

SHORT COMMUNICATION

Evaluation of pain perception latencies following metabolic alteration of plasma pH

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Pain has been a subject of intense and continuous research over the years. Several approaches have been employed in understanding and management of pain ranging from peripheral to central modulation as well as systemic to molecular mechanism of integration. This study is therefore aimed at investigating the role of altered plasma pH in the perception of experimental pain in both chronic and acute model. The results indicated significant ($p < 0.05$) prolonged nociceptive activity by nerve endings at increasing alkalinity and acidity of the plasma in both models of experimental pain used. In conclusion, plasma condition should be an important consideration in the management of pain because introduction of exogenous substances could shift the homeostatic equilibrium and could eventually affect latency and integration of nociception.

Key words: Alkalosis, acidosis, nociception, homeostasis, plasma.

INTRODUCTION

Pain is the second most common reason people visit doctors, exceeded only by colds and upper respiratory infections. Albert Schweitzer is noted to have said 'Pain is an even worse master than death (Marcus and Arbeiter, 1994). The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". The sensation of pain plays a physiological role, warning us about threats to the physical integrity of our body (Chapman and Gavin 1999). Several management or treatment options have been put forward in the management of pain ranging from peripheral to central interventions. However, most of these interventions are either unaffordable or not effective. A thorough knowledge of plasma chemistry could be a helpful criteria in the management of pain. The body continually strives to balance pH or maintain homeostasis and when this balance is compromised as a result of lack of physical

activities, environmental pollutants and diets, the threshold of nociception is altered (Baroody, 1991). This study is therefore aimed at evaluating pain perception when plasma pH is shifted either towards acidosis or alkalosis.

MATERIALS AND METHODS

Animals

A total of 30 male albino rats (100 to 120 g) were used for the study. They were bred and housed in the pre-clinical animal house of the College of Health Sciences, Ladoke Akintola University of Technology Ogbomoso, Nigeria under a 12/12 h light-dark cycle at room temperature. The animals were fed standard mouse cubes and distilled water *AD LIBITUM*.

Induction of metabolic acidosis

A total of 10 animals were used in this group. Metabolic acidosis

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Table 1. Effects of altered plasma pH on pain perception latencies in rat. Data represent mean \pm SEM in N = 10 and *P < 0.05 considered significant when compared with the control.

Parameter	Mean plasma pH	Tail-withdrawal latencies (s)	Formalin test	
			Early phase (s)	Late phase (s)
Control	7.40 \pm 0.01	5.08 \pm 0.22	9.80 \pm 0.45	27.06 \pm 0.13
Induced acidosis	7.10 \pm 0.01	10.90 \pm 0.22*	17.40 \pm 0.40*	61.15 \pm 0.12*

Table 2. Effects of altered plasma pH on pain perception latencies in rat. Data represent Mean \pm SEM in N = 10 and *P < 0.05 considered significant when compared with the control.

Parameter	Mean plasma pH	Tail-withdrawal latencies (s)	Formalin test	
			Early phase (s)	Late phase (s)
Control	7.37 \pm 0.34	3.37 \pm 0.56	9.08 \pm 8.6	21.12 \pm 2.4
Induced Alkalosis	7.59 \pm 0.15	5.08 \pm 0.71*	17.35 \pm 8.5*	27.41 \pm 2.5*

was induced by administration of 0.28 M of ammonium chloride (NH₄Cl) in drinking water for 3 days (Chambrey et al., 2005; Quentin et al., 2004). Acidosis is confirmed with the use of digital pH meter.

Induction of metabolic alkalosis

A total of 10 animals were used in this group. Metabolic alkalosis was induced by administration of 0.1 mg/kg of a stimulant laxative, bisacodyl (Dulcolax) orally for 3 days (McEnvoy, 2005). Alkalosis is confirmed with the use of digital pH meter.

pH measurement

After the treatments, blood samples were collected into heparinized sample bottles from the animals through the retro-orbital sinus with the aid of capillary tube. pH was measured using digital pH meter (Model 215 pH meter, Denver Instrument Company).

Tail-withdrawal test

The test was carried out using a modification of the tail-flick method (D'Amour and Smith, 1941). The animal was gently hand-held with a piece of towel, and the terminal 3 cm segment of the tail was immersed in a water bath maintained at 52 \pm 2°C. The time taken for the animal to flick its tail out of water was taken as the tail withdrawal latency.

Formalin test

Using a standard method (Hunskar and Hole, 1997), 20 μ l of 1% formalin was injected into the dorsal surface of the left hind paw of the rats. The times spent for licking the paws within the first 5 min long post-injection interval (early phase) and within 10 min starting from the 20th min post formalin (late phase) were measured. The animals were observed in a glass box 50 \times 50 \times 50 cm in dimension. The box is cleaned with methylated spirit to avoid bias due to the odour of the previous animal.

RESULTS

Effects of altered pH (metabolic acidosis) on pain perception latencies

As shown in Table 1, pain perception latencies of animals in both tail-withdrawal and formalin tests were increased as the plasma pH tends towards increasing acidity.

Effects of altered pH (metabolic alkalosis) on pain perception latencies

As shown in Table 2, pain perception latencies of animals in both tail-withdrawal and formalin tests were increased as the plasma pH tends towards increasing alkalinity.

DISCUSSION

From this study, there was significant increase in nociceptive activities of the treated animals when compared with the control in tail flick latency. Also, the response to formalin shows that there was an increase in perceived intensity of noxious stimuli in early phase. The early phase seems to be predominantly dominated by C-fibre activation due to peripheral stimulus while the late phase appears to be dependent on the combination of inflammatory reaction in the peripheral tissue and functional changes in the dorsal horn of the spinal cord. These functional changes seem to be initiated by the C-fibre barrage during the early phase (Carl, 2002). This observation is consistent with both increasing acidity and alkalinity induced in the experimental animals.

The kidney plays a significant role in maintenance of homeostasis in the body by excreting excess H⁺ and re-absorption of HCO₃⁻ among other endogenous regulatory

mechanisms, however in the presence of excess H^+ and HCO_3^- occasioned by introduction of exogenous agents in diet or drugs, homeostatic equilibrium is altered and in the instance of this disturbance, neuronal integration and activities are affected, leading to prolonged nociceptive activity.

Conclusion

Plasma chemistry as well as exogenous agents introduced into the plasma should be important factors of consideration in the management of pain.

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