Original Article

Pain response during fasting and postprandial conditions in healthy young Indian males

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Abstract

Background and Aim: The amount of pain perceived in response to a pain stimulus varies from person to person, and under different conditions in the same person. It can be estimated in terms of cardiovascular reactivity (CVR) and pain sensitivity (PS). The cold pressor task has been successfully used to induce experimental pain in human subjects. Low blood glucose levels have been associated with increased scores of anger and frustration. Therefore, in the present study we have compared the response to experimental pain produced, in subjects in their fasting and fed states.

Methods: Cold pressor task was performed on 86 subjects in the fasting and ½-h postprandial (PP) states. The pain response was measured in terms of changes in pulse and blood pressure as CVR parameter and pain threshold, tolerance, and rating as PS parameters. Data were analyzed by comparing CVR and PS in fasting and ½-h PP condition by Student's *t*-test, Pearson's correlation and multiple regression analysis.

Results: Pain threshold and tolerance increased significantly in the ½-h PP state without significant change in the CVR. Significant positive correlation was obtained between blood glucose level and PS. Multiple regression analysis also showed significant independent contribution of blood glucose to pain threshold and tolerance.

Conclusion: Increase in blood glucose levels in the ½-h PP state increases the pain threshold and tolerance, making it easier for the subjects to bear pain.

Key words: Cold pressor task, experimental pain, fasting, pain threshold, pain tolerance

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INTRODUCTION

The intensity of pain perceived by an individual in response to a painful stimulus depends on the biology of the noxious event, and on physical, psychological, and social factors related to the individual. Experimental pain can be produced in human subjects by cold pressor task (CPT), a simple noninvasive procedure.[1] The amount of pain perceived by an individual can be estimated in terms of cardiovascular reactivity (CVR) (change in heart rate and blood pressure) and pain sensitivity (PS) (pain threshold, pain tolerance, and pain rating).[1,2]

The utility of psychological and behavioral interventions in pain management is closely investigated due to the undesirable side effects associated with prolonged use of most analgesics. Methods of enhancing pain tolerance and decreasing pain rating without the use of drugs involve behavioral techniques, acute elicitation of the relaxation response, and mental distraction.

Low blood glucose levels have been associated with aggression and frustration.[3] Therefore, this study compares CVR and PS in fasting and ½-h postprandial (PP) conditions. Experimental pain was produced by performing CPT, in the fasting and ½-h PP state.

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MATERIALS AND METHODS

Selection of volunteers

The study protocol was approved by the Institute's Ethics Committee. This study was carried out in Teerthanker Mahaveer Medical College, Moradabad, during a period of 6 months. Convenience sample of subjects was selected from student volunteers enrolled at Teerthanker Mahaveer University, Moradabad. Since only 26 females volunteered for the study compared to 150 male volunteers, the study was conducted on male volunteers only.

Subjects of age 18–25 years and body mass index between 18.5 and 24.9 kg/m^2 were selected. Subjects with self-report of acute/chronic illness, history of bone injury in the nondominant hand, or on antipyretic or analgesic medicines were excluded from the study. Subjects with resting pulse >90/min and resting blood pressure >140/90 mm Hg were also not included in the study, to eliminate subjects with preexperiment sympathetic stimulation. After screening the volunteers according to the mentioned inclusion and exclusion criteria, 110 subjects were selected for the study. Written informed consent was obtained from selected volunteers before beginning the study. The participants were asked to report at 8 am, at least 8-h after last meal.

Estimation of plasma glucose

Two milliliter venous blood sample was taken from each subject, 5 min before performing the CPT in fasting and PP condition. Plasma glucose was estimated using estimation kit from Reactivos GPL based on glucose oxidase-peroxidase method.

Subjects with fasting plasma glucose values of 70 mg/dl or less were not included in the study as sympathetic stimulation occurs at this level of blood glucose. This ensured that the increase in heart rate and blood pressure was solely due to experimental pain produced by CPT.

Observations from subjects with fasting plasma glucose higher than 110 mg/dl or with ½-h PP (1/2-h PP) plasma glucose higher than 200 mg/dl were excluded from statistical analysis as such high glucose levels may be due to impaired glucose tolerance.

Cold pressor task

The CPT was performed by the method described by Kumar *et al*.,[2] on each subject in the fasting condition and again, ½-h after ingestion of 75 g glucose in 300 ml water. Heart rate and blood pressure were recorded manually, before and immediately after performing the CPT. Time of immersion, pain threshold (time duration in seconds after which subject first reported feeling pain), pain tolerance (time duration in seconds for which the subject tolerated the pain) was recorded using two separate stop watches and pain rating was obtained on visual analogue scale (amount of pain reported by the subject at the end of CPT on a scale of 0 [no pain] to 10 [maximum pain bearable]) from each subject, immediately after CPT.[1]

On the basis of plasma glucose level and time of immersion during CPT, follwing subjects were excluded from the study.

- Subjects with fasting plasma glucose lower than 70 mg/dl (12 subjects were excluded), or higher than 110 mg/dl (2 subjects were excluded)
- Subjects with ½-h PP glucose higher than 200 mg/dl (5 subjects were excluded)
- Subjects with a total time of immersion <10 s during CPT (5 subjects were excluded).

Statistical analysis of data

Data analysis was carried out on observations obtained from 86 subjects using Microsoft Excel version 2007 (Microsoft Office, United States), and Student's *t*-test was used to compare the data obtained in the fasting and ½-h PP states. The data have been presented as mean ± standard deviation. SPSS version 14 (SPSS Software Inc., Chicago, IL, USA) was used. Pearson's correlation analysis and multiple regression to establish a relationship between blood glucose and PS parameters. $P < 0.05$ was considered as significant.

RESULTS

Basal parameters recorded before conducting the CPT are presented in Table 1. There was a significant increase in pulse in the ½-h PP condition. The mean value of systolic blood pressure (SBP) decreased in the ½-h PP condition, but this decrease was not significant. A slight but significant decrease in resting diastolic blood pressure (DBP) was observed in the ½-h PP condition.

Cardiovascular reactivity on subjection to CPT was recorded in terms of change in pulse (dPulse), SBP (dSBP) and DBP (dDBP). Table 2 depicts the CVR along with the PS (in terms of pain threshold, pain tolerance and pain rating) in the fasting and ½-h PP

Table 1: Basal parameters before performing the cold pressor task

Parameters	Fasting	½-h postprandial	*P*
Plasma glucose (mg/dl)	85.57±12.01	150.80±14.69	<0.001
Pulse (/min)	77.58±7.46	81.63±7.09	<0.001
SBP (mm Hg)	123.47±8.82	121.91±9.11	0.256
DBP (mm Hg)	80.93±5.65	77.63±5.94	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure. The values are expressed in mean±SD. $P > 0.05$ was considered significant.

condition. The CVR decreased significantly in the ½-h PP condition. Pain threshold and pain tolerance increased significantly, and pain rating decreased significantly in the ½-h PP state. The interrelationship between blood glucose and PS parameters during fasting and ½-h PP condition is presented in Table 3. Blood glucose levels and PS parameters (pain threshold and pain tolerance) were positively and significantly correlated during fasting and ½-h PP condition. Pain rating was negatively but not significantly correlated with blood glucose. Result of multiple regression analysis demonstrated significant and independent contribution of blood glucose level to pain threshold and pain tolerance [Table 4].

DISCUSSION

Significant increase in resting pulse rate in ½-h PP condition is in accordance with the histamine-induced PP tachycardia reported in vertebrates.[4] Decrease in blood pressure during PP state was due to the vasodilation produced by histamine. PP hypotension has been reported in normal geriatric population.[5] This study shows that PP decrease in blood pressure also occurs in normal young men. The PP hypotension may also contribute to tachycardia.

Pain sensitivity decreased in the ½-h PP condition as the subjects showed higher threshold and tolerance. Blood glucose was positively and significantly correlated with pain threshold and tolerance. However, since there was no significant correlation between blood glucose and pain rating, increase in blood glucose did not affect the pain rating. Multiple regression analysis [Table 4] showed independent significant contribution of blood glucose on pain threshold and tolerance during fasting and ½-h PP condition. Apparently, subjects tolerated pain for a longer time with no increase in pain rating. Decreased PS during PP state is probably responsible for the decrease CVR in this state. Although the subject tolerated pain for a longer duration, heart rate and blood pressure did not increase in that proportion.

The increased histamine in the PP condition could have an analgesic effect via the H_3 receptor.[6,7] Carbohydrate-rich meal results in increased insulin level in blood, promoting protein synthesis and leading to decreased amino acid level in blood. Consequently, the permeability of blood-brain barrier to tryptophan increases, causing increased synthesis of serotonin.[8] Serotonin inhibits pain transmission in the dorsal horn of the spinal cord by the raphe spinal pathway and increases the pain threshold.[9] Since serotonin is anxiolytic, it may also decrease PS by relieving anxiety in the PP state. Recently, sweet taste-induced analgesia has been demonstrated in humans by functional magnetic resonance imaging.[10] Any or all of these factors may contribute to the decreased PS in the PP state.

Limitation of the study

Due to the lack of sufficient numbers of female subjects, this study was conducted on young male subjects only. However, since the PS is different in males and females,[2] the study needs to be performed on a larger scale including subjects of both sexes.

CONCLUSION

Comparison of pain response in fasting and ½-h PP states depicts decreased PS without any corresponding increase

Table 2: Cardiovascular reactivity and pain sensitivity data in fasting and ½-h postprandial conditions

Parameter	Fasting	Postprandial	*P*
dPulse (/min)	7.67±6.55	3.23±2.26	<0.001
dSBP (mm Hg)	5.72±4.93	3.53±2.62	<0.001
dDBP (mm Hg)	5.53±4.39	4.07±3.57	0.02
Pain threshold (s)	23.97±8.99	28.92±11.11	0.002
Pain tolerance (s)	62.69±26.78	72.97±28.35	0.01
Pain rating (VAS)	6.60±1.47	6.09±1.48	0.02

dPulse: Change in pulse, dSBP: Change in systolic blood pressure, dDBP: Change in diastolic blood pressure, VAS: Visual analogue scale. The values are expressed in mean±SD. *P* > 0.05 was considered significant

Table 3: Correlation between blood glucose and pain sensitivity parameters

Parameters	Fasting		½-h postprandial	
	r	*P*	*r*	*P*
Pain threshold	0.406**	<0.001	0.514**	<0.001
Pain tolerance	0.491**	<0.001	0.578**	<0.001
Pain rating	−0.024	>0.05	−0.020	>0.05

P<0.05 was considered as significant

Table 4: Multiple regression analysis of pain sensitivity parameters (as dependent variables) with blood glucose levels (as independent variable) in fasting and ½-h postprandial condition

Parameters	Fasting				½-h postprandial			
	Standardized regression coefficient beta	95% CI		*P*	Standardized regression coefficient beta	95% CI		*P*
		Lower limit	Upper limit			Lower limit	Upper limit	
Pain threshold	0.406	0.156	0.453	<0.001	0.514	0.248	0.530	<0.001
Pain tolerance	0.491	0.673	1.516	<0.001	0.578	0.787	1.483	<0.001
Pain rating	−0.024	−0.029	0.024	>0.05	−0.020	−0.024	0.020	>0.05

P<0.05 was considered as significant. CI: Confidence interval

in CVR in the PP state, suggesting that it is more difficult to bear pain on an empty stomach with low blood glucose. Persons with high PS may be advised to avoid complete fasts during episodes of chronic or acute pain.

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