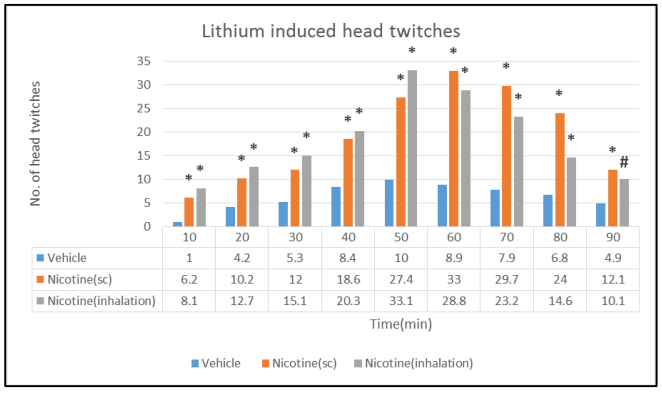

Fig 1: Role of serotonergic activity in antidepressant action of nicotine

Discussion: The behavioral model used in our studies to evaluate serotonergic activity of nicotine was lithium induced head twitches. Lithium produces head twitches by increasing

the synaptic concentration of serotonin [5]. Head twitches can be used to study serotonin (5-HT) neuron activity. Several drugs are used to induce head twitches in rats i.e. 5 hydroxytryptophan (5-HTP) by increasing the free concentration of serotonin at its receptor site and 5 methoxytriptamine by directly mimicking endogenous 5-HT at its receptor sites [5].

In the present study, it was found that head twitches were seen in rats treated with lithium chloride. Nicotine administered by both the routes potentiated head twitches in rats. This indicates increase in synaptic serotonin levels with both nicotine (s.c.) and inhalational route.

Limitation: Not estimate timely concentration of serotonin (5-HT) in blood as well as in CSF during experimental procedure.

Conclusion

1) Serotonin mediated lithium induced head twitches was seen with both nicotine (s. c.) and nicotine (inhalational) compared with that of vehicle treated group.
2) Nicotine administered by inhalational route showed short lasting action than nicotine administered subcutaneously.

References

1. Manuel Garcìa Barroso. Depression: Clinical Definition and Case Histories. The International Journal of Transpersonal Studies. 2003; 22:89-99.
2. Baldessarini RJ. Drug therapy of depression and anxiety disorders. In Brunton LL, Lazo JS, Parker KL, editors. Goodman & Gilman's the pharmacological basis of therapeutics. 11th ed. New York: McGraw-Hill, Medical Publishing Division, 2006, 429-459.
3. Victor I. Reus. Mental Disorders. In. Psychiatric disorders: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 17th ed.: McGraw-Hill, Medical Publishing Division, 2008, 2710-2723.
4. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-IV, 4th ed., text revision. APA Press, Washington, D.C, 2000.
5. Wielosz M, Klenrok Z. Lithium induced head twitches. J. Pharm. Pharmacol. 1979; 31:410-411.
6. Eric JN, Michel B, Ralph JD, Amelia JE, Stephen JG, Lisa MM. Neurobiology of Depression. Neuron. March 2002; 34:13-25.
7. Shirayama Y, Chaki S. Neurochemistry of the nucleus accumbens and its relevance to depression and antidepressant action in rodents. Current Neuropharmacology. 2006; 4:277-291.
8. Richards D. Prevalence and clinical course of depression: A Review, Clinical Psychology Review, 2011. doi: 10.1016/j.cpr.2011.07.004
9. Rao KV. Biostatistics- A manual of statistical methods for use in health, nutrition and anthropology. Jaypee Brothers, 2nd Ed. 2007, 226-260.