Ability of an Upright-Supine Test to Differentiate Skew Deviation From Other Vertical Strabismus Causes

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Objective: To determine the sensitivity and specificity of a new upright-supine test to differentiate skew deviation from trochlear nerve palsy and other causes of vertical strabismus in a large number of patients.

Methods: The study consisted of 125 consecutive patients who sought treatment from January 1, 2008, through December 31, 2010, for vertical strabismus of various causes: skew deviation (25 patients), trochlear nerve palsy (58 patients), restrictive causes (14 patients), and other causes (eg, myasthenia gravis and childhood strabismus) (28 patients). Twenty healthy participants served as controls. The deviation was measured by the prism and alternate cover test using a near target at 1/3 m in both the upright and supine positions. A vertical strabismus that decreased by 50% or more from the upright to supine position constituted a positive test result.

Results: The upright-supine test result was positive in 20 of 25 patients with skew deviation (sensitivity, 80%) but negative in all patients with trochlear nerve palsy, restrictive, or other causes (specificity, 100%).

Conclusions: The upright-supine test is highly specific for differentiating skew deviation from other causes of vertical strabismus. This test could be added as a fourth step after the 3-step test, and if the result is positive, neuroimaging should be considered if indicated clinically.

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Skew deviation is vertical strabismus caused by a supranuclear lesion that disrupts the vestibulo-ocular reflex projections from the utricles in the inner ears to ocular motor nuclei (ie, the utriculo-ocular reflex). It is typically caused by damage to the brainstem, cerebellum, or peripheral vestibular system (ie, the inner ear and its afferent projections). The utricles lie roughly in the horizontal plane when the head is in the upright position; they normally detect static positions (tilts) of the head. In a previous study, it has been observed that the magnitude of vertical misalignment and ocular torsion in skew deviation is dependent on head position; it decreased substantially when patients changed from an upright to a supine position. Conversely, in patients with trochlear nerve palsy, the vertical strabismus and ocular torsion changed minimally between these 2 positions.

METHODS

STUDY PARTICIPANTS

The medical records of all adult (≥18 years of age) and pediatric (<18 years of age) patients who sought treatment for vertical strabismus at the University Health Network – Toronto Western Hospital, The Hospital for Sick Children, and private offices in Toronto, Ontario, Canada, from January 1, 2008, through December 31, 2010, were reviewed. The patients’ clinical history, ophthalmic and neurologic findings, and test results (eg, tests for myasthenia gravis, thyroid ophthalmopathy, or other orbital diseases) were recorded.

Skew deviation was diagnosed in patients who fulfilled all the following clinical criteria: (1) a vertical misalignment that is comitant, incomitant, or alternating (ie, positive or negative 3-step test result) with or without head tilt posture or fundus torsion; (2) no deficiency of depression in adduction; (3) presence of associated symptoms and signs suggestive of brainstem or cerebellar involvement;
Unilateral peripheral trochlear nerve palsy was diagnosed in patients who fulfilled all of the following clinical criteria: (1) deficient depression of the hypertropic eye in adduction; (2) incomitant hypertropia that increased with adduction of the hypertropic eye and with head tilt toward the hypertropic eye, with or without excyclotorsion (ie, positive 3-step test result); (3) absence of any other neurologic symptoms and signs; and (4) absence of any intracranial lesion on MRI. Fifty-eight patients (47 adults and 11 children) were included. Their mean (SD) age was 39.3 (19.5) years (range, 4-77 years). Twenty-three were female.

Restrictive strabismus was diagnosed based on a positive forced duction test result. In addition, all patients exhibited a compressed pattern of motility in the affected eye that did not obey the muscle sequelae of paralytic strabismus on the Hess/Lees chart.
Fourteen patients (10 adults and 4 children) were identified in this category, including those with scleral buckle that caused muscle or soft-tissue entrapment (5 patients), orbital fracture with muscle entrapment in the fracture site (4 patients), Graves disease (3 patients), and Brown syndrome (superior oblique tendon sheath syndrome; 2 patients). The mean (SD) age was 46.7 (26.3) years (range, 7-81 years). Five were female.

The other causes of vertical strabismus included conditions that were not attributable to any of these diagnoses. Twenty-eight patients (10 adults and 18 children) were identified, including those with myasthenia gravis (2 patients), oculomotor nerve palsy (1 patient), strabismus after cataract surgery (1 patient), monocular elevation deficit (1 patient), and vertical strabismus that occurred in the context of typical childhood strabismus (23 patients; eg, inferior oblique muscle overaction, dissociated vertical deviation, partially accommodative esotropia, and intermittent exotropia). The mean (SD) age was 20.9 (21.3) years (range, 4-81 years). Eighteen were female.

Twenty healthy individuals (mean [SD] age, 33.9 [18.4] years; age range, 4-70 years; 10 female), without any vestibular, neurologic, or eye diseases, served as controls. The research protocol was approved by the research ethics boards of the University Health Network and The Hospital for Sick Children and adhered to the tenets of the Declaration of Helsinki.

MEASUREMENT OF VERTICAL DEVIATION

The magnitude of vertical strabismus was measured by the prism and alternate cover test. While sitting upright with the head erect (participants were not allowed to adopt their usual abnormal head posture, if present), the participant fixated on a single-letter optotype (12-point font size) located 1/3 m away in the midsagittal plane at eye level. Prisms of increasing power were placed over the deviated eye while the cover alternated between the eyes. The highest prism strength where no refixation movement occurred was recorded in prism diopters (PD). The test was repeated with the participant in a supine position.

Figure. Percentage changes in vertical deviation from the upright to supine position for each group. A positive percentage change indicates an increase in vertical deviation from the upright to supine position, whereas a negative percentage change indicates a decrease in vertical deviation from the upright to supine position. The horizontal dashed line represents the 50% decrease threshold used to define a positive upright-supine test result. The bottom and top of the box indicate the 25th and 75th percentiles, respectively, and the band near the middle of the box indicates the 50th percentile or the median (the median and 75th percentile in the trochlear nerve palsy group, the median in the restrictive group, and the median and 25th and 75th percentiles in the healthy groups are 0%). The error bars indicate the 10th and 90th percentiles (in the skew deviation group, the 25th and 10th percentiles are −100% and the 90th percentile is 0%). Black circles indicate outliers.

The primary outcome measure was the percentage change in deviation measured from the upright to supine position. The percentage changes for all 5 groups were compared using analyses of variance. Significant effect was analyzed further using post hoc Tukey honestly significant difference tests. All statistical analyses were performed using the SAS statistical software, version 9.2 (SAS Institute Inc, Cary, North Carolina). The significance level was set at P < .05.

On the basis of the results of a previous study,3 a positive upright-supine test result was defined as a 50% or greater decrease in the vertical deviation measured from the upright to supine position. Sensitivity of the upright-supine test was calculated by dividing the number of patients with skew deviation who exhibited a positive result by the total number of patients with skew deviation. Specificity was calculated by dividing the number of patients with vertical strabismus other than skew deviation (ie, trochlear nerve palsy, restrictive strabismus, and other causes combined) who exhibited a negative result by the total number of patients with vertical strabismus other than skew deviation.

STATISTICAL ANALYSIS

The Figure shows the percentage change in vertical deviation from the upright to supine position for each group. A positive percentage change indicated an increase in vertical deviation from the upright to supine position, whereas a negative percentage change indicated a decrease in vertical deviation from the upright to supine position. The mean (SD) changes in vertical deviation were –63.3% (39.0%) in skew deviation, –2.8% (21.5%) in trochlear nerve palsy, 8.4% (23.0%) in restrictive strabismus, –0.6% (15.5%) in other causes of vertical strabismus, and 0% in healthy controls (analysis of variance, P < .001). Post hoc Tukey honestly significant difference tests revealed that patients with skew deviation exhibited a significantly different mean percentage change in vertical deviation when compared with each of the other groups (P < .001). No significant differences were found among patients with trochlear nerve palsy, patients with restrictive strabismus, patients with other causes of vertical strabismus, and healthy controls.

In patients with skew deviation, the deviation disappeared completely (ie, 100% decrease) in 9 of 25 patients (36.0%) and decreased 50% or more but less than 100% in 11 of 25 patients (44.0%) when changing from the upright to supine position. The mean (SD) decrease in vertical deviation for these 20 patients with a positive upright-supine test result was –79.1% (22.1%). Of the remaining 5 patients with skew deviation who had a negative upright-supine test result, 3 had no change (1 had a right hypertropia of 5 PD, 1 had a left hypertropia of 2 PD, and 1 had a right hypertropia of 8 PD), 1 had a 33% decrease of right hypertropia from 3 PD upright to 2 PD supine, and 1 had a 33% increase of left hypertropia from 9 PD upright to 12 PD supine. Four of these 5 patients had a lesion that involved the midbrain (1 had a pilocytic astrocytoma with vertical gaze palsy and bilateral ptosis; 1 had a midbrain infarct with vertical gaze palsy, facial nerve palsy, and ataxia; 1 had a lacunar infarct in the thalamus, midbrain, and cerebellar hemisphere with ataxia; and 1 had a cerebellar arteriovenous malformation and vasogenic edema in the mid-
In this investigation, we found that skew deviation is the only condition in which the vertical misalignment decreased by at least 50% when the patients changed from an upright to a supine position. All other vertical strabismus, including trochlear nerve palsy, restrictive strabismus, ocularmotor nerve palsy, myasthenia gravis, and vertical strabismus that occurred in the context of typical childhood strabismus, had a negative upright-supine test result. However, only 2 patients had myasthenia gravis, which is known to mimic nearly all other ocular motility disorders. Therefore, the test may not be 100% specific in all clinical populations. In addition, the study is limited because the examiners were not masked. Nevertheless, the high specificity of the upright-supine test in the current series of patients suggests that this test holds promise as an additional diagnostic step to aid the differentiation of skew deviation from other causes of vertical strabismus.

What is the physiologic basis of this new upright-supine test? Skew deviation has been attributed to an asymmetric disruption of the utriculo-ocular pathway. The utriculo-ocular pathway originates from the otolithic receptors of the utricle in the inner ear, which project to the vestibular nuclei. The second-order neurons in the vestibular organ or its afferent activities of the utriculo-ocular reflex such that any imbalance of utricular (otolithic) input is minimized. This, in turn, may lead to a reduction of vertical misalignment in skew deviation in the supine position. Conversely, in isolated unilateral peripheral trochlear nerve palsy and other causes of vertical strabismus, the utriculo-ocular pathway remains intact. Thus, the magnitude of vertical deviation does not change significantly between the upright and supine positions. We observed a few patients with trochlear nerve palsy who had a larger amount of change in vertical deviation between positions (ie, the 4 outliers in the Figure) that could not be readily explained. Nevertheless, none of them had a decrease in vertical strabismus that was 50% or greater between positions, an observation found exclusively in patients with skew deviation. Therefore, a 50% or greater decrease in vertical strabismus between positions appears to be a specific criterion to differentiate skew deviation from all other causes of vertical strabismus.

We found that 5 patients with skew deviation had a negative upright-supine test result. Interestingly, 4 of these patients had a lesion affecting the midbrain. We speculate that their vertical strabismus may have resulted from a combination of skew deviation and nuclear-fascicular trochlear nerve palsy, which may explain why the upright-supine test result was negative.

Clinical differentiation between skew deviation and trochlear nerve palsy is important because the treatment of patients with these conditions is different. Trochlear nerve palsy is typically diagnosed with the 3-step test. In contrast, the vertical strabismus in skew deviation may be comitant or incomitant, and in some cases, it may even be alternating on lateral gaze (ie, bilateral abducting hypertropia). It may mimic trochlear nerve palsy during the 3-step test with increased hypertropia on contralateral gaze and with ipsilateral head tilt; however, it may also increase on ipsilateral gaze or with contralateral head tilt, or it may remain unchanged with gaze direction or head tilt. Conversely, a long-standing trochlear nerve palsy with spread of comitance may simulate a comitant skew deviation. In addition, in both conditions, the head is usually tilted toward the side of the hypertropic eye, although the head tilt in trochlear nerve palsy is a compensatory mechanism to minimize diplopia, whereas that in skew deviation is part of the pathologic process seen in ocular tilt reaction. Furthermore, because both conditions may result from brain trauma or from lesions in the posterior fossa, differentiating skew deviation from trochlear nerve palsy can be challenging.

Fundus examination may be useful to differentiate between the 2 conditions. The fundus is usually excyclotorted in the hypertropic eye in trochlear nerve palsy, but it is usually incyclotorted in the hypertropic eye (excyclotorted in the hypertropic eye) in skew deviation. However, objective assessment of fundus torsion requires pupillary dilation and indirect ophthalmoscopy, which may not be readily available or feasible for nonophthalmologists, including neurologists and orthoptists. It is also difficult to assess fundus torsion in uncooperative patients.

Most patients with skew deviation exhibit other neurologic signs that would prompt their physicians to perform neuroimaging. However, subtle neurologic signs may sometimes be missed by general ophthalmologists and orthoptists, and brain MRI may not always be readily available. Some patients with skew deviation may have an iso-
lated vertical strabismus and a positive 3-step test result without any detectable neurologic signs. In the present study, we encountered 2 patients with acute onset of vertical deviation as a result of cerebellar hemorrhage who exhibited a positive 3-step test result that mimicked a trochlear nerve palsy, but they had a positive upright-supine test result that suggested skew deviation. The upright-supine test is thus an additional test that would be useful to alert physicians to rule out skew deviation even if the patients have typical features of trochlear nerve palsy. The test is simple and quick to perform by covering each eye alternately while patients fixate a near target at 1/3 m (eg, using a near vision card at patients’ arm length) in both the upright and supine position, with or without the use of prisms. Unlike fundus torsion, this test does not require pupillary dilation or indirect ophthalmoscopy. In some instances, we have also performed the upright-supine test by tilting the patient’s head backward while the patient sat upright (so that the head’s anteroposterior axis and thus the plane of the uiricles were aligned with the earth-vertical axis). We found the same results whether the vertical strabismus measurement was performed with the whole body or the head only in a supine position.

In the present study, we only included patients with neurologic signs to establish an unequivocal diagnosis of skew deviation. It would be interesting to investigate whether the upright-supine test would be useful in a more clinically relevant and challenging scenario—one in which a patient has an isolated vertical strabismus, a positive 3-step test result, and an absence of neurologic signs. A prospective study is currently under way to evaluate the added value of the upright-supine test beyond the classic 3-step test in this challenging scenario. This prospective study will also investigate the overall sensitivity and specificity of the combined use of the 3-step test, fundus torsion, and upright-supine test to differentiate skew deviation from trochlear nerve palsy.

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REFERENCES


**Archives Web Quiz Winner**

Congratulations to the winner of our July quiz, Arun Lakshmanan, MS, DNB, FRCS, MRCOphth, Department of Ophthalmology, Queens Medical Centre, Nottingham, England. The correct answer to our July challenge was cerebrotendinous xanthomatosis. For a complete discussion of this case, see the Small Case Series section in the August *Archives* (Monson DM, De-Barber AE, Bock CJ, et al. Cerebrotendinous xanthomatosis: a treatable disease with juvenile cataracts as a presenting sign. *Arch Ophthalmol*. 2011; 129[8]:1087-1088).

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