Original Article

A comparative study of pheniramine and lorazepam for physiological and cognitive/psychomotor task impairment

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Abstract

Context: Pheniramine is being used harmfully in combination with opiates and benzodiazepines through injecting route. **Aims:** The present study is an attempt to compare the physiological and psychomotor/cognitive task performance on pheniramine and lorazepam. **Settings and Design:** The study used a double blind randomly allotted cross-over design. **Materials and Methods:** The doses of the drugs used were placebo (normal saline) - 2 ml, Pheniramine maleate - 45.5 mg, Lorazepam - 2 mg. The assessments were made at base line and then at 15 min., 120 min and 240 min. The subjects were assessed for the socio-demographic profile, drug use history, physiological parameters (pulse rate, BP, respiratory rate), and psychomotor/cognitive tasks. **Statistical Analysis used**: Analysis was carried out using SPSS ver 10.0. In between, drug comparisons were done using one-way ANOVA (multiple comparisons). **Results:** Physiological and cognitive/psychomotor tasks performance did not show any significant difference between pheniramine, lorazepam and placebo. **Conclusions:** The findings suggest the pheniramine and lorazepam have comparable impairment on physiological and cognitive/psychomotor task performance.

Key words: Lorazepam, pheniramine, psychomotor functions

INTRODUCTION

Anti-histaminics, because of well-established central nervous system effects, are associated with potential abuse liability. Moreover, most of the anti-histaminics are available freely, either individually or as a component of the over-the-counter (OTC) preparations in India. Overdose related poisoning has been reported for certain anti-histaminics like diphenhydramine.[1] There is marked variability in the result of abuse liability studies of various anti-histaminic compounds. Moreover, different studies carried out on the same anti-histaminic compound have come up with variable results.[2]

Pheniramine abuse has been reported from India[3] and is used in combination with buprenorphine by the injecting drug users.[4-6] Buckley *et al.*, compared toxicity and use of pheniramine with other antihistamines.[7] There have been reports citing possible higher abuse liability of pheniramine as compared to other anti-histaminics. However, no abuse liability study was available for pheniramine till recently. We have published first such study[8] in which pheniramine was found to be comparable to lorazepam in with regards to its abuse liability potential.

Abuse liability study paradigm recommends use of a negative control (placebo) and a positive control (drug with known abuse liability).[8] We have used normal saline (as negative control) and lorazepam (as positive control) in this

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study. We present the findings from the physiological and cognitive performance tests used in our experimental study. It was interesting to find no significant differences between pheniramine and lorazepam on most of these parameters.

MATERIALS AND METHODS

The study was carried out at the National Drug Dependence Treatment Centre, AIIMS, an apex institute on drug-dependence treatment in an inpatient setting. The study included 22 male subjects meeting the inclusion criteria and was approved by the institute's ethical committee. The subjects were included following an informed consent for participation in the study. The subjects having any contraindication to the use of lorazepam or pheniramine and those suffering from serious medical illness or psychiatric illness were not included in the study.

All the study subjects administered the three study drugs (i.e. pheniramine, lorazepam and normal saline) in a double blind random order. An adequate wash out period of five drug half lives was given in between any two administrations. We used 45.5 mg pheniramine, 2 mg lorazepam and 2 ml normal saline which were administered intravenously.

The study subjects were clinically observed for vital clinical parameters, adverse effects of lorazepam and pheniramine and any other untoward clinical events.

We collected information on pulse rate, blood pressure and respiratory rate. Psychomotor/cognitive performance measures used in the study were as follows:

Digit symbol test

This is a subtest of Weschler Adult Intelligence Scale (Revised). In this test, the subject is required to draw the geometric pattern associated with the nine digits present on the chart after allowing him to see the chart for a specified time period (scores are the number of correct patterns drawn and number of patterns attempted). Scores are reported as percentage of the pre-drug scores (number correct and number attempted).

Balance task

This task measures the subject's ability to stand upright on one foot with his eyes closed and arms extended to the sides at shoulder height. The scores for this task is the sum of the time the subject was able to remain erect without touching the raised foot to the floor when tested for 30 sec on each foot; maximum possible score being 60 sec. Scores are reported as percentage of pre-drug scores.

Reaction time

The task used to assess the reaction time requires the subjects to press the telegraphic keys in response to a flash of light. The results include number of correct responses and the mean reaction time in milliseconds.

Picture recall/recognition

This is a subtest of PGI memory scale. The task involves memorization of 10 pictures from a set of 20 pictures of easily recognizable objects. Maximum possible score for each recall/recognition test is 10.

These assessments were made at baseline (before administration of drugs) and then at 15, 120 and 240 min. The complete battery of the tests was applied at all the assessments.

The descriptive analysis was carried out for all the variables recorded in the study. To compare the three drugs one-way analysis of variance (ANOVA) multiple comparisons were used for the observations at baseline, 15, 120 and 240 min. SPSS version 10.0 was used to carry out the analysis. Level of statistical significance was kept at $P < 0.05$.

RESULTS

The average age of the study subjects in the study was 32.26 ± 4.48 years.

Physiological parameters

Pulse rate

The pulse rate of the three groups (pheniramine, lorazepam, placebo) was compared separately for the base line, 15 min, 120 min and 240 min using the one-way ANOVA multiple comparisons [Table 1].

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 0.53 (lesser in pheniramine group) in the pulse rate at base line which was statistically insignificant ($P = 1.00$). This difference was 1.07 (more in pheniramine) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 0.27 (more in placebo group) which was statistically insignificant ($P = 1.00$) and the difference at 240 min was 0.80 (more in placebo group) which was statistically insignificant ($P = 1.00$).

Lorazepam vs. placebo

As compared to the placebo there was no difference in the pulse rate at base line ($P = 1.00$). This difference was 3.20 (more in lorazepam group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 1.20 (more in lorazepam group) which was statistically insignificant (1.00) and the difference at 240 min was 0.93 (more in lorazepam group) which was statistically insignificant ($P = 1.00$).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 0.53 (lesser in pheniramine group) in the pulse rate at base line which was statistically insignificant ($P = 1.00$). This difference was 2.13 (more in lorazepam group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 1.47 (more in lorazepam group) which was statistically insignificant (1.00) and the difference at 240 min was 0.53 (more in pheniramine group) which was statistically insignificant ($P = 1.00$).

Respiratory rate

The respiratory rate of the three groups (pheniramine, lorazepam, placebo) were compared for in between group comparisons separately for the base line, 15 min, 120 min and 240 min using the one-way ANOVA multiple comparisons [Table 2].

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 0.20 (lesser in pheniramine group) in the respiratory rate at base line which was statistically insignificant ($P = 1.00$). This difference was 0.20 (more in pheniramine group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min there was no difference in the two groups (1.00) and the difference at 240 min was 0.27 (more in pheniramine group) which was statistically insignificant ($P = 1.00$).

Lorazepam vs. placebo

As compared to the placebo there was a difference of 0.33 in the respiratory rate (more in lorazepam group) at base line which was statistically insignificant ($P = 0.95$). This difference was 0.67 (more in lorazepam group) at 15 min which was statistically insignificant ($P = 0.21$), at 120 min the difference was 0.47 (more in lorazepam group) which was statistically insignificant (0.61) and the difference at 240 min was 0.33 (more in lorazepam group) which was statistically insignificant ($P = 1.00$).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 0.13 (lesser in pheniramine group) in the pulse rate at base line which was statistically insignificant ($P = 1.00$). This difference was 0.46 (more in lorazepam group) at 15 min which was statistically insignificant ($P = 0.60$), at 120 min the difference was 0.47 (more in lorazepam group) which was statistically insignificant (0.61) and the difference at 240 min was 0.07 (more in pheniramine group) which was statistically insignificant ($P = 1.00$).

Blood pressure

The blood pressure of the three groups (pheniramine, lorazepam, placebo) were compared for in between group comparisons separately for the base line, 15 min, 120 min and 240 min using the one-way ANOVA multiple comparisons [Tables 3 and 4].

Systolic blood pressure

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 0.27 (higher in pheniramine group) in the systolic blood pressure at base line which was statistically insignificant ($P = 1.00$). This difference was 1.33 (more in pheniramine group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min there was no difference in the two groups ($P = 1.00$) and the difference at 240 min was 0.27 (more in placebo group) which was statistically insignificant ($P = 1.00$).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 0.67 (higher in placebo group) in the systolic blood pressure at base line which was statistically insignificant ($P = 1.00$). This difference was 0.67 (more in placebo group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 1.07 (more in placebo group) which was statistically insignificant (1.00) and the difference

Table 1: In between group comparisons of the three drugs: Pulse rate

	Drug (i)	Drug (j)	Mean difference (i-j)	Std. error	Sig.	95% confidence interval	
						Lower bound	Upper bound
Base line	Placebo	Pheniramine	0.53333	3.14826	1.000	-7.3174	8.3840
	Placebo	Lorazepam	0.00000	3.14826	1.000	-7.8507	7.8507
	Pheniramine	Lorazepam	–0.53333	3.14826	1.000	-8.3840	7.3174
15 min.	Placebo	Pheniramine	–1.06667	3.45591	1.000	-9.6845	7.5512
	Placebo	Lorazepam	–3.20000	3.45591	1.000	-11.8179	5.4179
	Pheniramine	Lorazepam	–2.13333	3.45591	1.000	-10.7512	6.4845
120 min.	Placebo	Pheniramine	0.26667	3.36178	1.000	-8.1165	8.6498
	Placebo	Lorazepam	–1.20000	3.36178	1.000	-9.5832	7.1832
	Pheniramine	Lorazepam	–1.46667	3.36178	1.000	-9.8498	6.9165
240 min.	Placebo	Pheniramine	0.80000	3.17797	1.000	-7.1248	8.7248
	Placebo	Lorazepam	–0.93333	3.17797	1.000	-8.8581	6.9915
	Pheniramine	Lorazepam	0.53333	3.14826	1.000	-7.3174	8.3840

Table 2: In between group comparisons of the three drugs: Respiratory rate

	Drug (i)	Drug (j)	Mean difference (i-j)	Std. error	Sig.	95% confidence interval	
						Lower bound	Upper bound
Base line	Placebo	Pheniramine	–0.20000	0.32982	1.000	–1.0225	0.6225
	Placebo	Lorazepam	–0.33333	0.32982	0.954	–1.1558	0.4891
	Pheniramine	Lorazepam	–0.13333	0.32982	1.000	–0.9558	0.6891
15 min.	Placebo	Pheniramine	–0.20000	0.35989	1.000	–1.0975	0.6975
	Placebo	Lorazepam	–0.66667	0.35989	0.213	–1.5641	0.2308
	Pheniramine	Lorazepam	–0.46667	0.35989	0.605	–1.3641	0.4308
120 min.	Placebo	Pheniramine	0.00000	0.36107	1.000	–0.9004	0.9004
	Placebo	Lorazepam	–0.46667	0.36107	0.610	–1.3671	0.4337
	Pheniramine	Lorazepam	–0.46667	0.36107	0.610	–1.3671	0.4337
240 min.	Placebo	Pheniramine	–0.26667	0.37317	1.000	–1.1972	0.6639
	Placebo	Lorazepam	–0.33333	0.37317	1.000	–1.2639	0.5972
	Pheniramine	Lorazepam	–0.06667	0.37317	1.000	–0.9972	0.8639

Table 3: In between group comparisons of the three drugs: Systolic blood pressure

	Drug (i)	Drug (j)	Mean difference (i-j)	Std. error	Sig.	95% confidence interval	
						Lower bound	Upper bound
Base line	Placebo	Pheniramine	–0.26667	2.16485	1.000	–5.6651	5.1317
	Placebo	Lorazepam	0.66667	2.16485	1.000	–4.7317	6.0651
	Pheniramine	Lorazepam	0.93333	2.16485	1.000	–4.4651	6.3317
15 min.	Placebo	Pheniramine	–1.33333	2.34035	1.000	–7.1694	4.5027
	Placebo	Lorazepam	0.66667	2.34035	1.000	–5.1694	6.5027
	Pheniramine	Lorazepam	2.00000	2.34035	1.000	–3.8361	7.8361
120 min.	Placebo	Pheniramine	0.00000	2.34252	1.000	–5.8415	5.8415
	Placebo	Lorazepam	1.06667	2.34252	1.000	–4.7748	6.9081
	Pheniramine	Lorazepam	1.06667	2.34252	1.000	–4.7748	6.9081
240 min.	Placebo	Pheniramine	0.26667	2.20360	1.000	–5.2284	5.7617
	Placebo	Lorazepam	1.46667	2.20360	1.000	–4.0284	6.9617
	Pheniramine	Lorazepam	1.20000	2.20360	1.000	–4.2951	6.6951

Table 4: In between group comparisons of the three drugs: Diastolic blood pressure

	Drug (i)	Drug (j)	Mean difference (i-j)	Std. error	Sig.	95% confidence interval	
						Lower bound	Upper bound
Base line	Placebo	Pheniramine	–0.80000	1.24467	1.000	–3.9038	2.3038
	Placebo	Lorazepam	0.40000	1.24467	1.000	–2.7038	3.5038
	Pheniramine	Lorazepam	1.20000	1.24467	1.000	–1.9038	4.3038
15 min.	Placebo	Pheniramine	–0.13333	1.22548	1.000	–3.1893	2.9226
	Placebo	Lorazepam	0.53333	1.22548	1.000	–2.5226	3.5893
	Pheniramine	Lorazepam	0.66667	1.22548	1.000	–2.3893	3.7226
120 min.	Placebo	Pheniramine	–0.40000	1.09332	1.000	–3.1264	2.3264
	Placebo	Lorazepam	0.26667	1.09332	1.000	–2.4597	2.9930
	Pheniramine	Lorazepam	0.66667	1.09332	1.000	–2.0597	3.3930
240 min.	Placebo	Pheniramine	–2.00000	1.24535	0.347	–5.1055	1.1055
	Placebo	Lorazepam	0.26667	1.24535	1.000	–2.8388	3.3722
	Pheniramine	Lorazepam	2.26667	1.24535	0.228	–0.8388	5.3722

at 240 min was 1.47 (more in placebo group) which was statistically insignificant ($P = 1.00$).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 0.93 (higher in pheniramine group) in the systolic blood pressure at base line which was statistically insignificant ($P = 1.00$). This difference was 2.00 (more in pheniramine group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 1.07 (more in

pheniramine group) which was statistically insignificant (1.00) and the difference at 240 min was 1.20 (more in pheniramine) which was statistically insignificant ($P = 1.00$).

Diastolic blood pressure

Pheniramine vs. Placebo

As compared to the placebo there was a mean difference of 0.80 (higher in pheniramine group) in the diastolic blood pressure at base line which was statistically insignificant ($P = 1.00$). This difference was 0.13 (more in pheniramine group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 0.40 (more in pheniramine group) which was statistically insignificant (1.00) and the difference at 240 min was 2.00 (more in pheniramine) which was statistically insignificant ($P = 0.35$).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 0.40 (higher in pheniramine group) in the diastolic blood pressure at base line which was statistically insignificant ($P = 1.00$). This difference was 0.53 (more in placebo group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 0.27 (more in pheniramine group) which was statistically insignificant (1.00) and the difference at 240 min was 0.27 (more in pheniramine) which was statistically insignificant ($P = 1.00$).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 1.20 (higher in pheniramine group) in the diastolic blood pressure at base line which was statistically insignificant ($P = 1.00$). This difference was 0.67 (more in pheniramine group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 0.67 (more in pheniramine group) which was statistically insignificant (1.00) and the difference at 240 min was 2.27 (more in pheniramine) which was statistically insignificant ($P = 0.23$).

Psychomotor/Cognitive performance

Reaction time

The reaction time of the three groups (pheniramine, lorazepam, placebo) were compared for in between group comparisons separately for the base line, 15 min, 120 min and 240 min using the one-way ANOVA multiple comparisons [Table 5].

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 0.01 (higher in placebo group) in the reaction time at base line which was statistically insignificant ($P = 1.00$). This difference was 0.01 (more in pheniramine group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was not observed ($P = 1.00$) and the difference at 240 min was 0.01 (more in pheniramine) which was statistically insignificant ($P = 1.00$).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 0.01 (higher in lorazepam group) in the reaction time at base line which was statistically insignificant ($P = 1.00$). This difference was 0.01 (more in lorazepam group) at 15 min which was statistically insignificant ($P = 1.00$), at 120 min the difference was 0.01 (more in lorazepam group) which was statistically insignificant (1.00) and the difference at 240 min was not observed ($P = 1.00$).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 0.01 (higher in lorazepam group) in the reaction time at base line which was statistically insignificant ($P = 1.00$). This difference was not observable at 15 min ($P = 1.00$), at 120 min the difference was 0.01 (more in lorazepam group) which was statistically insignificant (1.00) and the difference at 240 min was 0.01 (more in pheniramine) which was statistically insignificant ($P = 1.00$).

Balance task

The balance task performance of the three groups (pheniramine, lorazepam, placebo) were compared for in between group comparisons separately for the base line, 15 min, 120 min and 240 min using the one-way ANOVA multiple comparisons.

Pheniramine vs. placebo

As compared to the placebo there was a difference of 0.13 sec (more in pheniramine group) in the two groups at the base line which was statistically insignificant ($P = 1.00$). A mean difference of 0.06 sec (higher in placebo group) in the duration of balance task at 15 min statistically insignificant ($P = 1.00$). At 120 min the difference was 0.47 (more in placebo group) which was statistically insignificant (1.00) and the difference at 240 min was 0.33 (more in placebo group) which was statistically insignificant ($P = 1.00$).

Lorazepam vs. placebo

As compared to the placebo there was no difference in the two groups at the base line ($P = 1.00$). A mean difference of 2.20 sec (higher in placebo group) in the duration of balance task at 15 min statistically insignificant ($P = 1.00$). At 120 min the difference was 0.13 (more in lorazepam group) which was statistically insignificant (1.00) and the difference at 240 min was 0.33 (more in lorazepam) which was statistically insignificant ($P = 1.00$).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference

Table 5: In between group comparisons of the three drugs: Cognitive tasks

		Pheniramine vs. placebo			Lorazepam vs. placebo			Pheniramine vs. lorazepam		
		15 min	120 min	240 min	15 min	120 min	240 min	15 min	120 min	240 min
Reaction time		↑ 0.16	↑ 0.33	↓ 0.58	↔	↔ 1.00	↓ 0.33	↔	↔ -	↔ -
Balance task		↓ 0.33	↓ 0.14	↓ 0.25	↓ 0.21	↑ 0.72	↑ 0.16	↑ 0.16	↔ 1.00	↑ 0.82
DSST	Total	↓ 0.18	↓* 0.01	↔ 1.00	↑ 0.46	↓ 0.45	↑ 0.79	↑ 0.77	↓ 0.74	↓ 0.06
	Correct	↓ 0.15	↓ 0.12	↑ 0.81	↓ 0.46	↓ 0.45	↑ 0.79	↓ 0.54	↓ 0.20	↓ 0.50
	%age correct	↓ 0.65	↑ 0.40	↑ 0.63	↑ 0.40	↓ 0.76	↓ 0.08	↓ 0.33	↓ 0.44	↑* 0.04
Picture R/R	Total	↓ 0.33	NA	NA	↑ 0.72	NA	NA	↓ 0.75	NA	NA
	Correct	↓ 0.33	NA	NA	↓ 0.33	NA	NA	↑ 0.67	NA	NA
	%age correct	↓ -	NA	NA	↑ 0.33	NA	NA	↓ 0.33	NA	NA

DSST - Digit symbol substitution test, Picture R/R - Picture recall/recognition test, (↑ increased, ↓ decreased, ↔ no change, *statistically significant values, NA - not assessed)

of 0.13 (higher in pheniramine group) in the duration of balance task at base line which was statistically insignificant (P = 1.00). This difference was 2.13 ses at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 0.60 (more in lorazepam group) which was statistically insignificant (1.00) and the difference at 240 min was 0.67 (more in lorazepam) which was statistically insignificant (P = 1.00).

Digit symbol substitution test

The digit symbol substitution test (DSST) performance of the three groups (pheniramine, lorazepam, placebo) were compared for in between group comparisons separately for the base line, 15 min, 120 min and 240 min using the one-way ANOVA multiple comparisons for the total number of responses, correct responses and percent correct responses.

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 0.53 (higher in placebo group) in the total number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 2.07 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 1.47 (more in placebo group) which was statistically insignificant (1.00) and the difference at 240 min was 0.20 (more in placebogroup) which was statistically insignificant (P = 1.00).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 0.27 (higher in placebo group) in the total number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 1.13 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 0.40 (more in placebo group) which was statistically insignificant (1.00) and the difference at 240 min was 0.6o (more in lorazepam group) which was statistically insignificant (P = 1.00).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 0.27 (higher in lorazepam group) in the total number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 0.93 (higher in lorazepam group) at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 1.07 (more in lorazepam group) which was statistically insignificant (1.00) and the difference at 240 min was 0.40 (more in lorazepam group) which was statistically insignificant (P = 1.00).

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 0.87 (higher in placebo group) in the correct number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 2.33 (higher in placebo group) at 15 min which was statistically insignificant (P = 0.72), at 120 min the difference was 1.40 (more in placebo group) which was statistically insignificant (1.00) and the difference at 240 min was 0.40 (more in pheniramine group) which was statistically insignificant (P = 1.00).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 0.53 (higher in placebo group) in the correct number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 1.13 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 0.80 (more in placebo group) which was statistically insignificant (1.00) and the difference at 240 min was 0.13 (more in lorazepam group) which was statistically insignificant (P = 1.00).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 0.33 (higher in lorazepam group) in the correct number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 1.20 (higher

in lorazepam group) at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 0.60 (more in pheniramine group) which was statistically insignificant (1.00) and the difference at 240 min was 0.27 (more in pheniramine group) which was statistically insignificant (P = 1.00).

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 1.00 (higher in placebo group) in the total number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 1.22 (higher in placebo group) at 15 min which was statistically insignificant (P = 0.72), at 120 min the difference was 0.29 (more in placebo group) which was statistically insignificant (1.00) and the difference at 240 min was 0.40 (more in pheniramine group) which was statistically insignificant (P = 1.00).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 0.73 (higher in placebo group) in the total number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 0.29 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 0.64 (more in placebo group) which was statistically insignificant (1.00) and the difference at 240 min was 0.98 (more in placebo group) which was statistically insignificant (P = 1.00).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a mean difference of 0.27 (higher in lorazepam group) in the percentage correct number of attempts in DSST at base line which was statistically insignificant (P = 1.00). This difference was 0.93 (higher in lorazepam group) at 15 min which was statistically insignificant (P = 1.00), at 120 min the difference was 0.34 (more in pheniramine group) which was statistically insignificant (1.00) and the difference at 240 min was 1.37 (more in pheniramine group) which was statistically insignificant (P = 0.91).

Picture recall/ recognition test

The picture recall/ recognition test performance of the three groups (pheniramine, lorazepam, placebo) were compared for in between group comparisons separately for the base line, 15 min, 120 min and 240 min using the one-way ANOVA multiple comparisons for the total number of responses, correct responses and percent correct responses.

Pheniramine vs. placebo

As compared to the placebo there was no difference the total attempts in picture recall/ recognition test at base line (P = 1.00). This difference was not observed at 15 min (P = 1.00).

Lorazepam vs. placebo

As compared to the lorazepam there was a difference of 0.07 (higher in placebo) in the total attempts in picture recall/ recognition test at base line which was statistically insignificant (P = 1.00). This difference was 0.07 (higher in lorazepam group) at 15 min which was statistically insignificant (P = 1.00).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a difference of 0.07 (higher in pheniramine group) in the total attempts in picture recall/ recognition test at base line which was statistically insignificant (P = 1.00). This difference was 0.07 (higher in lorazepam group) at 15 min which was statistically insignificant (P = 1.00).

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 0.07 (higher in placebo group) in the correct responses in picture recall/ recognition test at base line which was statistically insignificant (P = 1.00). This difference was 0.20 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 0.07 (higher in placebo group) in the correct responses in picture recall/recognition test at base line which was statistically insignificant (P = 1.00). This difference was 0.20 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00).

Pheniramine vs. lorazepam

As compared to the lorazepam there was no difference in the total responses in picture recall/ recognition test at base line (P = 1.00). This difference was not observed at 15 min (P = 1.00).

Pheniramine vs. placebo

As compared to the placebo there was a mean difference of 1.18 (higher in placebo group) in the correct responses in picture recall/ recognition test at base line which was statistically insignificant (P = 1.00). This difference was 2.00 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00).

Lorazepam vs. placebo

As compared to the placebo there was a mean difference of 1.84 (higher in placebo group) in the percentage correct responses in picture recall/ recognition test at base

line which was statistically insignificant (P = 1.00). This difference was 2.00 (higher in placebo group) at 15 min which was statistically insignificant (P = 1.00).

Pheniramine vs. lorazepam

As compared to the lorazepam there was a difference of 0.67 (higher in pheniramine group) at base line in the percentage correct responses in picture recall/ recognition test at base line which was statistically insignificant (P = 1.00). This difference was not observed at 15 min (P = 1.00).

DISCUSSION

The current study aimed at assessment of abuse liability of pheniramine. Abuse of this drug has been reported in combination with buprenorphine through injecting route. We used the recommended standard protocol for the current study.[8]

Normal saline was used as negative control and lorazepam was used as positive control. All the study subjects were administered all three drugs in random sequence in a double blind manner. Also adequate washout period was given in between two administrations.

We assessed physiological parameters as well as cognitive performance following administration of all the three drugs. Studies on drug abuse liability assessment recommend use of such instruments.[8]

The findings of the current study were interesting as no significant differences were observed between pheniramine and placebo for most of the physiological and cognitive performance tasks.

Administration of pheniramine as well as lorazepam was associated with changes in all these parameters at 15, 120 and 240 min. However, in between group comparison failed to find any significant differences on most of the parameters. The only significant differences observed were for percentage of correct responses on DSST at 240 min after administration.

Both anti-histaminics and benzodiazepines have been associated with abuse.[3-5] Moreover, easy availability of these medications makes them a likely candidate of drug of abuse. The comparable findings of pheniramine and lorazepam observed in the current study on different physiological and cognitive performance test highlight the similarity in terms of the effects of these two drugs on human body. It is interesting to find comparable impairment of the different cognitive and motor performance task with pheniramine and lorazepam. Hence, it is imperative to assess those presenting with abuse of either of these drugs for possible signs of impairment on these parameters.

We have used lower doses of both pheniramine and lorazepam in the current study due to safety reasons. It would be interesting to compare these drugs at higher doses as the drug abusers are more likely to use them in higher doses due to emergence of tolerance to the psychological effects of these drugs.

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