Looking under every rock:
Duchenne muscular dystrophy and traditional Chinese medicine

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Abstract

Traditional Chinese medicine has been advocated to alleviate symptoms in Duchenne muscular dystrophy. To investigate this hypothesis, a pilot study was carried out in Beijing on 10 DMD boys treated with various regimens, including pills, decoctions, massages and acupuncture at various stages of their disease course. Despite the limited scientific impact of such a study, it seems as if the benefit, if any, is minimal. Moreover, some indirect clinical clues such as the cushingoid appearance found in a few patients suggest these drugs may also contain corticosteroids to some extent.

Keywords: Traditional Chinese medicine; Duchenne muscular dystrophy; Pilot study; Corticosteroids

1. Introduction

Fifteen years after the discovery of the DMD gene, an etiological treatment is still not available. As a result, a number of parents from Western countries are turning to alternative therapies including empirical regimens such as Chinese traditional medications. Indeed many potent drugs, such as quinine, digitalis, salicylic acid, or pervincamine, were derived from empirical plant medicines.

Chinese medicine derives from ancient times and is in part based upon an empirical pharmacopoeia consisting of a great number of vegetal, animal and mineral remedies, many of which are compiled in the famous Great Herbal, a document dating back to AD 1552 and still in use in China today [1,2]. The molecular basis of the pharmacological efficacy of an increasing number of old Chinese traditional remedies is currently being unraveled as well as their putative side effects. This is exemplified by the discovery of several potent drugs in oncology, either of mineral origin, such as arsenic trioxide [3] or of vegetal origin, such as taxol, indirubin and camptothecin [4,5].

Despite the discovery of the genetic defect in Duchenne muscular dystrophy 15 years ago and in the absence of any etiological treatment, a growing number of patients and relatives from Western countries have been turning to alternative empirical therapies such as Chinese traditional medications with various and somewhat contradictory outcomes. This prompted us to investigate the phenomenon more in depth and to hypothesize that these medications when applied to DMD patients might contain active and possibly innovative compounds.

Under the umbrella of the Duchenne Parent Project (DPP)—Holland, a preliminary pilot study was undertaken at Wangjing Hospital in Beijing where an internist, Prof. Xia, had a longstanding experience in traditional therapeutic interventions for DMD. The aims of the study were to (i) assess the diagnosis of her DMD patients on molecular grounds; (ii) substantiate any therapeutic effect and, if any; (iii) determine its pharmacological basis.
2. Methods

A team comprising one clinician (J.A.U.), two molecular biochemists (Q.S.F., J.C.K.) and one parent of the DPP-Holland (E.V.) was sent over to Beijing in 1998. Our Chinese clinical counterpart was simply asked to select the DMD patients in whom she thought the treatment had been optimally efficient. Ten patients with the clinical diagnosis of DMD or BMD were thus identified and examined both in Beijing and in the Northern province of Jilin by one of us (J.A.U.). For practical reasons, only brief manual muscle testing and an overall clinical evaluation were achieved. No functional scoring nor pulmonary tests were performed.

In the absence of proper dystrophin immunostaining in Beijing at that time, each patient was sampled for DNA studies in order to help confirm the diagnosis of DMD. Blood specimens were therefore taken and processed in Shanghai (F.Q.S.) for DNA extraction and subsequently analyzed in Paris (D.R.) where a standard search for the most frequent gene defects was performed (multiplex-PCR screening of 19 exons to detect exonic deletions, and Southern blot to detect exon duplications).

Unfortunately, no detailed individual prescription or written protocol were made available to us. We merely knew that for at least two consecutive months the 10 patients had been under different regimens comprising (i) two different types of capsules containing Chinese traditional ingredients: ‘herbal tea’, Ginseng balls (commercial brand), vitamin C, E, and Inosin (unknown dosages); (ii) acupuncture; and (iii) massage and exercise. The two types of capsules were then analyzed by T. Meier’s group in Switzerland (MyoContract Ltd., Liestal) to look for the presence of possible natural steroids.

3. Results

Nine sporadic cases aged between 7 and 15 years showed clinical symptoms and features consistent with DMD (onset in childhood, progressive proximal muscle weakness, and pseudohypertrophic calves). The last case was more suggestive of Becker muscular dystrophy given the delayed age of onset and the slower progression of the disease. Clinically, all patients were ambulant except one. However, three of them were close to loss of ambulation at age 9, 10 and 14, respectively. The majority (8/10), had limited contractures of the feet and not only in the youngest patients. The presence of overt hypercorticism was noted in three patients with significant weight gain, cushingoid appearance, hyperpilosity and short stature. Other side effects such as cataracts or bone fractures were unreported but had not been screened specifically.

In six cases, a frame-shift mutation of the dystrophin gene was found: five deletions and one duplication (see Table 1). This proportion—60%—is in accordance with the rate of gross abnormalities found in the DMD gene. The remaining cases may harbor point mutations but the screening has not been performed yet. Alternatively, they might pertain to non-dystrophinopathic conditions such as sarcoglycanopathies.

Through highly sensitive bioassay extraction of two types of capsules, there was strong evidence for the presence of at least two glucocorticoids (see the following paper by Courdier-Fruh et al.) thus confirming the clinical symptoms of hypercorticism demonstrated in some patients.

4. Discussion

From this preliminary study, it is not possible to draw any definitive conclusions regarding the beneficial effect of Chinese traditional herbal medicine in DMD patients.

From a clinical viewpoint, we have only been able to identify trends in this small population. Based on our personal experience with age-matched ambulant DMD boys, we noted an overall mild degree of contractures even though this remains very subjective. One cannot rule out the influence of non-therapeutic factors such as the ethnic background or the positive impact of massages and/or acupuncture. In terms of ambulation, the beneficial effect of the Chinese medications is even more questionable. Most patients were under 10 and apparently not far off the natural course of DMD. The only exception was an adolescent aged 15 still able to walk a few steps unaided but in whom no gross rearrangement in the DMD gene was detected. He could therefore correspond to an intermediate form of DMD or to another molecular type of muscular dystrophy. More importantly, it seems as if some of the compounds given to these children contain steroid-like substances with mild but overt clinical hypercorticism as shown in three out of our 10 cases. At this stage, there is no clue as to whether these compounds are of major interest as compared to ‘regular’ glucocorticoids prescribed in the Western world in DMD patients and that are known to slow down the disease course transiently.

On the whole, the clinical muscle or functional improvement, if any, is not dramatic and would require further studies. Ideally, controlled double-blind studies would be necessary but are rather difficult to consider in the current Chinese context where evidence-based medicine is not yet the rule. Meanwhile, it may be wise to collect more information from a larger number of patients undergoing these interventions not only in China but also worldwide. Assessing the respective benefit of each component of those Chinese medical protocols may also pose difficulties but would be useful.

This pilot study did not bring a miracle drug but was nevertheless useful to illustrate the requirements and the obstacles encountered in the scientific appraisal of Chinese
traditional medication in DMD in general. Parents of DMD boys who are tempted to have access to these drugs should be informed accordingly of their effects and potential hazards since the potential toxicity of some of these Chinese traditional medicines has clearly been demonstrated elsewhere in other conditions [6,7].

**Acknowledgements**

This pilot study was supported by the Duchenne Parent Project in Holland and briefly reported at the DPP meetings in the USA (Pittsburgh, June 2001), and in the Netherlands (Amsterdam, October 2002). We are extremely grateful to Prof. Y.Q. Xia for her invaluable help in this study.

**References**


**Table 1**

Summary of the clinical data in the 10 DMD/BMD patients seen in China

<table>
<thead>
<tr>
<th>Case</th>
<th>Id.</th>
<th>Age at examination (fall 1998)</th>
<th>DMD gene defect</th>
<th>Clinical diagnosis</th>
<th>Clinical status</th>
<th>Hypercorticism</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>GHB</td>
<td>10</td>
<td>Del 46-47</td>
<td>DMD</td>
<td>Ambulant. Very few muscle contractures.</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>WB</td>
<td>9</td>
<td>Dup 13-17</td>
<td>DMD</td>
<td>Ambulant. Very few muscle contractures.</td>
<td>0</td>
</tr>
<tr>
<td>VI</td>
<td>WJL</td>
<td>7</td>
<td>Del 51</td>
<td>DMD</td>
<td>Ambulant. Can run. Very few muscle contractures.</td>
<td>0</td>
</tr>
<tr>
<td>VII</td>
<td>CB</td>
<td>18</td>
<td>Not found</td>
<td>BMD</td>
<td>Ambulant. Reportedly stabilization of symptoms.</td>
<td>0</td>
</tr>
<tr>
<td>VIII</td>
<td>ZTY</td>
<td>14</td>
<td>Not found</td>
<td>DMD</td>
<td>Partially ambulant. Able to walk a few steps at home unaided.</td>
<td>+ +</td>
</tr>
<tr>
<td>IX</td>
<td>ZC</td>
<td>10</td>
<td>Not found</td>
<td>DMD</td>
<td>Almost off his feet. No improvement reported. Marked contractures.</td>
<td>0</td>
</tr>
<tr>
<td>X</td>
<td>YZY</td>
<td>9</td>
<td>Not found</td>
<td>DMD</td>
<td>Almost off his feet. Few muscle contractures.</td>
<td>0</td>
</tr>
</tbody>
</table>