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Original Article

Physiology Section

Effect of Age on Response to Experimental Pain in Normal Indian Males

INDU SAXENA[1], MANOJ KUMAR[2],ABHIJEET SINGH BARATH[3], ANJALI VERMA[4], SUMIT GARG[5], MANOJ KUMAR[6]

ABSTRACT

Background and Objectives: Response to experimental pain depends on the nature of the pain stimulus, as well as on gender, racial, cultural and socioeconomic factors. This study investigates the effect of age on pain sensitivity and cardiovascular reactivity produced by experimental pain. We have also compared the values of body mass index (BMI) and resting blood pressure of volunteers with the normal values.

Materials and Methods: The study was conducted on 83 Indian males of different age groups. The volunteers were divided into 4 groups: Children, Young Adults, Middle-Aged Adults and Old Adults; and their basal parameters (BMI, resting pulse and blood pressure) were recorded. Selected volunteers were subjected to cold pressor task (CPT). Pain sensitivity (PS) (pain threshold, tolerance and pain rating on a visual analog scale) and cardiovascular reactivity (CVR) (increase in pulse and blood pressure) were recorded.

Results: Many volunteers had abnormal values of BMI and resting blood pressure and had to be excluded from the study. PS and CVR between different groups were compared by one-way ANOVA. Significant differences in PS were observed, with highest pain sensitivity in Children and lowest in Old Adults. No significant differences were observed in the CVR.

Conclusion: The high numbers of volunteers with abnormal basal parameters (BMI and resting blood pressure) show an urgent need to educate the general public about the dangers and risk factors of obesity and hypertension. Less exposure of children to painful encounters may be responsible for their high pain sensitivity while higher values of resting blood pressure and decreased sensitivity of the sensory systems with advancing age may be responsible for the hypoalgesia observed in old adults.

Keywords: Adults, Children, Elderly, Experimental approaches, Pain measurement

INTRODUCTION

The sensation of pain is a universal phenomenon and is an indication of disease or tissue damage. The intensity with which pain is perceived by an individual varies widely, being influenced by the nature of the noxious stimulus, as well as by genetic [1], racial [2], cultural [3], and socioeconomic [4] factors. Gender differences in pain perception have been observed, with women exhibiting lower pain tolerance than men [5]. Elderly people tend to suffer more from chronic and acute pain episodes that may be due to higher prevalence of degenerative changes in the musculoskeletal system. However, the effect of age on pain sensitivity is unclear, with various studies reporting decrease, increase or no change in pain sensitivity with age [6-9]. One factor responsible for the discrepancies in the results may be the different methods used to induce experimental pain. Woodrow et al., used a pressure tolerance test on the Achilles tendon [6], Harkins et al., have used painful thermal stimuli [7], and Li et al., conducted an observational study on patients requiring 18-gauge intravenous catheter placement as a part of their treatment [8]. Besides these, laser, radiation, electric current and visceral distension have also been used as pain stimuli [9]. Various animal and human pain studies related to aging have been reviewed by Yezierski [10]. In this study, we have investigated the pain response in four different age groups using cold pressor task to induce experimental pain. The cold pressor task (CPT) is a simple, non-invasive technique that has been safely used to produce experimental pain in children and adults [11]. Cardiovascular reactivity (CVR, i.e., increase or decrease in the heart rate and/or blood pressure) and pain sensitivity (PS, i.e., pain threshold, pain tolerance and pain rating) were used to estimate the intensity of pain perceived by an individual [4]. We also took this opportunity to determine the number of persons with abnormal values of body mass index and resting blood pressure, and to establish if such persons were aware of their condition.

MATERIALS AND METHODS

Permission to conduct this study was obtained from the Ethical Committees of AIIMS, Jodhpur and TMMC & RC, Moradabad, India where this work was done. Inclusion of female subjects would have involved recruiting three types of subjects: those that had not attained menarche (Children), menstruating females of reproductive age group (Young Adults and Middle Aged Adults), and those who had attained menopause (Old Adults). Besides, response to experimental pain in menstruating women is known to vary with the phase of the menstrual cycle [12]. Therefore only male individuals aged 6 to 75 years, of North Indian origin were requested to volunteer for this study.

A total of 140 persons agreed to volunteer for this study. The basal parameters (height, weight, resting pulse, and blood pressure) and a personal history of disease and medication were recorded for each individual. The following inclusion and exclusion criteria were observed while recruiting volunteers for the study:

Inclusion Criteria

- Body mass index (BMI) between 18-23 kg/m^2 in case of adults. In case of children, normal range was established for age [13].
- Resting blood pressure < 140/90 mm Hg for adults [14]. In case of children, normal range of blood pressure for age and height was obtained from A Pocket Guide to Blood Pressure Measurement in Children [15]. Hypertensive children were excluded from the study.

Exclusion Criteria

- History of chronic or acute illness at the time of experiment,
- Individuals who had taken antipyretic or analgesic medicine in the past 12 hours
- Smokers, tobacco chewers, and persons consuming alcoholic beverages daily or frequently,
- In our past studies, some persons with a history of bone injury in the hand that was immersed in cold water reported a longer lasting pain, therefore persons with a history of bone injury in the non-dominant hand were excluded from this study.

On the basis of the above criteria, 83 persons were selected for the study, and written informed consent was obtained from each selected subject, or his parent (in case of children below 18 years of age).

The subjects were divided into four groups on the basis of their age: Children (CH): 8-13 years; Young Adults (YA): 18-25 year; Middle-Aged Adults (MAA): 35-45 year; and Old Adults (OA): 55-70 year.

Cold pressor task (CPT) was performed on each individual [12]. The subject was seated comfortably in a quiet room maintained at 22-26°C. After 10min, his resting pulse and blood pressure were measured manually, in the sitting position, using a sphygmomanometer and stethoscope.

The subject was asked to immerse his non-dominant hand in the cold water bath, maintained at 0-1 degree Celsius, up to 2cm above wrist, palm down and fingers spread out. He was asked to report the time when he felt the pain (pain threshold) and to remove his hand from the water whenever he chose not to bear the pain anymore. Pain tolerance was calculated by subtracting pain threshold from the total time of immersion. Pain threshold and total time of immersion were recorded in seconds using two separate stop watches. Heart rate and blood pressure were recorded manually before and immediately after the CPT. The subject was asked to grade the pain experienced during CPT on a visual analog scale (VAS) [12]. The cardiovascular reactivity was obtained in terms of increase in pulse (dPulse) and systolic (dSBP) and diastolic (dDBP) blood pressure, and pain sensitivity was obtained in terms of pain threshold, pain tolerance, and pain rating.

Data from persons with total time of immersion greater than 30 seconds was used for analysis. Therefore, data of 4 children with total time of immersion less than 30s was excluded from analysis [16]. [Table/Fig-1] shows the total number of volunteers of each age group, the number of individuals excluded due to different criteria, and the number of subjects from whom data was finally obtained for analysis (total 79 in number). Pre-hypertensive individuals (both children and adults) were included in this study.

The parameters of cardiovascular reactivity (increase in pulse and blood pressure) and pain sensitivity (pain threshold, pain tolerance, and pain rating on VAS) in different age groups were compared by one-way ANOVA using SPSS version 21. P-Values less than 0.05 were considered significant.

Group	Volun-teers	BMI < NV	BMI > NV	Pulse >100 (/min)	RSBP > NV	RDBP > NV	Immersion Time <30s	Subjects Selected
Children	33	7	3	3	2	2	4	17
Young Adults	32	0	9	1	4	4	0	21
Middle-Aged Adults	35	0	15	0	7	12	0	22
Old Adults	40	0	18	0	18	13	0	19
Total	140	7	45	4	31	31	4	79
%	100	5	32.14	5.7	22.14	22.14	2.9	56.43

[Table/Fig-1]: Total number of volunteers of each age group, number of individuals excluded due to different criteria, and number of subjects finally selected for the study
BMI: Body mass index, RSBP: Resting systolic blood pressure, RDBP: Resting diastolic blood pressure, NV: Normal Value for that age

RESULTS

Pain sensitivity parameters (pain threshold, pain tolerance and pain rating) are summarized as mean ± SD in [Table/Fig-2] and one-way ANOVA has been used to compare the values of each parameter between the groups. Highly significant differences (p-value <0.001) were observed in Pain Threshold and Pain Tolerance, the Bonferroni post-hoc analyses have been presented in the table. No significant differences were obtained in Pain Rating (p-value 0.624).

Cardiovascular reactivity to pain was obtained in terms of increase in pulse and blood pressure. The increase in pulse (dPulse) and systolic (dSBP) and diastolic (dDBP) blood pressure are presented as mean ± SD in [Table/Fig-3]. The mean values obtained for each parameter between the four groups have been compared by one-way ANOVA. No significant differences were obtained (p-values >0.05).

Parameter	Group				p-Value
	Children (CH)	Young Adults (YA)	Middle Aged Adults (MA)	Old Adults (OA)	
Pain Threshold (s)	9.24 ± 3.85*#	17.71 ± 7.34$	15.91± 10.36£	33.11 ± 12.74	<0.001
Pain Tolerance (s)	31.65± 9.45 #	50.90 ± 41.71$	38.23± 16.55£	139.95 ± 118.10	<0.001
Pain Rating (VAS)	6.82 ± 1.47	6.71 ± 1.76	7.23 ± 1.51	7.16 ± 1.01	0.624

[Table/Fig-2]: Comparison of Pain Threshold, Pain Tolerance and Pain Rating between the four groups of subjects by one-way ANOVA
Significance between:
*: CH and YA: 0.04,
#: CH and OA, $: YA and OA and £: MA and OA: <0.001

Parameter	Group				p-Value
	Children	Young Adults	Middle Aged Adults	Old Adults	
dPulse (/min)	7.53 ± 6.15	3.71 ± 6.43	5.27 ± 4.84	4.95 ±1.93	0.163
dSBP(mmHg)	5.29 ± 5.96	4.86 ± 7.31	5.64 ± 1.71	7.26 ±3.90	0.491
dDBP(mmHg)	5.65 ± 5.11	4.29 ± 4.39	5.18 ± 2.36	2.74 ±1.91	0.08

[Table/Fig-3]: Comparison of cardiovascular reactivity parameters between the four groups of subjects by one-way ANOVA

DISCUSSION

[Table/Fig-1] shows the percentage of persons in different age groups having abnormal values of BMI and resting blood pressure. In case of children, BMI values normal for age were selected according to the criteria given by Khadilkar et al., [13]. In case of adults, BMI ranging form 18 to 23 kg/m^2 was considered normal. Values of BMI lower than normal were observed in 7 children and in none of the adults. Values of BMI higher than the normal value for age were observed in all four age groups. Many such persons were unaware of their overweight or obese status.

In case of adults, systolic blood pressure higher than 120 mmHg was considered pre-hypertensive, higher than 140 mmHg was considered hypertensive. Diastolic blood pressure values above 80 mmHg were considered pre-hypertensive while those above 90 mm Hg were considered hypertensive [14]. Measurement and analysis of blood pressure in children was done according to A Pocket Guide to Blood Pressure Measurement in Children [15]. Majority of the pre-hypertensive/hypertensive volunteers (both young and old) were unaware of their condition. Most of the children and some of the adults were having their blood pressure measured for the first time. It is possible that white coat hypertension was present in at least some of these individuals. Guardians of hypertensive children and the hypertensive adults were informed and advised to consult a physician. Surprisingly, the incidence of high blood pressure was more in children of low socioeconomic status than in those belonging to affluent families.

Of the 18 pre-hypertensive/hypertensive children, only one had BMI higher than normal for age and height, suggesting that the high blood pressure observed in the selected group of children was not linked to obesity. In all other age groups, obesity with high blood pressure was more common (YA: 7; MAA: 8; OA: 15).

Obesity is the sixth most important risk factor contributing to the overall burden of diseases throughout the world [16,17]. Various population studies suggest that at least two-third cases of hypertension are due to obesity [16-19]. The problems due to undiagnosed obesity and hypertension need to be tackled immediately [20]. Fifty per cent of the patients are unaware of their obese status in the United States, and the number is probably even more in India [21,22]. Health risks associated with obesity include type 2 diabetes mellitus, gall bladder diseases, dyslipidemia, metabolic syndrome, breathlessness, hypertension, coronary artery disease, sleep apnea, stroke, and congestive heart failure [18,20,21]. Obesity has also been linked with glomerulopathy [23] and weight loss by morbidly obese individuals was found to be associated with significant reduction of urinary protein excretion [24].

Health measures taken by the government have been successful in decreasing mortality due to communicable diseases; however, rapidly changing lifestyles have resulted in increasing the mortality due to non-communicable diseases [25]. Health policy makers of the country need to provide sufficient resources for the control and prevention of the existing communicable diseases, as well as for the increasing incidence of non-communicable diseases. Since the programs for the prevention and control of communicable diseases drain the meagre resources, India faces a serious handicap in planning and initiating programs to combat non-communicable diseases. Surveillance of cardiovascular diseases involves a lot of human and financial resources for its sustainability. Surveillance targeted at special settings (schools, workplaces, hospitals) can be carried out by the medical students in the form of small projects (e.g., the Short Term Studentship program established by the Indian Council of Medical Research to develop research skills in the dental and medical students). Such programs can also include educating the general public about risk factors of CVD and other non-communicable diseases.

Comparison of the pain sensitivity parameters [Table/Fig-2] showed highly significant differences in Pain Threshold and Pain Tolerance between the four groups of subjects. Lowest mean values of Pain Threshold and Pain Tolerance were observed in Children. It is possible that due to their young age, children have less experience of painful encounters and are therefore more pain sensitive. Old Adults had the highest mean values of Pain Threshold and Pain Tolerance. Diminished pain sensitivity has been demonstrated in hypertensive animals and humans [26]. Bruehl et al., have shown that reduced pain sensitivity precedes the development of frank hypertension [27]. Duschek et al., have reported increased pain sensitivity in persons with low blood pressure [28]. McCubbin et al., suggest exaggerated opioid analgesia in persons at high risk of hypertension [29]. Altered blood pressure control mechanisms in the early stages of hypertension may be linked to altered neuropeptide regulation of pain. The mean Pain Threshold was higher in Young Adults group compared with the Children, and the mean Pain Tolerance was higher compared to both Children and Middle-aged Adults [Table/Fig-2]. Questioning the subjects about their daily physical activity revealed that subjects of the YA group were physically more active than the subjects of CH and MAA groups. Lower pain sensitivity (higher Pain Threshold and Pain Tolerance) has been demonstrated in athletes compared to non-athletes [30,31], therefore, therefore greater level of physical activity may be partly responsible for the decreased pain sensitivity in this group. Sensitivity in sensory systems is known to decrease with increase in age. A decrease in the number of peripheral receptors along with the deterioration of the supporting tissues [10] may also be responsible for the decreased pain sensitivity observed in old age.

There was no significant difference in the Pain Rating between the groups, indicating that subjects of all four groups preferred to tolerate a maximum pain of almost equal perceived intensity. Also, the range of Pain Rating was wide in each group, so that differences were not generated.

No significant differences were observed in the parameters of cardiovascular reactivity [Table/Fig-3]. In spite of the longer duration of pain tolerated by the OA group, the CVR of this group was similar to that of the other groups. Since there was no significant difference in the Pain Rating, it is possible that similar perception of pain intensity produced similar CVR in the different age groups.

Since the number of subjects in each age group was relatively small (17-22 subjects), and each age group included subjects belonging to different socioeconomic backgrounds, a larger study with a socioeconomically more homogenous group of subjects is required.

CONCLUSION

A part of this study may be considered as a pilot study for the survey of undiagnosed obesity and hypertension in Indian males of different age groups. There appears an urgent need to screen the general population for these parameters and to educate them about the risk factors of CVD. People must be encouraged to adopt healthier life styles.

Children were most sensitive to pain, while the old adults were the least sensitive.

There was no significant difference in the cardiovascular reactivity parameters between the groups, indicating that similar pain ratings (PR) produced similar effect on CVR. This suggests that the CVR is an indication of the pain rating.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Deparment of Biochemistry, AIIMS Jodhpur, Rajasthan, India.
2. Professor, Department of Physiology, TMMC & RC, Moradabad, Uttar Predesh, India.
3. Student, AIIMS Jodhpur, Rajasthan, India.
4. Demonstrator, Department of Physiology, TMMC & RC, Moradabad, Uttar Predesh, India.
5. Assistant Professor, Department of Physiology, SIMS, Hapur, Uttar Predesh, India.
6. Social Worker, Department of Community Medicine, TMMC & RC Moradabad, Uttar Predesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Manoj Kumar,
Professor, Department of Physiology, Teerthanker Mahaveer Medical College & Research Center,
Nh-24, Paskbara, Moradabad, Up- 244001, India.
E-mail : premmanoj2001@yahoo.co.in

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