Original Research Article

Evaluation of analgesic activity of glucose in Swiss Albino mice

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ABSTRACT

Background: Pain is the first and foremost symptom which alerts us about the underlying diseases, injuries or inflammation. Varied treatments are followed for pain relief worldwide. Nowadays tramadol, a centrally acting opioid analgesic is used widely. There are evidences that sweet substances like sucrose produce analgesia through endogenous opioid system. Sucrose has been proved to produce analgesic effect in healthy neonates and also in animals. Likewise, analgesic effect of glucose has also been studied but only limited no. of studies available.

Methods: Swiss Albino mice of either sex (20-30g) were procured from the central animal house of KFMS and R, Coimbatore. Animals were maintained under controlled temperature and light conditions with food and water ad libitum. Mice were kept in the department to get acclimatized. 24 mice were divided into 4 groups (n=6). Drugs were given orally after 12hours of fasting. Group I was the control. Group II received standard-tramadol (40mg/kg). Group III received glucose (200mg/kg). Group IV received glucose (400mg/kg).

Results: The latency period of glucose was significant (p<0.001) compared to controls and standard was significant (p<0.001) when compared to glucose by hot plate method.

Conclusions: Analgesic activity of glucose may be due to both central and peripheral inhibition of PG synthesis. This has been proved in previous studies. This study showed that glucose can be used as an add-on in non-diabetic patients with better compliance.

Keywords: Analgesia, Acetic acid, Glucose, Hot plate, Tramadol

INTRODUCTION

Pain is the most common ailment for which patients seek medical advice. Analgesics are drugs which decrease pain sensation by increasing the nociceptive threshold to external stimuli without altering consciousness. Both pharmacological and non-pharmacological interventions are available for management of pain. There are two main classes of analgesics currently available, the non steroidal anti-inflammatory drugs (NSAIDs) and Opioid analgesics, but they have significant side-effect like gastric ulceration/bleeding, analgesic nephropathy, increased risk of myocardial infarction, stroke and respiratory depression, constipation, physical dependence, addiction, respectively. Pain is the first and foremost symptom which alerts us about the underlying diseases, injuries or inflammations. To cure sometimes, to relieve often, to comfort always", is a 15th century French description of the role of the physician. Nowadays pain management is a specialized field in patient care. Varied treatments are followed for pain relief worldwide. Nowadays Tramadol, a centrally acting opioid analgesic is used widely. Sweet substances like sucrose produce analgesia through endogenous opioid system has been widely acknowledged. It has been proved to produce analgesic effect in healthy neonates and also in animals. Various studies have shown that administration of oral sucrose, a disaccharide, raises the pain threshold, presumably mediated by endogenous opioids and could be used for that purpose. However, sucrose is not routinely used for pain.

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Likewise, analgesic effect of glucose has also been studied, but only by limited no. of studies are available. Glucose is a monosaccharide widely used by intravenous (IV) route in intensive care unit but not as an oral solution. The present study was undertaken to find out the effect of oral administration of glucose, in different strengths, on pain relief.

METHODS

The study was conducted in Department of Pharmacology, Karpagam Faculty of Medical Sciences after having obtained Ethical clearance from Animal Ethical Committee at Karpagam Faculty of Medical Sciences and Research, Coimbatore. All the animals were handled carefully as per the CPCSEA guidelines.

Chemicals

Tramadol (ACME Laboratories Ltd)-Standard drug and 0.6% Acetic Acid, Normal saline were used.9

Experimental animals

The 48 Swiss albino mice of either sex (20-30g) were procured from the central animal house of KFMS and R, Coimbatore. They were kept in polypropylene cages in 12:12 hours light:dark cycle, provided with standard laboratory diet and had water ad libitum. Food was withdrawn 12 hours before and during experimental hours.

Acetic acid induced writhing test

The 24 Swiss albino mice were taken for this study. The mice were divided into 4 groups of 6 animals in each. Group I was used as control receiving 0.5 ml normal saline. Group II was given standard drug Tramadol 10mg/kg. Group III, IV received glucose in doses of 200 and 400mg/kg respectively. Mice were intragastrically administered with test and control drugs 30 min before intraperitoneal injection of acetic acid (0.6%). Then mice were placed in separate bell shaped transparent glass jars and numbers of abdominal contractions (writhes) were counted over a period of 10 minutes commencing 10 min after injection of acetic acid. The difference in number of writhes in test group was compared with standard treated and control treated groups.10 The percentage increase/decrease in number of writhing (as index of analgesia) was calculated. The Percentage Inhibition was calculated by formula:

\[ \text{% Inhibition} = \left( \frac{(Wc-Wt) \times 100}{Wc} \right) \]

Where \( Wc \) = No. of writhes in control group, \( Wt \) = No of writhes in test group.

Eddys hot plate method

The 24 Swiss albino mice weighing 20-30g were used. Mice were intragastrically administered with test and control drugs .1 hr after the ingestion of drugs mice were placed on the hot plate, which consists of electrically heated surface. Temperature of the hot plate was maintained at 55°C.

Responses such as jumping, withdrawal of the paws and licking of the paws were observed. The time period (latency period) when animals were placed and until responses occur was recorded by the stopwatch. The latency period was recorded after 0, 60, 90 and 120 min. These values were compared with the standard drug tramadol and control normal saline. This model evaluates the central pain.11

Statistical analysis

The experimental data were expressed as mean±SEM. Statistical analysis was carried out by one way analysis of variance (ANOVA). A level for \( p < 0.05 \) was considered to be statistically significant. IBM SPSS statistics © IBM Corporation 2012 software was used for statistical analysis purpose.

RESULTS

Acetic acid induced writhing test

Glucose which was given orally 30 min before intraperitoneal injection of acetic acid significantly reduced the number of writhes. Significant inhibition of the writhing response was observed after the administration of glucose 400mg/kg when compared to normal saline control group.

The number of writhes of glucose was less when compared to control whereas the number of writhes of standard drug (Tramadol) were less when compared to glucose and normal saline. When compared to control, the percentage inhibition of glucose was 58.33% at 200mg/kg, 66.66% t 400mg/kg and that of the standard was 83.96% (Table 1).

Table 1: Analgesic activity by acetic acid induced writhing in Mice.

<table>
<thead>
<tr>
<th>Groups</th>
<th>No. of writhes</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I (control)</td>
<td>36.23±2.32</td>
<td>-</td>
</tr>
<tr>
<td>Group II (standard)</td>
<td>6.03±2.43</td>
<td>83.33</td>
</tr>
<tr>
<td>Group III</td>
<td>15.34±2.23</td>
<td>58.33</td>
</tr>
<tr>
<td>Group IV</td>
<td>12.66±2.04</td>
<td>66.66</td>
</tr>
</tbody>
</table>

Each value is the mean±SEM for 6 mice, a \( P < 0.05 \); b \( P < 0.01 \); c \( P < 0.001 \) compared with control. Data were analyzed by using One-way ANOVA

Eddys hot plate method

Thus, the latency period of glucose was significantly (\( P < 0.001 \)) good when compared to control at time period 60-120 min, whereas the latency period of the standard was more significant (\( P < 0.001 \)) when compared to glucose at all-time intervals of experimentation (Table 2).
Table 2: Analgesic activity by hot plate method in mice.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Reaction time in seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 min</td>
</tr>
<tr>
<td>Group I (Control)</td>
<td>3.02±0.02</td>
</tr>
<tr>
<td>Group II (Standard)</td>
<td>3.23±0.08</td>
</tr>
<tr>
<td>Group III</td>
<td>3.24±0.04</td>
</tr>
<tr>
<td>Group IV</td>
<td>3.42±0.05</td>
</tr>
</tbody>
</table>

Each value is the mean±SEM for 6 mice, a P<0.05; b P<0.01; c P<0.001 compared with control. Data were analyzed by using One-way ANOVA.

DISCUSSION

The present study was conducted to evaluate the analgesic activity of glucose and to explore the mechanism of action. Pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage. Pain is produced by the excitation of nociceptors or their afferent free nerve endings. There are two types of pain, fast pain and slow pain, mediated through Aδ fibers and C fibers. Nociception is the mechanism; whereby noxious peripheral stimuli are transmitted to the central nervous system. Nociceptive fibers terminate in the superficial layers of the dorsal horn, forming synaptic connections with transmission neurons running to the thalamus. Nociceptors release glutamate, substance P contributing to neurogenic inflammation.

Gate control theory is constituted by transmission in dorsal horn. The dorsal horn transmission is inhibited by descending inhibitory pathways from the midbrain (periaqueductal grey area) and brain stem (nucleus raphe magnus). Enkephalin and 5-hydroxytryptamine are the main transmitters in this pathway. It causes both presynaptic and postsynaptic inhibition of incoming Type C and Type Aδ pain fibers where they synapse in the dorsal horn. Sweetening substances mainly modulates endogenous opioids and serotonin. β-endorphin, met-enkephalin, leu-enkephalin and dynorphin are the main endogenous opioids. The two enkephalins are found in the brain stem and spinal cord are known to involve in analgesia.

Nerve fibers derived from the periventricular nuclei and from the periaqueductal grey area secrete enkephalin at their endings. Fibers originating in this area send signals to the dorsal horns of the spinal cord neurons to secrete enkephalin. The enkephalin cause both pre synaptic and postsynaptic inhibition of incoming Type C and Aδ pain fibers where they synapse in the dorsal horns. Thus, the analgesic system block pain signals at the initial entry point to the spinal cord.

The use of different methods for evaluating pain is important because analgesic effect may be due to one or more mechanisms. For this reason in this study we have used hot plate method for supraspinal analgesia and acetic acid induced writhing for spinal analgesia.

There is also a role for nitric oxide (NO) pathway in pain modulation in animals and humans. NO also mediates the peripheral and central antinociceptive effect of analgesic compounds such as opioids. The NO-cyclic guanosine monophosphate (NO/cGMP) signalling pathway has also been shown to play a pivotal role in developing tolerance to opioid analgesia. Nevertheless, the role for NO in nociception is very complex and diverse. Both inhibitory and promotive actions of NO have been reported in nociception and pain. Glucose, a sweetening agent produces analgesia by inhibiting PG synthesis, modulating endogenous opioids. It can be used as an add on drug for pain in non diabetic patients.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Animal Ethics Committee at Karugumal University Faculty of Medical Sciences and Research, Coimbatore, India

REFERENCES


