Head-up tilt testing in children

See page 1618 (issue 22/17) for the article to which this Editorial refers

The article by Kouakam et al.[1] in issue 22/17 is a prospective observational study of syncope recurrence in 101 children (mean age 12.6 ± 3; range 7–18 years) undergoing head-up tilt testing for investigation of recurrent unexplained syncope or presyncope. Data are presented for patients recruited between 1990 and 1998, and followed-up for an average of 4 years. Head-up tilt was initially positive in 67 patients, 58 of whom had a diagnosis of vasovagal pre-syncope or syncope and nine of psychogenic syncope. Forty-three of 67 tilt-positive patients were treated in a non-randomized manner with either beta-blockers, disopyramide, midodrine, dual-chamber pacemaker or psychotherapy. Treatment decisions were based on symptom severity. The only significant predictor of syncope recurrence was the number of pre-treatment syncopal events. Syncope recurrence during the follow-up period was independent of the head-up tilt test responses and of treatment decision.

Fifteen per cent of children will have a syncopal episode before adulthood[3]. The causes of syncope in children and adolescents are similar to those described for adults, although the relative frequency and prognosis of individual diagnoses vary. Fortunately, the majority of syncopal events in young persons are isolated and benign[3]. Traditional investigations (including 12 lead ECG, 24 h Holter monitoring, EEG, glucose tolerance test, echocardiography and CT head scanning) have a diagnostic yield of less than 60% in adults[4]. In children, the reported diagnostic rate of conventional testing is even less[5].

The use of tilt testing as an investigative tool in children with unexplained or suspected vasovagal syncope was first reported in the early 1990s[6–8]. Pongiglione et al. (1990), tilted 20 subjects (ages 7–22, mean 12.5 years), to 90° for 15 min and if symptoms (pre-syncope or syncope) did not develop a head-up tilt was repeated during isoproterenol infusion. A diagnosis was achieved in 16 (4 passive, 12 isoproterenol) patients[6]. Thilenius et al. (1991) then reported a series of 35 patients with unexplained pre-syncope or syncope (ages 8–19) who had a head-up tilt to 60° for 10 min, followed by isoproterenol provocation if a passive head-up tilt was negative. A diagnosis was achieved in 70% of patients[7].

Several other investigators have since published their experience of the head-up tilt test in children and young adults. The heterogeneity of published studies mirrors that in adults. There is wide variation in the populations studied and in the head-up tilt testing protocols that is reflected in the diversity of results obtained. Several factors, including age, angle and duration of tilt, time of day and intravenous cannulation alter the results[9]. Positive diagnostic rates in children vary from 10% to 44% for passive head-up tilt[10–12]. When tilting is augmented by isoproterenol, positive rates increase to 80%[6].

In the few paediatric studies that have included a control group, sensitivity for passive tests varies from 43% to 49% and specificity from 93% to 100%[8,10,13]. Isoproterenol infusion increases test sensitivity up to 77% at the expense of a small reduction in specificity (87%)[14]. For comparison, the reported sensitivity and specificity of passive head-up tilt in adults is approximately 25% and 90%, respectively, and for isoproterenol head-up tilt 41% to 64% and 27% to 100%[15–21].

The mean time to symptoms during head-up tilt in children has been reported to be from less than 10 min (patients in 90° upright position) to 48 min (60° tilt) and is largely dependent upon the angle and length of tilt[8,13]. In the study by Kouakam et al., the mean time to symptoms during 60° passive head-up tilt was 28 (± 16) min. It has been postulated that given the lower centre of gravity in children, orthostatic stress during head-up tilt is less than that for adults[22]. Passive tilt test durations of 30–45 min at 60° to 80° have become widely accepted in laboratories evaluating older adolescents and adult patients[22]. Further diagnostic data on tilt angle and duration in the paediatric population is required.

Provocation with isoproterenol is used to increase diagnostic accuracy as part of the tilt protocol in the majority of centres[6,7,11,14]. Kouakam et al. tilted their patients to 60° for 45 min and if no symptoms occurred isoproterenol was administered. This is consistent with the consensus from published data for
<table>
<thead>
<tr>
<th>Authors</th>
<th>Title</th>
<th>Journal reference</th>
<th>No. of subjects treated</th>
<th>Age (years) (mean)</th>
<th>Tilt angle (degrees)/duration (mins)</th>
<th>Intervention (no. of paced patients in brackets)</th>
<th>Placebo/control group</th>
<th>Length of follow-up (mean, months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thilenius OG, Quinones JA, Husayni TS et al.</td>
<td>Tilt test for diagnosis of unexplained syncope in pediatric patients</td>
<td>Pediatrics 1991; 87: 334–8</td>
<td>17</td>
<td>range 8–19</td>
<td>60/10</td>
<td>Atenolol, propranolol, fludrocortisone</td>
<td>No</td>
<td>Not documented</td>
</tr>
<tr>
<td>Grubb BP, Temes-Armos P, Moore J et al.</td>
<td>The use of head-up tilt table testing in the evaluation and management of syncope in children and adolescents</td>
<td>PACE 1992; 15: 742–8</td>
<td>21</td>
<td>14; range 8–17</td>
<td>80/30 min</td>
<td>Fludrocortisone, metoprolol, transdermal scopolamine, dual chamber pacemaker (1)</td>
<td>No</td>
<td>20</td>
</tr>
<tr>
<td>Balaji S, Oslizlok PC, Alken MC et al.</td>
<td>Neurocardiogenic syncope in children with a normal heart</td>
<td>J Am Coll Cardiol 1994; 23: 779–85</td>
<td>100</td>
<td>13</td>
<td>90 (standing)/20</td>
<td>Fludrocortisone, salt replacement, pseudoephedrine, pacemaker (2)</td>
<td>No</td>
<td>18 median; range 4–40</td>
</tr>
<tr>
<td>Scott WA, Pongiglione G, Bromberg B et al.*</td>
<td>Randomized comparison of atenolol and fludrocortisone acetate in the treatment of paediatric neurally mediated syncope</td>
<td>Am J Cardiol 1995; 76: 400–2</td>
<td>58</td>
<td>13</td>
<td>80/15</td>
<td>Atenolol, fludrocortisone</td>
<td>No</td>
<td>6</td>
</tr>
<tr>
<td>Mangru NN, Young ML, Mas MS et al.</td>
<td>Usefulness of tilt table test with normal saline infusion in management of neurocardiac syncope in children</td>
<td>Am Heart J 1996; 131: 953–5</td>
<td>50</td>
<td>14; range 6–24</td>
<td>80/30</td>
<td>Fludrocortisone, salt, beta-blockers (including metoprolol), pacemaker (3)</td>
<td>No</td>
<td>12</td>
</tr>
<tr>
<td>McLeod KA, Wilson N, Hewitt J et al.*</td>
<td>Cardiac pacing for severe childhood neurally mediated syncope with reflex anoxic seizures</td>
<td>Heart 1999; 82: 721–5</td>
<td>12</td>
<td>range 2–14</td>
<td>Not documented</td>
<td>Pacemaker— all patients received dual chamber device which was programmed to ODO, VVI, or DDD for 4 month periods</td>
<td>Yes (crossover)</td>
<td>12</td>
</tr>
</tbody>
</table>

*Refers to studies whereby treatment is randomized.
optimal sensitivity and specificity. Clearly further large studies of both patients and healthy controls are required to improve the diagnostic yield in children. Of note, to the best of our knowledge, there are no reports of using glyceryl trinitrate provocation during tilting in paediatric patients. In a recent randomized controlled trial comparing 20-min glyceryl trinitrate provoked head-up tilt with 40-min passive head-up tilt in adult patients with unexplained syncope, a diagnostic test was 10 times more likely during a 20-min glyceryl trinitrate-head-up tilt.

Current guidelines for blood pressure monitoring during head-up tilt recommend beat-to-beat recordings continuously during the entire study. Finger plethysmography is the least invasive technique and has been validated in adults. In children the sphygmomanometer has been widely used in clinical practice, whereas plethysmography requires further validation during head-up tilt. However, there are reports of high accuracy and repeatability of finger plethysmography in paediatric patients over the age of 6 years.

Management of vasovagal syncope in children is similar to that in adults. Conservative measures (adequate hydration, awareness of premonitory symptoms), salt replacement, fludrocortisone, beta-blockers, transdermal scopolamine, disopyramide, midodrine and sertraline have all been used in children, with varying success. In the majority of studies, treatment is administered on an empirical basis or guided by tilt table testing. There is some evidence that beta-blocker therapy is more effective in patients who have isoproterenol tilt-induced syncope than in those who experience syncope during passive tilt alone. Scott et al. randomized a uniform cohort of 59 children (mean age 13-12 ± 3.1 years) with recurrent syncope and a positive tilt test to atenolol or fludrocortisone. At the end of the 6-month follow-up, 83% of patients had either a resolution of or a reduction in symptoms. There was no difference in outcome observed between the two treatment groups.

There are observational reports of cardiac pacing in children with prolonged asystole during head-up tilt. The total number of patients studied is small (less than 20) and there are conflicting results. McLeod et al., reported a randomized controlled trial of cardiac pacing for severe childhood vasovagal syncope associated with reflex anoxic seizures. Pacing significantly reduced episodes of loss of consciousness associated with seizures.

Table 1 is a summary of published studies reporting treatment in children and/or adolescents with recurrent unexplained syncope and tilt-proven vasovagal syncope. The table highlights the small number of patients studied, the varying angle and duration of head-up tilt employed, and the non-randomized administration of treatments.

In the present study by Kouakam et al., 43 of 67 head-up tilt-positive patients were treated empirically with oral fluids, beta-blockers, disopyramide, midodrine, psychotherapy, or dual-chamber pacemaker. The remaining 24 head-up tilt-positive patients and all head-up tilt-negative patients received no treatment. During follow-up (96% of patients were followed prospectively for an average of approximately 4 years) there was no difference in syncope recurrence between head-up tilt-negative or head-up tilt-positive patients — either treated or untreated. This raises important issues about whether children should receive pharmacological therapy or cardiac pacing. In adults without pharmacological therapy, syncope recurrence is similar in those with a positive vs those with a negative head-up tilt. Further randomized placebo-controlled trials of treatment with long-term follow-up are required to determine the benefits, if any, of treatment.

Head-up tilt testing is an established, safe diagnostic tool for the investigation of children with unexplained clinically significant syncope. The majority of studies include patients over the age 6 years, but younger children, if co-operative, can be successfully tilted. Testing should be performed under controlled circumstances by experienced staff and not delegated to the most junior doctor/nurse/technician.

The paper by Kouakam et al.[1] contributes significantly to the current literature on paediatric vasovagal syncope. The authors conclude that historical syncope is the only predictor of syncope recurrence. This information will be useful for clinicians as well as both patients and parents. The principal strength of the study is the long duration of prospective follow-up of both head-up tilt-positive and head-up tilt-negative patients. However, because treatment strategies were not randomized it is still unclear what role tilt testing plays in treatment stratification. Furthermore, it raises important questions regarding optimal treatment strategies for vasovagal syncope in children.

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References