Clinical Evaluation and safety of Liv.52 Drops in the management of loss of appetite in children: A subset analysis

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ABSTRACT
Loss of appetite is a common complaint of mothers who bring their children for pediatric consultation. A number of pharmacological agents like cyproheptadine are used to correct this problem, but a number of adverse effects are known to occur with this medication. Liv.52 is a novel herbal formulation recommended for hepatic diseases and anorexia. Present study was carried out to evaluate the safety and efficacy of Liv.52 drops in the management of loss of appetite in children. Results indicated that Liv.52 drops improved appetite significantly in the children. It also led to general well being of the children. There were no adverse effects attributed to Liv.52 drops.

INTRODUCTION
Appetite is the internal driving force for the search, choice and ingestion of food. Subjective sensation of hunger, satiety, other appetite sensations and desire to eat specific type of food may be influenced by a number of different internal factors including physiological and psychological variables. Many reasons can cause a child to experience a loss of appetite during the first six years. Most of them are quite normal with no reason to alarm. When children do not feel well, they invariably have loss of appetite. Sometimes, it is difficult to distinguish a normal reduction in food needs from loss of appetite. If the child looses weight and exhibits other symptoms, it may be an appetite problem. External factors such as prior meals, physical activity, temperature, and weather may influence the subjective sensations. Feeding behavior is the result of the complex central nervous system, integration of central and peripheral neural hormonal and neurochemical signals relating to the brain and metabolic states. Serotonin plays an important role in regulation of appetite and the subsequent releases of growth hormone. Changes in circulating glucose concentrations appear to elicit meal initiation and termination by regulating activity of specific hypothalamic neurons that respond to glucose. Loss of appetite in children is a very common complaint of mothers. Medications like cyproheptadine are commonly used to improve appetite. But this may lead to untoward effects like decrease in growth hormone release and inhibition of steroid release.

Hence there is a need of a safe and effective appetite stimulant. A number of herbal formulations are claimed to have appetite stimulation and Liv.52 drops is one such formulation. Present study was carried out to assess the efficacy and safety of Liv.52 drops in improvement of appetite in children.

MATERIALS AND METHODS
This open clinical evaluation was carried out in the out patient department of Paediatrics, Medical College, Kolkata in 2002. This protocol of this study was approved by local ethics committee and the parents of the children were free to withdraw from the study if they choose so. Seventy children of either sex entered into this study after informed consent obtained from one of the parents. Children with history of loss of appetite of at least one month duration
were included in the study. They underwent detailed clinical examination, hematological examination and liver function tests {serum bilirubin and serum glutamic pyruvic transaminase (SGPT)}.

Parents were advised to administer Liv.52 drops to their children in a dose of 15-20 drops twice daily, orally for a period of 12 weeks. Children were examined on a fortnightly basis for a period of three months. During this follow up, subjective evaluation of appetite, nausea, and fatigue was carried out using visual analogue scale. Anthropometric evaluation like body weight and height were also carried out. Blood examination and liver function tests were conducted initially and repeated at the end of the study.

The primary end point was subjective decrease in loss of appetite leading to increase in body weight. The secondary end point was general well beingness and adverse effects if any. Parents were asked to maintain a diary of feeding details of their children on daily basis. Adverse effects as reported by the parents were recorded during the course of the study.

**Statistical analysis:** Results were analysed statistically using Analysis of Variance.

**RESULTS**

Seventy children entered the study, three children were lost during follow up. Sixty seven children completed the study protocol of three months duration. Compliance to medication was evaluated by examining the returned medication container (Table 1).

Most of the children (40 male and 27 females) exhibited a significant improvement in their appetite score and by the end of the study period, only six out of 67 children had history of loss of appetite at the end of 3 months (Table 2). Seven of the children who had nausea at the entry of the study (n=30) had similar symptoms by the end of the study period. Weight loss seen in 60 children at entry was found in five children at 12 weeks and this change was significant (Figure 1). Fatigue was improved by treatment with Liv.52 drops. There was a significant increase in hemoglobin and serum proteins (Table 3 and Figure 2). Similarly there was a significant fall in eosinophil count by the end of the study (Table 3).

**Table 1: Demographic patients on entry**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Number (n)</th>
<th>Male : Female ratio</th>
<th>Mean age (Years)</th>
<th>Mean weight (Kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n)</td>
<td>67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male : Female ratio</td>
<td>40:27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (Years)</td>
<td>1.45 ± 0.23</td>
<td>Range 4 months to 3 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean weight (Kg)</td>
<td>4.2 ± 0.9</td>
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</tbody>
</table>

**Table 2: Effect of Liv.52 drops on clinical parameters in children with loss of appetite (n=67)**

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Number of patients showing clinical symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>67</td>
</tr>
<tr>
<td>Vomiting/Nausea</td>
<td>30</td>
</tr>
<tr>
<td>Weight loss</td>
<td>60</td>
</tr>
</tbody>
</table>

*p<0.01 as compared to baseline parameter
Statistical analysis by Fisher’s Exact Test.

**Table 3: Effect of Liv.52 drops on biochemical parameters in children with loss of appetite**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g%)</td>
<td>9.65 ± 1.89</td>
<td>11.34 ± 2.1*</td>
</tr>
<tr>
<td>Eosinophil (%)</td>
<td>5.20 ± 1.4</td>
<td>3.82 ± 1.6*</td>
</tr>
<tr>
<td>Total proteins (g%)</td>
<td>6.12 ± 0.92</td>
<td>6.72 ± 0.32*</td>
</tr>
</tbody>
</table>

*p<0.01 as compared to baseline parameter
Statistical analysis by Paired ‘t’ test
DISCUSSION
From the moment of birth, feeding becomes an important way for a parent to show love and affection. For many, feeding their child is an act full of meaning. It represents caring for the health and life of a child.

Present study indicates that Liv.52 drops have appetite improvement activity in children. For evaluation of appetite, visual analogue scales were used which are reliable for appetite research. Appetite is a complex phenomenon arising from a sequence of interactions among...
peripheral and central mechanism. The gastrointestinal tract contains chemo and mechanoreceptors that relay the information about its nutrient content to the brain mainly via the vagus nerve. Impairment of appetite or satiety may arise from peripheral or central mechanisms. Medications like cyproheptadine can improve appetite but they are known to inhibit release of growth hormone which can be detrimental to the children. In addition, it is known to decrease insulin synthesis in experimental animals. 

Liv.52 is an herbal formulation and is being used in various indications for the past many years. It has a number of ingredients that are known to improve appetite. *Cichorium intybus* is known to contain zinc which may be responsible to improve appetite. Its other ingredients are known to improve appetite by taking care of metabolism and liver functions. It is possible that the appetite stimulation by Liv.52 drops may be a synergistic effect by its various ingredients. Present study also indicates that Liv.52 drops improve fatigability, nausea and vomiting commonly seen in children and thus bring about general well-beingness of children.

Present study also indicates that this formulation is very safe and effective in the management of loss of appetite in the children.

**References**