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Research Article

AGEING COLD PRESSOR RESPONSE

***Deepinder Kaur Gandhi[1], Kawalinder Kaur**[2], **Jaswinder Singh**[3], **Anupama Mahajan**[4] and **Seema**[5]
[1,2]*Physiology Department, Sri Guru Ram Das Institute of Medical Sciences and Research (SGRD IMSAR), Amritsar*
[3]*Anaesthesia Department, Government Medical College, Amritsar*
[4,5]*Anatomy Department, (SGRD IMSAR), Amritsar*
**Author for Correspondence*

ABSTRACT
There is much clinical evidence to suggest that the sympathetic activity varies with ageing. The present study examined the relation between blood pressure reactivity to cold stimulus in different age groups. The study involved 100 healthy subjects who were divided into four different age groups (Group A, 15-30 years, Group B 31-45 years, Group C 46-60 years, and Group D above 60 years). The autonomic insufficiency was ruled out in all. Cold pressure response (CPR) was measured with the changes in blood pressure in response to a painful stimulus generated by placing the hand in cold water. During comparison the values for the systolic blood pressure (S.B.P) and Diastolic blood pressure (DBP) in this test showed progressive increase from younger to older age group (Group A to Group D) suggesting significant increase in sympathetic activity in elderly.

Key Words: *Cold Pressure Response, Ageing, Sympathetic Activity*

INTRODUCTION
Automatic responses to stress prepare the body for fight or flight. Corticotropin-releasing factor (CRF) in the central nervous system activates autonomic and adrenocortical responses to stressors. The general response to day-to-day stressors like exercise, pain and cold lead to activation of the sympathetic nervous system with inhibition of the parasympathetic nervous system. When stress becomes severe then adreno medullary release of epinephrine ensues. As stress increases even further, then CRF not only activates the sympathetic nervous system but leads to the release of adreno corticotropic hormones.
Psychological stress not only tends to increase epinephrine, it also tends, to increase sympathetic nerve activity to the heart leading to increased cardiac output. As we age, norepinephrine release in response to the cold pressor test increases. Less epinephrine is released from the adrenal medulla in the elderly, however epinephrine blood levels are similar because of diminished clearance of epinephrine from the circulation with advanced age.

The cold presser response is an indicator of sympathetic activity after cold stress. The cold pressor test (CPT) triggers in healthy subjects a vascular sympathetic activation and increase in blood pressure. This autonomic function test varies with the process of ageing. Ageing which is a natural process of merely growing older in a temporal sense is a general physiological process. Healthy ageing is associated with various changes in the automatic functioning (Sympathetic and parasympathetic activity) in the body. Studies of sympathetic nervous system activity in healthy human subjects demonstrated an age-related increase in resting plasma, nor epinephrine levels which is caused by an increase in nor epinephrine spillover at sympathetic nerve endings and by a decrease of its clearance (Frank *et al*., 2000, Durand S et al 2004). Another factor that contribute to the affect of age on cold stress is pressor responses to core body temperature-reducing levels of cold stress in older than in younger adults by showing that pressor responses to a much less severe level of cold stress induces marked and consistently higher systolic and mean blood pressure responses in older than in younger adults (Hess *et al.,* 2009). Also with the ageing the process of atherosclerosis may attenuate the production of endothelial derived releasing factors i.e., Nitric Oxide (No) and vessels are likely to exhibit greater constrictor response even to the same levels of vasoconstrictors as in young.

Ageing brings a decline in the sensory modalities including pain and touch, two sensory modalities involving A and C fibres (Wickre maratch MM *et al.,* 2006). The observed decline in function of the sensory system is observed above 65 years of age, there is evidence that pain-related functions start to decline around middle age. (Lariviere *et al.,* 2007). The result showed a decline of function of the endogenous pain inhibitory system in middle age adults and above 65 years old. Work done over the past few years gives us an indication of affect of ageing on the cold pressor response so a formal study was planned to be carried out on healthy subjects of different age groups to study the effect of ageing on cold pressor response.

MATERIALS AND METHODS

The present study was conducted on 100 healthy subjects taken from Amritsar district. The subjects were categorised into 4 different groups. (Groups A, Group B, Group C and Group D). Each consisting of 25 subjects.

Group	Age in years
A	15-30
B	31-45
C	46-60
D	Above 60

All the subjects were tested under similar laboratory conditions. Subjects were allowed to acclimatize themselves to the experimental and environmental conditions. During that period detailed history and medical examination was carried out. The nature of test was explained to the subjects before hand. For sympathetic activity the cold pressor response (CPR) was noted by a test.

Test

The cold pressor response which consists to placing the hand in cold water as painful stimulus, is used to study the autonomic response of different individuals (Lebalance et al, 1975). The afferent fibres for-this response are the pain fibres "(which are stimulated by placing the hand in cold water) and the efferent fibres are sympathetic fibres.

Procedure

The test was done as one per method of Le balance et al, 1975). The nature of test was explained to the subjects and were reassured that the tests would not do any harm.

Resting Blood pressure was recorded with the subject sitting comfortably. Subject was then asked to immerse his hand in cold water and the temperature was maintained at 1-4 degree centigrade throughout the procedure. Blood pressure measurements were made from the other arm at 30 seconds interval for a period of 2 minutes. After two minutes, the subject was allowed to remove his hand. Maximum increase in the systolic and diastolic pressure were determined and results recorded. An increase in the systolic blood pressure of greater than or equal to 15 mmHg will be considered normal. In any condition where there is deficient sympathetic outflow the cold pressor test will be expected to show a smaller rise.

RESULTS AND DISCUSSION

The data obtained revealed that the SBP and DBP changes in the cold pressor test showed progressive increase from Group A to Group D.. Between Group A and Group B SBP and DBP changes in cold pressor response were statistically highly significant ($P<0.001$). Between group B and C SBP and DBP changes in cold pressor response were statistically highly significant SBP ($p<0.001$) and DBP ($p<0.01$). Between group C and D the SBP changes in the cold pressor response were statistically highly significant ($p<0.001$) while the DBP changes are not significant ($P>0.05$). This showed that sympathetic activity increases with age.

Our results of increase sympathetic activity with age are comparable with the studies carried out by Blandini F etal (1992) Ng et al (1993), Jensen Urstad et al (1997), Jaquet et al (1998), Mat sukawa et

al (1998) Mehta Ahiya V. (1999), Selvamurthy et al (1999),tte C et al (2005), Hess KL et al (2009), Mourot L et al (2009) Srivastava RD et al (2010), Laflamme YT and Marchand S (2012).

Table 1 Comparative study of Cold Pressor Response in different age groups

Group	**COLD PRESSOR RESPONSE**							
	SYSTOLIC BLOOD PRESSURE (S.B.P.)				DIASTOLIC BLOOD PRESSURE (D.B.P.)			
	Mean	S.D.	P-value	Sig.	Mean	S.D	p-valve	Sig.
A	10.80	3.26			6.88	2.38		
			<0.001	HS			<0.001	HS
B	15.20	3.21			12.88	3.90		
			<0.001	HS			<0.01	HS
C	18.30	2.74			16.72	4.08		
			<0.001	HS			>0.05	NS
D	22.80	3.06			17.04	3.01		

S.B.P. : Systolic Blood Pressure
D.B.P. : Diastolic Blood Pressure
S : Significant
HS : Highly Significant
NS : Not Significant

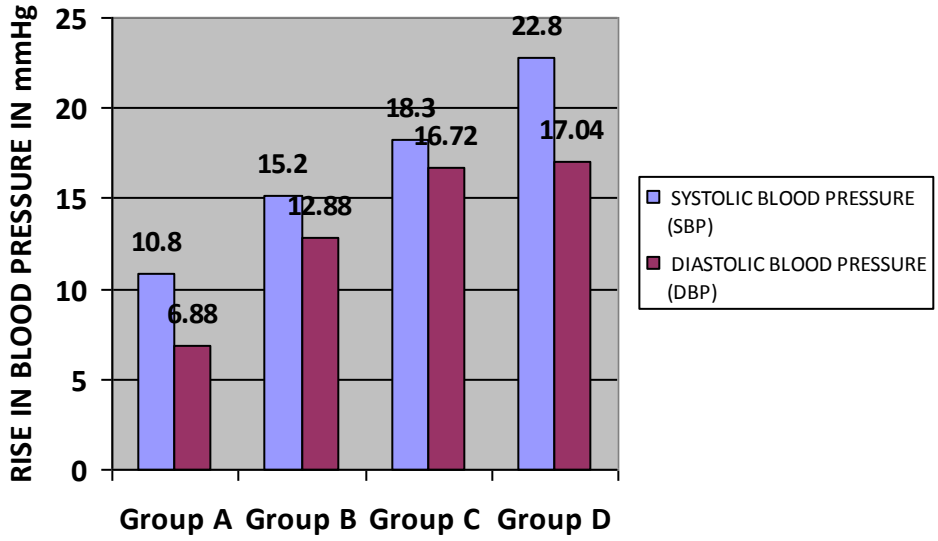

Figure 1: Showing Comparison of Mean ± S.D valves of change in Blood Pressure During cold pressor response in different age groups.

Blandini F et al (1992) studied the levels of free plasma nor adrenaline, adrenaline and dopamine in response to tour tests stimulating the sympatho-adreno medullary activity and found that the elderly showed an increased nor adrenergic responsiveness when compared with the young subjects, confirming the existence of an 'up-regulation' of the peripheral sympathetic tone in old people.
Ng et al (1993) studied the muscle sympathetic nerve activity (MSNA) at rest and found that (MSNA) increases with age and was progressively higher in the young women, older women and older men. Jensen, Urstad et al (1997) studied the effect of age and gender on Heart rate variability by 24 hour ECG recodings (20-70 years of age) in men and women and found that age and to lesser degree gender are important determinants in healthy subjects.
Jaquet et al (1998) studied the relationship between ambulatory blood pressure levels. within subject blood pressure variability and age in men and women, it was explored that systolic blood pressure was higher in the elderly than in the young group. In comparison to the young subjects both elderly men and women had higher diastolic blood pressure. Blood pressure variability while subjects were awake was higher in the elderly, women in particular. Matsukawa et al (1998) concluded that muscle sympathetic nerve activity increases with age in women and men and that the activity was markedly lower in young women then in men but is markedly acclerated with age. Mehta Ahuja V. et al (1999) concluded that there was significant increase in sympathetic activity in males along with other factors. Selvamurthy et al (1999) evaluated some of the physiological correlates responsible for functional alternation with advancement of age. The result revealed that the cold pressor response showed more or less similar rise in both systolic and diastolic blood pressure upto age of 55 years thereafter, a highly significant increase was noticed.
Mourot *et al.,* (2009) studied the effect of the cold pressor est on cardiac autonomic control in normal subjects and found higher sympathetic activity at the skin level during cold pressor test in the group with decreased heart rate. Srivastava *et al.,* (2010) showed comparison of cold pressor response in young versus elderly males and young versus elderly females yielding comparable rise in systolic blood and diastolic blood pressure with age. Otte *et al.,* (2005) studied the cortical response to challenge in difficult age groups. The result demonstrated that ageing increases the cortisol response to challenge. This effect of age on cortisol response is almost three-fold stronger in women than men. Hess *et al.,* (2009) studied the affects of ageing on cardiovascular responses to cold stress in humans and the results indicated that there is a greater pressor response to non-internal body temperature reducing cold stress with age in humans that may be mediated by increased levels of central arterial stiffness. Laflamme YT and Marchand S (2012) studied effect of ageing in post menopausal women and found that for identical cold pain stimulus post menopausal women reported significantly more pain during cold pressure test.

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