Comparative Study of CNS Effects of Opium in Homeopathic Potencies with Pentazocine in Mice

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Abstract Opium is a drug being used in modern medicine as well as in homeopathy. Despite of the same source, both the pathies have different principles and indications. Opium is an alkaloid having main action on CNS. So in this study, we evaluated the effect of different dilutions of Opium in homeopathic potencies on CNS in mice and compared with that of Pentazocine. We divided forty mice of either sex into 7 groups (6c, 30c, 200c, 1 M, 0/1 LM, dispensing alcohol, Pentazocine). Test drugs were given orally. Different actions on CNS were evaluated by using Actophotometer for locomotor activity, Analgesiometer for analgesic activity and Straub test for opioid. Our result showed that pharmacological actions of Opium seen in modern medicine were not seen with different dilutions of Opium, in homeopathic potencies. 30c and 200c dilutions may be having secondary curative that is CNS stimulant action (reversal of CNS depression due to alcohol) as per homeopathic principles.

Keywords Opium, Homeopathic Drugs, Locomotor Activity

1. Introduction

Homeopathy is a form of an alternative medicine, first proposed by German physician Samuel Hahnemann in 1796, in which practitioners use homeopathic medicines in highly diluted preparations. It is based on the principle of law of similar. Homeopathic medicines, which produce certain symptoms in healthy individuals, are given in diluted form to the patients having similar symptoms. Homeopathic remedies are prepared by serial dilutions by giving forceful strokes, i.e. (succussion) \(^2\) after each dilution under the assumption that this increases the effect. Dilution often continues until none of the original substance remains.

Depending on the dilution, homeopathic remedies may not contain any pharmacologically active molecules and for such remedies to have pharmacological effect would violate fundamental principles of science. Modern homeopaths have proposed that water has a memory \(^3\) that allows homeopathic preparations to work without any of the original substance or the duality of action theory \(^4\) however; there are no verified observations or scientifically plausible physical mechanisms for such a
phenomenon. While some individual studies have positive results, systematic reviews of published trials fail to demonstrate its efficacy conclusively [5, 6]. Furthermore, higher quality trials tend to report less positive results, and most positive studies have not been replicated or show methodological problems [6]. The lack of convincing scientific evidence supporting homeopathy's efficacy use of remedies lacking active ingredients have caused homeopathy to be described as pseudoscience, quackery, and a cruel deception.

Opium is an alkaloid derived from plant source [7], and is being used in modern medicine as well as in homeopathy. Despite the same source, the indications in both the pathies are different. Opium has main action on central nervous system. In homeopathy, opium is used for painless condition, drowsy or sleepy people, for apoplexy, constipation, typhoid and colic [8]. But systematic research work has not been done to evaluate the effect of different dilutions or whether effects are comparable with that of morphine. So preclinical animal experiments are necessary to evaluate whether these dilutions really have action or not.

So this study was undertaken with the aim to evaluate the effect of different dilutions of opium (6c, 30C, 200c, 1M, 0/1 LM -homeopathic preparation) on CNS in mice and to compare these actions with conventional mixed opioid agonist-antagonist Pentazocine, used in modern medicine.

2. Materials and Methods

Study was initiated after Institutional Animal Ethics Committee approval (5/2010). Mice of either sex weighing 20-40 grams were divided into Seven groups with 6 animals in each group (6c, 30c, 200c, 1M, 0/1 LM, dispensing alcohol, Pentazocine).

They were housed in animal room, with alternating light-dark cycle of 12 hr each. All the drugs in homeopathic potencies were given orally 0.2ml, by mice feeding needle. All drugs were provided by Homeopathy College, BVDU, Pune.

Following tests were performed to compare activity of opium in various homeopathic potencies with conventional mixed opioid agonist-antagonist, Pentazocine.

2.1. Locomotor Activity

Mice pretreated with drugs or control were placed in locomotor activity chamber to which photoelectric cells were attached (Digital Actophotometer). Locomotor activities of the mice were recorded over a period of 10 minutes. Difference in the activity before and after giving drugs was calculated.

2.2. Hot Plate Method

Mice were divided into seven groups as mentioned above. Animals were placed on the hotplate which was maintained at 55ºC. The time between placement on the hot plate and the occurrence of either licking of the paws, shaking or jumping off from the plate was recorded as response latency. Reaction time for licking or lifting of fore & hind paws was calculated before & after giving the drug i.p. at 30, 60, 120 min. A cut off time of 30 sec was followed to avoid any thermal injury to the paws.
2.3. Straub’s Test

All the groups were given respective drug subcutaneously. The observations were continued for a period of 30 min following injections. Tail rose vertically (angle>45) was considered as + positive Straub test. The mice from (all groups) were scored all or none for straub’s tail reaction.

2.4. Statistics

One way analysis of Variance (ANOVA) followed by Dunnett test was used for statistical analysis by using graph pad prism version 5.

3. Results

![Graph 1: Locomotor Activity by Actophotometer](image1)

Figure 1: Locomotor Activity by Actophotometer

Maximum CNS depressant activity was seen in 1M, alcohol and 6c group.

![Graph 2: Analgesic Activity by Analgesiometer](image2)

Figure 2: Analgesic Activity by Analgesiometer

No statistically significant analgesic activity was seen with Opium in any homeopathic potency.
Table 1: Straub Test

<table>
<thead>
<tr>
<th>Drug</th>
<th>6c</th>
<th>30c</th>
<th>200c</th>
<th>1M</th>
<th>0/1lm</th>
<th>Alc</th>
<th>Pentazocine</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of mice showing Straub's test</td>
<td>16.67</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>66.6666667</td>
<td></td>
</tr>
</tbody>
</table>

Straub's test was negative with Opium in all homeopathic potencies.

4. Discussion

Opium is an extract of the exudates derived from seedpods of the Opium poppy, Papaver somniferum. Opium is a complex chemical cocktail containing sugars, proteins, fats, water, meconic acid, wax, latex, gums, ammonia, sulphuric and lactic acids, and numerous alkaloids, most notably morphine (10% - 15%), codeine (1% - 3%), noscapine (4% - 8%), papaverine (1% - 3%) and the baine (1% - 2%) [12]. All of the latter, apart from the baine, are used medicinally as analgesics. Morphine is by far the most prevalent and important alkaloid in opium. It binds to and activates μ-opioid receptors in the brain, spinal cord, stomach and intestine [13].

In modern medicine Opium and its derivatives are used medicinally as analgesics. The opioid analgesics are of inestimable value because they reduce or abolish pain without causing loss of consciousness. They also relieve cough, spasm, fever and diarrhea [13]. Opium is also one of the chief remedies of materia medica in homeopathy used for comatose conditions, painless condition, drowsy or sleepy people, for apoplexy, constipation, typhoid, colic in homeopathy [8]. Source is same (seedpods of the Opium poppy, Papaver somniferum) even for homeopathic preparation [8].

4.1. Locomotor Activity

As in both the pathies Opium is used for its CNS action hence we explored the effect of drug on locomotor activity. As seen in results, significant difference was seen in locomotor activity amongst all groups. Lowest activity (CNS depression) was seen with 6c, 1M and alcohol group (Figure 1). 6c is the only group which contain detectable amount of Opium [14]. Decrease in locomotor activity in this group may be related to additive action of Opium and alcohol as both drugs have CNS depressant action [15]. 30c, 200c and 1M also showed gradually decreasing CNS depressant action but less CNS depressant action than 6c and alcohol. Though these potencies do not contain any drug (below Avogadro's number) [16]. As dilution increases potency go on increasing as per homeopathic principle. CNS depressant activity was seen may be due to increase in potency or due to presence of alcohol. Decrease motor activity seen in 0/1LM group is in fact it is different scale and 0/1LM similar to mother tincture may be having detectable amount of drug [17]. All homeopathic drugs used dispensing alcohol for their preparation. As Opium is class IV drug [14] - (1:5 powdered drug + strong alcohol 88%) dispensing alcohol is used as vehicle. Same we used for control group. CNS depressant activity may be due to its alcoholic content. The role of alcohol in homeopathic preparation remains to be explored. CNS depressant activity is correlated more with presence of alcohol.

Surprisingly when CNS depression was compared among all groups, more locomotor activity (less CNS depression) was seen in all opium groups than dispensing alcohol group as shown in Figure 1. This may be due to the dual nature of opium that is drug may be reversing the effect of alcohol when given together. This is also called as secondary curative action [18] which was seen particularly with 30c and 200c group (Figure 1). According to homeopathic principle, each drug have two actions; primary action which produces certain symptoms in pharmacological doses and secondary action that produces exactly opposite set of symptoms where drug is given in very small/diluted doses.
This Fundamental claim of homeopathy is based on the principle that smaller doses produce stimulating effect on biological activity and higher doses cause inhibition.

Example, primary action of opium is deep sleep, constipation and secondary action of opium is long lasting wakefulness and diarrhea [19]. Our results indicate that CNS depressant activity of alcohol is reversed or decreased by 30c and 200c groups of homeopathic preparations. These observations are in accordance with Hanheman who advocated 30c dilution for most of the purpose [20]. In materia medica it is mentioned that opium is used for comatose patient or for sopor, painlessness, apoplexy etc. [8]. This use may be related to secondary curative action of opium as mentioned above.

4.2. Analgesic Activity

In Hot plate model, nociceptive reaction toward thermal stimuli in mice is a well validated model for detection of opiate analgesics as well as several types of analgesic drugs from spinal origin [9]. No statistically significant analgesic activity was seen with opium in all homeopathic potencies whereas Pentazocine showed significant analgesic activity (Figure 2). In homeopathy, opium does not have any analgesic indication [19]. This is also according to modern medicine principle that drug will produce its action only if it is given in certain amount. (Pharmacological doses)

4.3. Straub’s Test

Which is characteristic for opioid group showed negative results by all homeopathic preparations (Table 1) as these preparations do not contain any active ingredient to act on opioid receptors present on anococcygeus muscle.

4.4. Summary

These differences in all above mentioned tests are due to the fact that homeopathic drug do not contain any significant amount of drug or drug properties are lost while preparation. So conventional CNS actions of Opium (analgesic, CNS depression) as seen in allopathic medicine was not seen with different dilutions of Opium in homeopathic potencies. But only secondary curative action of Opium was seen in our findings. This may be due to the method of preparation of homeopathic drugs, that is Potentisation-(Dilution) and Succussion-Forceful striking (liquid Vehicle)

It is well mentioned in literature that after forceful striking, power of the medicine increases. Shaking and agitating the mixture is an important part of the potentiating process. Samuel Hahnemann believed that this was a key part of the homeopathic practice and that it would "release dynamic forces from the diluents which were preserved and intensified with subsequent dilutions" So while conducting preclinical animal experiments or clinical trials to evaluate the effect of different dilutions of homeopathic preparations, one has to consider homeopathic indications.

Limitations: - 1. We had not procured Morphine as test drug as it is reserved drug instead of that we used clinically used conventional morphine derivative Pentazocine. 2. Succesed alcohol with different potencies should be used instead of dispensing alcohol.

5. Conclusion

Pharmacological actions of Opium seen in modern medicine were not seen with different dilutions of Opium in homeopathic potencies. 30c and 200c dilutions are having secondary curative action as per the homeopathic indications.
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References


