Use of intravenous paracetamol infusion versus placebo in acute brain injury

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Abstract

Background: Traumatic brain injuries (TBI) are main causes of mortality and disability worldwide, particularly in children and young adults. They lead to changes in temperature, cerebral blood flow, the pressure inside the skull and consciousness. Patients with TBI experience febrile episodes which lead to previous consequences so it should be resolved prophylactically by use an appropriate antipyretic, but remains important deficiency of coherent evidence about active therapies in the acute care of patients with TBI.

Objectives: Early administration of intravenous paracetamol to patients to reduces core body temperature following intense traumatic brain injury contrast to placebo (normal saline).

Patients & Methods: Involved in this study 20 patients of both sex, aged from 18 to 65 years, who were accepted to the intensive care unit for sharp brain injury. A prospective study was carried out in intensive care unit in AL Hussein medical city in Karbala during the period from first of November 2016 to the 28th of February 2017. Eligible patients were randomly selected & classified to two groups A & B which (10 patients each group). Group A received (0.9 %) of sodium chloride (normal saline) each (6/24) hours and group B received 1 gram of intravenous Paracetamol every (6 /24) hours. The result included Temperature, pulse rate and systolic & diastolic of blood pressure, which were measured prior to administration of the study drug, hourly
during the period of study (24 hours) & till 2 hours after the final dose of the study. The data were analyzed by using T-test.

**Results:** By using T-test of two groups. Shows this study that there is little or no significant decrease in patient’s temperature in group B who were given paracetamol (P>0.05) except at (first dose) of paracetamol (P<0.05), while there is no change in group A who were given normal saline (P>0.05). This study also shows significant decrease in diastolic blood pressure in group B at (first & second dose) of paracetamol (P<0.05), while there is no significant change in group A (P>0.05). When we monitored the pulse rate parameter & systolic blood pressure, we noticed that there is no significant change in its value in the two groups (P>0.05).

**Conclusion:** Was concluded that there is little or no significant decrease in patient’s temperature in group B who were given paracetamol, while there is no change in group A who were given normal saline.
Introduction:

Traumatic brain injury (TBI) is the main cause of mortality and disability worldwide, particularly in children and young adults. Males suffer TBI further than females. Reasons comprise falls, violence and vehicle accidents. The brain trauma may occur from of a focal hit on the head, by a sudden acceleration or deceleration inside the cranium or by combination of both sudden impact and movement. Secondary injury result from the brain trauma, after the damage several of events which occur in the minutes to daysthat causes changes in the pressure and cerebral blood flow inside the skull, contribute to the damage result from the initial injury. Some of imaging technique used to diagnosis with treatment include CT scan and MRI (magnetic resonance imaging), treatment needed for TBI may be minimal or may involve interventions such as medication, emergency surgery or surgery year, depending on the injury. Physical, speech, occupational, recreation and vision therapies may be used for rehabilitation. Counseling, supported employment, and community support services may also be useful [1].

System classified TBI by its pathological feature [2]. Lesion may be extra-axial, or intra-axial. The injury from TBI can be focal or diffuse, confined for specific area or distribute in a more general manner. It is popular for both kinds of injury to find in a given case. Diffuses injuries of brain manifest with minimal damage in neuroimaging studies, which lesion can be see in microscopy technique postmortem [3]. Type of diffuse injury contain edema and diffuse axonal injuries, which is widespread damages to axon include white matter tract and projection to the cortex [4] [5]. Types of diffuse injuries contain concussions and diffuse axonal injury, widespread damage to axon in area including white matter and the cerebral hemisphere [5] [6] [7]. Focal injury may be make symptom related to the function of the damage area. One type from focal injury, cerebral lacerations, occur when the tissue is cut or torn. In like injury, cerebral contusions (bruising of brain tissue), blood is mixed among tissue. In contrast to, intracranial hemorrhage comprise bleeding that is not mixed with tissue [8] [9]. Patient with TBI frequently experience febrile episode that may be of infectious or non-infectious origin. Neurogenic fever is a non-infectious origin from fever in the patient with TBI. Until recently, NF was thought to be in relation rare consequence of TBI. Neurogenic fever result from a disruption in the hypothalamic set point temperature
which result in an abnormal elevation in temperature of body and is reasoning to be caused by damage to the hypothalamus\textsuperscript{[10][11]}. TBI result in several different types of damage, and at this point it is unclear if one particular type is connected with an elevation incidence of NF. From cadaveric studies it is known, that hypothalamic injuries is common in patients after TBI as 42.5\% of the brainprosecuted was evidence of hypothalamic damage\textsuperscript{[12]}. Most reports characterizes the patient with NF as being relatively bradycardia, have a notable lossof perspirations, having a plateau-like temperature curve (no diurnal variation) which long to little days to little weeks, the temperatures being characteristic too high with resistant for antipyretic medications\textsuperscript{[11][13][14]}. Acetaminophen is used for elimination the mild to moderate pain. Intravenous form of paracetamol used to pain of sudden onset in the patients in emergency department\textsuperscript{[15]}. Use of paracetamol in combination with caffeine is first line therapy in treatment tension or migraine headache\textsuperscript{[16]}. The major mechanisms propose is the suppression of cyclooxygenases COX and recent findingpropose that it is highly selective for COX2. For of its selectivity for COX2, it does not significantly suppress the producing of the pro clotting thromboxanense. But when compared with aspirin or other NSAID, its peripheral anti-inflammatories activity is usually limited by several factor, one of which is the high level of peroxides found in inflammatory lesion\textsuperscript{[17]}.

The author recognize the active metabolite is NAPQI, however this reactive compound should reply not only with the thiol in TRPA1, but also with any other suitableredy nucleophile that it occur to encounter. It is proposition that thiol group in cysteine protease, e.g. the proteases that take part in the dealing of procytokine, like those resulting IL-1B and IL6, might be the target giving rise to overall analgesic effect\textsuperscript{[18][19]}. The COX enzyme is responsible for the metabolism of arachidonic acid to prostaglandin H2 which an stable molecule that is, in turn, modulate to various other pro-inflammatory compounds. This step blocked byanti-inflammatory like the NSAIDS. Only when appropriately oxidized is the COX enzyme highly active\textsuperscript{[20]}. Because paracetamol minimize the oxidize form of the COX enzyme, which stop it from forming pro-inflammatory chemicals. Therefore, this leads to decrease amount of prostaglandin E2 in the CNS, which result decreasing the hypothalamic set-point in the thermoregulatory center\textsuperscript{[21]}.

**Patients & Methods:**

A prospective study was carried out in intensive care unit in AL Hussein medical city in Karbala during the period from first of November 2016 to the 28\textsuperscript{th} of February 2017. 20 patients were included, who were send to the intensive care unit for acute brain insult according to the consent of the relative of the patient.

**Inclusion criteria:**

- Age more than 18 & less than 65.
- Abnormal brain CT (defined by the presence of hemorrhage, contusion, infarction and edema).
Within 48 hours of injury.

**Exclusion criteria:**

- Allergy to paracetamol.
- Date of chronic liver disease from chronic alcohol abuse.
- Acute or chronic renal failure.
- Hemodynamic insecurity (known as systolic blood pressure < 90 mmHg in spite of vasopressor utilize).
- Dormant patient predictable to die within 24 hours.

Eligible patients were randomly selected & divided to two groups A & B which (10 patients each group). Group A received (0.9 %) of sodium chloride (normal saline) every (6/24) hours and group B received 1 gram of intravenous Paracetamol every (6/24) hours. Temperature measurements were done by core temperature probe, pulse rate and non-invasive blood pressure and were measured prior to administration of the study drug hourly during the period of study (24 hours) & till 2 hours after the last dose of the study.

**Results:**

**Table 1. Shows normal saline effect on the parameters (temperature, Pulse rate, SBP and DBP) with time.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>12 am</th>
<th>6 am</th>
<th>12 am</th>
<th>6 am</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>37.75±1.707</td>
<td>38.15±1.833</td>
<td>37.65±2.114</td>
<td>37.70±2.000</td>
</tr>
<tr>
<td>Pulse rate</td>
<td>101.00±5.079</td>
<td>101.30±3.947</td>
<td>104.50±2.414</td>
<td>108.00±5.960</td>
</tr>
<tr>
<td>SBP</td>
<td>129.50±5.500</td>
<td>126.50±7.925</td>
<td>126.90±5.758</td>
<td>131.00±6.182</td>
</tr>
<tr>
<td>DBP</td>
<td>81.50±4.349</td>
<td>74.50±4.179</td>
<td>83.00±2.603</td>
<td>78.00±2.708</td>
</tr>
</tbody>
</table>
Results represents mean± standard deviation of (temperature, Pulse rate, SBP and DBP) with time of normal saline; non-significant change which \( P \leq 0.05 \).

### Table 2. Shows paracetamol effect on the parameters (temperature, Pulse rate, SBP and DBP) with time.

Results represents mean± standard deviation of (temperature, Pulse rate, SBP and DBP) with time of paracetamol; non-significant change which \( P \leq 0.05 \).

### Table 3. Shows differences between paracetamol effect and normal saline effect on parameters (temperature, Pulse rate, SBP and DBP).

Results represents mean± standard deviation of (paracetamol and normal saline); Superscripts (*) represent significant change \( P \leq 0.05 \) between groups.
Discussion

Acute brain injuries are common problem in our population which have many complications and consequences on injured persons such as increase in their temperature which lead to disturbance in consciousness and increase in intracranial pressure which it causes mortality one in three of those who are maximum severely affected and a large ratiowho that survive have long term physical or mental inability, this consequences expose patient to more serious problem so it must be resolved.[22] We used paracetamol in an attempt to resolve this problem (increase temperature,disturbed intracranial pressure). This study shows that there is little or no significant decrease in patient’s temperature in group B who were given paracetamol ,while there is no change in group A who were given normal saline.Paracetamol is used for treatment the pain and fever which it is used in mild to moderate pain[23].

This study also shows significant decrease in diastolic blood pressure in group B, while there is no significant change in group A.Regarding the pulse rate parameter, was noticed that there is no significant change in its value in the two groups.In this study ,was also noticed that there is no significant change in the two groups when we monitored the systolic blood pressure.Our data were in agreement with other researches like[24][25][26].

References


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