

## Effect of black tea consumption on onset of action of benzodiazepines in children: A case–control study

Nihar Ranjan Mishra, Prakash Chandra Panda

From Department of Paediatrics, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Sambalpur, Odisha, India

**Correspondence to:** Nihar Ranjan Mishra, Department of Paediatrics, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Sambalpur, Odisha, India. Phone: +91-09337797072. E-mail: drnihar.mishra@gmail.com

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### ABSTRACT

**Introduction:** Benzodiazepines (lorazepam and diazepam) are the drugs that have calming effects, but caffeine of black tea is a stimulant. Hence, taking black tea along with benzodiazepines might block the calming effects of the latter. In our locality, giving black tea to the children is a regular sociocultural practice by their parents. **Objective:** To know the effect of black tea consumption on onset of action of benzodiazepines in children. **Methods:** An observational analytic matched case–control study was done in our department from January 2015 to June 2015 subjected to interview schedule by simple consecutive sampling, and data were analyzed using SPSS version 24 software after proper consent and ethical committee approval. Inclusion criteria of cases were any child taking black tea routinely between 1 and 15 years of age attending our outpatient department or inpatient department requiring intravenous (IV) benzodiazepines medications, and exclusion criteria were critically ill children, having chronic liver or kidney diseases, and children taking anticonvulsants regularly. Children of identical age groups, not taking black tea at all, requiring IV benzodiazepines were taken as controls. **Results:** An independent t-test showed a significant difference in the onset of action of lorazepam in black tea drinkers (M=5.44 h, standard deviation [SD]=2.43h) and in non-drinkers (M=1.65 h, SD=0.74h);  $t(99.06)=13.94h$ ,  $p=0.016$  and for diazepam in drinkers (M=1.65 h, SD=0.74h) and in non-drinkers (M=0.93 h, SD=0.37h);  $t(98.23)=16.58h$ ,  $p=0.005$ . **Conclusion:** Black tea delays the onset of actions of benzodiazepines. Hence, it is advisable not to give black tea to the children, and further studies on this aspect are warranted.

**Key words:** Benzodiazepines, Black tea, Caffeine

Black tea is used for improving mental alertness as well as learning, memory, and information-processing skills [1]. It is additionally used for treating headache and low blood pressure; preventing heart disease, including “hardening of the arteries” (atherosclerosis) and heart attack [1]; preventing Parkinson’s disease [2]; and reducing the risk of stomach and colon cancer, lung cancer, ovarian cancer, and breast cancer [3]. It is in addition used for type 2 diabetes and as a diuretic to increase urine flow [3]. Drinking black tea throughout the day helps to keep people alert, even after extended periods without sleep [4] and side effects due to the caffeine in black tea [5]. Furthermore, people who drink black tea or other caffeinated beverages all the time, especially in large amounts, can develop psychological dependence and might make the anxiety disorders worse [3,5].

Taking black tea along with benzodiazepines might block the calming effects of benzodiazepines such as alprazolam, clonazepam, diazepam, and lorazepam, which are central nervous system depressants [5,6]. The combination of coffee more specifically caffeine with diazepam can make the diazepam less effective [3] due to its stimulant effect. American College of Neuropsychopharmacology recommended that those, who suffer from anxiety, should reduce or eliminate caffeine from their

diets [7]. In our locality, giving black tea to the children is a social stigma, and we are facing a lot of problems in sedating children those who were taking black tea at their home. Hence, we planned this study to know whether there is any effect of black tea on benzodiazepines or not.

### METHODS

This observational, prospective, matched, case–control study was done in the Department of Paediatrics of a Tertiary Care Hospital of Western Odisha from January 2015 to June 2015. One hundred and twelve cases and controls (1:1) were taken by simple consecutive sampling. The study was undergone after taking proper consent from legal heir and Institutional Ethical Committee approval. Cases and controls were matched in respect to age, sex, and socioeconomic status. Children between 1 and 15 years of age, taking black tea regularly (at least once in a day for a period of 30 days before receiving the drug), were taken as cases. These were children who required benzodiazepines for various procedures such as computerized tomography and magnetic resonance imaging scan, lumbar puncture, and/or intercostal chest tube drainage. Cases those were critically ill, having chronic liver

and/or kidney diseases, and taking anticonvulsants regularly were excluded from the study. Children who were not taking black tea (not even a single time till receiving the drug) were taken as controls.

The benzodiazepine was given as intravenous (IV) lorazepam (0.1 mg/kg) or IV diazepam (200 µg/kg) single loading dose before the procedure. Selection of the drug was based on the availability of the drug in our hospital pharmacy at that time, and drugs were supplied free of cost to all the patients. One arm of each case and control received the same drug. Delay in onset of action (sedation) was defined as onset of action  $\geq 1$  h after giving the drugs (both lorazepam and diazepam). The drug was given by a trained nurse, and a resident recorded the time interval between drug administration and the onset of sedation (ability to tolerate the procedures as described before while maintaining normal cardiopulmonary efforts) in both the cases and controls. All relevant data were recorded in an excel sheet and were analyzed using SPSS version 24 software in terms of independent t-test, odds ratio (OR), and correlation statistics.

## RESULTS

Out of 112 cases, 64 received IV lorazepam and 48 received IV diazepam, and for 112 controls, number was same as that of cases. Sexual predilection of boy (64%) was more than that of girl (36%) in consuming black tea. 2×2 table (Table 1) drawn to calculate OR for IV lorazepam, IV diazepam, and for both to assess the delay in onset of action of benzodiazepines. The risk of developing delayed onset of action in cases in comparison to controls was thirty times more with IV lorazepam while it was four times with IV diazepam and eleven times with benzodiazepine drugs (both lorazepam and diazepam).

On using independent t-test, a significant difference in the onset of action of lorazepam was seen between cases (5.44±2.43 h) and controls (1.65±0.74 h);  $t(99.06)=13.94$  h,  $p=0.016$ . Similarly, a significant difference in the onset of action of diazepam was seen between cases (3.24±1.67 h) and controls (0.93±0.37 h);  $t(98.23)=16.58$  h,  $p=0.005$ . There was a significant difference in the onset of action of benzodiazepines between cases (6.67±2.52 h) and controls (1.98±0.73 h);  $t(96.81)=15.13$  h,

$p=0.001$ . Correlation statistics between age and onset of action of IV benzodiazepines (both lorazepam and diazepam) was positive and strong (0.971 and 0.832, respectively) and statistically significant ( $p=0.002$ , 0.021, respectively) (Fig. 1).

## DISCUSSION

Although few studies have assessed the effect of black tea consumption on the onset of action of benzodiazepines in adult population, we could not find any such study in children. A study published in 1983 examined the human participants in four controlled double-blind trials. Study participants took diazepam or a placebo capsule and then drank decaffeinated coffee, decaffeinated coffee with caffeine added, or decaffeinated coffee with theophylline added. Caffeine in doses of 250 and 500 mg counteracted the effect of the diazepam in a number of areas tested [8].

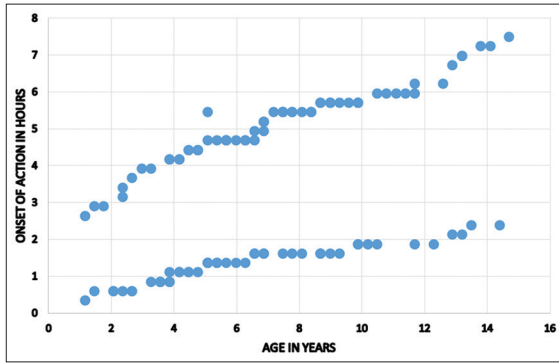
In our study, male children consumed more black tea than the females which may be due to sociocultural habits of male-dominated society of our region. The mean onset of action of lorazepam and diazepam was much higher in cases than the controls, which further supports the findings that the caffeine in the black tea interferes the action of benzodiazepines. This is in collaboration with a previous study done in 2009 [3]. The positive correlation of age with that of onset of action of IV benzodiazepines suggested that as the age advances, the frequency of tea consumption increases, which lead to a more delayed onset of action. This again suggests that the blood levels of the caffeine might be interacting with the benzodiazepines and this was supported by the previous studies [3,9,10].

In our locality, giving black tea to the children is a regular sociocultural practice by their parents and this leads to problems while sedating these children for various procedures. Hence, curtailing the black tea among rural areas of Western Odisha from diets of children should be encouraged. However, as this is a single-center, hospital-based study, therefore, it has its own limitations and results cannot be extrapolated to the general population. Furthermore, we could not measure the drug level before and after the study, which would be more accurate. Hence, a multicenter cohort study with a larger sample size is expected in upcoming future to solve these issues.

**Table 1: 2×2 table showing distribution of cases and controls on basis of onset of action of benzodiazepines (lorazepam, diazepam and both)**

Drug	Black tea consumption	Delay in onset of action			OR with 95% CI
		Yes	No	Total	
Lorazepam	Yes	52	12	64	30.33 (11.48-80.09)
	No	08	56	64	
	Total	60	68	128	
Diazepam	Yes	33	15	48	4.01 (1.71-9.38)
	No	17	31	48	
	Total	50	46	96	
Benzodiazepines	Yes	85	27	112	10.95 (5.88-20.38)
	No	25	87	112	
	Total	110	114	224	

OR: Odds ratio, CI: Confidence interval



**Figure 1: Correlation between onset of action of benzodiazepines with age of the children taking black tea regularly (lower line for diazepam and upper line for lorazepam)**

## CONCLUSION

Our study suggests that taking black tea interferes with the onset of actions of benzodiazepines (both lorazepam and diazepam), and the duration of black tea consumption is directly proportional to the prolongation of onset of action of benzodiazepines.

## REFERENCES

1. Smits P, Corstens FH, Aengevaeren WR, Wackers FJ, Thien T. False-negative dipyridamole-thallium-201 myocardial imaging after caffeine infusion. *J Nucl Med.* 1991;32(8):1538-41.
2. Alemdaroglu NC, Dietz U, Wolfram S, Spahn-Langguth H, Langguth P.

Influence of green and black tea on folic acid pharmacokinetics in healthy volunteers: Potential risk of diminished folic acid bioavailability. *Biopharm Drug Dispos.* 2008;29(6):335-48.

3. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: An updated systematic review. *Drugs.* 2009;69(13):1777-98.
4. Cook DG, Peacock JL, Feyerabend C, Carey IM, Jarvis MJ, Anderson HR, et al. Relation of caffeine intake and blood caffeine concentrations during pregnancy to fetal growth: Prospective population based study. *BMJ.* 1996;313(7069):1358-62.
5. Jeppesen U, Loft S, Poulsen HE, Brsen K. A fluvoxamine-caffeine interaction study. *Pharmacogenetics.* 1996;6(3):213-22.
6. Dlugosz L, Belanger K, Hellenbrand K, Holford TR, Leaderer B, Bracken MB. Maternal caffeine consumption and spontaneous abortion: A prospective cohort study. *Epidemiology.* 1996;7(3):250-5.
7. Rogers PJ, Hohoff C, Heatherley SV, Mullings EL, Maxfield PJ, Evershed RP, et al. Association of the anxiogenic and alerting effects of caffeine with ADORA2A and ADORA1 polymorphisms and habitual level of caffeine consumption. *Neuropsychopharmacology.* 2010;35(9):1973-83.
8. Mattila MJ, Nuotto E. Caffeine and theophylline counteract diazepam effects in man. *Med Biol.* 1983;61(6):337-43.
9. Smits P, Lenders JW, Thien T. Caffeine and theophylline attenuate adenosine-induced vasodilation in humans. *Clin Pharmacol Ther.* 1990;48(4):410-8.
10. McPartland JM, Guy GW, Di Marzo V. Care and feeding of the endocannabinoid system: A systematic review of potential clinical interventions that upregulate the endocannabinoid system. *Plos One.* 2014;9(3):e89566.

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