Dipsogenic Response and Infectious Process in Rats

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Abstract. Septic peritonitis is a severe infectious process. Symptoms suggest the need to establish a link with homeostasis of water intake for disease treatment. To determine the alterations between dipsogenic responses associated with infectious process in rats using the CLP model. Analysis shows that 24-h after infectious process induction by CLP, water intake (ml/per 100-g body weight) decreased when compared to results for control and sham vs. test time progression after CLP rats. However, 48-h and 72-h after CLP water intake increased to control levels. Based on these preliminary results, it can only be stated that the inhibition of thirst may be associated with the activation of central and systemic mechanisms or a combination of mechanisms. The recovery of the animals may be associated with well being, quality of life and nutritional support, and immune system. We are investigating the molecular mechanisms through cell signaling related to the alterations in water intake caused by infectious process.

Keywords: Infectious process, Thirst mechanism, Rat

INTRODUCTION. Peritonitis is an abdominal infection in which pathogenic microorganisms rapidly proliferate incurring a severe infectious process [5], and it presents in three forms: aseptic, septic and combined. Since anorexia is one of the symptoms of infectious process [3], there is a need to establish a link between the regulation of nutrient metabolism and homeostasis of thirst for disease treatment [9]. It is known that, the lateral hypothalamic area, the hypothalamic paraventricular nucleus, and the periaqueductal gray are all regions that receive a strong neural input from the lamina terminalis and are proposed as regions that participate in the manifestation of thirst. The cerebral mechanisms that subserve
the water intake responses are associated with the following: (a) hypertonicity, cellular dehydration, and osmoreceptor stimulation; (b) hypovolemia and extracellular dehydration; and (c) hormonal signals that may stimulate or inhibit thirst [7]. However, scientific studies of thirst mechanisms are hampered by the inability to measure it directly or to quantify it precisely. Because of this, the alteration of water intake mechanisms remains uncertain. Thus, in view of the complexity of the study of dipsogenesis, the objective of this work was to determine the possible alterations in dipsogenic responses associated with infectious process in rats.

MATERIAL AND METHODS - The infectious process by cecal ligation and puncture (CLP) as previously described by Wichterman et al., (1980) and illustrated by Zapparoli et al., (2011) is currently the most widely used animal experimental model for mild infection, because it mimics the clinical conditions of postsurgical [6]. The experiments were carried out in groups of male Wistar Hannover rats (CEMIB-UNICAMP): control or non-operated (n=5), sham-operated (n=5) and CLP (n=5) (eight weeks of age), which were allowed free access to tap water and standard rat chow (Nuvilab Radiated - Nuvital Nutrientes S/A, Brazil). The rats were housed under controlled climatic conditions, in accordance with current international bioethics and biosafety norms for animal experimentation and with the guidelines of the Brazilian College of Animal Experimentation (COBEA). The sham-operated and CLP animals received pre-induction anesthetic with atropine (0.02 to 0.04 mg/kg, ip) and after 10 min, ketamine (75-100 mg/kg body weight, ip) + xylazine (5-10 mg/kg body weight, ip). After the abolition of the corneal-palpebral and foot reflex, the animals were placed on a surgical thermal table and immobilized with clamps. A gel eye shield was then applied during anesthesia. Post-procedure CLP, the rats were then given the analgesic buprenorphine (0.05-0.1 mg/kg, sc, 12-12 h), and the animals were placed under an incandescent light. After recovery from anesthesia, the rats were subsequently housed individually in metabolic cages with free access to tap water and food and accompanied for 24-h, 48-h and 72-h post induction of mild infection. At the end of the experiment, the animals were sacrificed by hypoxia in a carbon dioxide chamber carried out according a euthanasia policy for rodents in the guide for the care and use of laboratory animals. The data were presented by values obtained at 24-h, 48-h, 72-h post induction of infectious process and body weight (per 100-g body weight) and water intake (ml/per 100-g body weight). The results are reported as Means±SD, determined using repeated measures ANOVA. Bonferroni’s t-test post-hoc analysis was used to determine the extent of the differences. *p= 0.00 was considered significant.

RESULTS - The Table 1 and Figure 1 show water intake and body weight in rats. Analysis shows that 24-h after infectious process induction by CLP, water intake decreased when compared to results for control and sham vs. test time progression after CLP rats. However, 48-h and 72-h after CLP, water intake of animals increased and returned to control levels (Table 1 and Figure1).
DISCUSSION - Considering that animals can go without food for up to 60 days, if not longer, the absolute requirement for daily water and the proposed pathophysiological correlates of its lack makes it a very important subject. Reduced physical activity and drinking are some of the behavioral alterations induced by infection. However, behavioral alterations may be associated with physiological changes, and the inhibitory effect on fluid intake could result from the activation of inhibitory hormones and neurotransmitters [8]. Thirst in mammals arises from mechanisms which involve volume reduction, in both intracellular and extracellular compartments, mediated by a combination of angiotensin II, vasopressin and osmoregulation [4]. Moreover, although infection may activate central mechanisms to reduce activity and ingestive behavior, it may also have a systemic effect, other than alteration in body temperature or arterial pressure, which could attenuate signals of dehydration and contribute to the inhibition of water intake. On the other hand, antidipsogenesis is induced by infection in the rat and it is mediated by central production of reactive oxygen species (nitric oxide), eicosanoids (prostaglandins), and possibly the release of various inflammatory mediators such as cytokines (e.g., TNF-α and interleukin-1β, interleukin-6) and the involvement of several biochemical pathways [7]. Therefore, based on the above results, it can only be stated that the inhibition of thirst may be mediated by the activation of central mechanisms, systemic dilution and expansion of fluid, or a combination of central and systemic mechanisms [10]. However, the ability of the animals to become tolerant to infection is crucial to the survival of the organism and to elicit controlled inflammatory responses. Also, the recovery of the animals may be associated with well-being and quality of life. Laboratory animals are housed under controlled climatic conditions. And balanced diet generally improves the body's ability to cope with bacterial translocation. Catabolic response and plasma cortisol levels are reduced, and disease progression is hindered due to a variety of nutrients with immunostimulatory actions [1] and associated with the production and synthesis of collagen and mechanical resistance in infectious process [2].

CONCLUSION - In view of the mortality caused by infectious process in mammal the homeostasis, diagnosis and initiation of therapy should be early in order to have a favorable prognosis. We are investigating the molecular mechanism and via of cellular signaling related to the alterations promoted for the infectious process and water intake to complement our preliminary physiological results.
TABLE I: Alterations of Body Weight and Water Intake in Rats

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Body weight (ml/100 g)</th>
<th>Water intake (ml/100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTROL</td>
<td>2.7±0.5</td>
<td>12.6±0.8</td>
</tr>
<tr>
<td>SHAM</td>
<td>2.6±0.4</td>
<td>11.9±0.7</td>
</tr>
<tr>
<td>CLP - 24 h</td>
<td>2.5±0.6</td>
<td>6.0±1.3*</td>
</tr>
<tr>
<td>48 h</td>
<td>2.6±0.1</td>
<td>10.3±0.9</td>
</tr>
<tr>
<td>72 h</td>
<td>2.6±0.7</td>
<td>12.1±0.5</td>
</tr>
<tr>
<td>(n=5)</td>
<td>Mean±SD</td>
<td>(&gt; 0.99)*</td>
</tr>
</tbody>
</table>

Figure 1: Alterations of Water Intake in Rats

TABLE 1 AND FIGURE 1: STUDY OF WATER INTAKE (ML/PER 100-G BODY WEIGHT) IN RATS. The data were presented by values obtained at 24-h, 48-h and 72-h post induction of infectious process. The number of animals in each group is shown in parentheses (n=5). The results are reported as Means±SD, determined using repeated measures ANOVA. Bonferroni’s t-test post-hoc analysis was used to determine the extent of the differences. * p = 0.00 was considered significant.
REFERENCES


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