Radiological assessment of the atlantoaxial distance in Down's syndrome

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Abstract

People with Down's syndrome are predisposed to atlantoaxial instability. As part of a study to determine whether those with Down's syndrome should be screened for atlantoaxial instability before they participate in sport, a series of 279 children, aged 6 to 17 years was investigated radiologically. Lateral radiographs of the cervical spine were taken in neutral position and in flexion. The magnification factor was assessed by means of a marker attached to the nape of the neck. After correction for magnification 15% of the patients were found to have an atlantoaxial distance greater than 4 mm on the flexion film, especially boys under 11 years of age. However, sex and age together explained at most 9% of the variation in atlantoaxial distance. The maximum distance found was 6.5 mm. The disagreement between the means of first and second measurements by the same (test-retest) and by another (inter-) observer was more for those taken in the neutral position than in flexion. On a group level the results for reliability were satisfactory.

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Atlantoaxial instability in Down's syndrome is a well known condition.^{1–3} Before those with Down's syndrome are allowed to participate in sports some physicians think it necessary to identify those at risk of accidental damage to the spinal cord. It is of great importance to the quality of life of children with Down's syndrome to assess the real need of restricting participation in sports for those who have an atlantoaxial distance exceeding 4 or 5 mm.^{4,5} To meet this need we initiated a research project into atlantoaxial instability in Down's syndrome. With this screening aspect in mind, it is relevant to study the reliability of radiological methods for measuring the distance between atlas and axis. So far the simplest way of measuring the atlantoaxial distance is by x ray imaging of the cervical spine on a lateral film, both in neutral position and in flexion, and by correcting the distance obtained for magnification. Hinck and Hopkins,⁶ and Locke *et al*⁷ have established normal values for the atlantoaxial distance in adults and children. Locke *et al* measured this distance in 200 normal children and studied the influence of sex, age, film to tube distance, position, and reader error. They found that in radiographs of the subject supine, made with a 40 inch tube to

film distance, no child had an atlas to dens distance greater than 4 mm. Changes in position, film to tube distance, and variance in reader measurements interacted in such a way that it was difficult to draw specific conclusions about these factors. Tube to film distance did not affect the atlas to dens distance in the neutral and flexion positions. In the extension position, however, there was a significant difference.⁷ As Locke *et al* based their conclusions on the results of a one centre study, the influence of the magnification was probably consistent. As far as we know only Selby *et al* paid special attention to the reliability and to the reproducibility of the atlantoaxial distance measurement in a group of children with Down's syndrome, by repeating the study within 10 minutes in 19 children.⁸ The results were different, and the authors assumed that changes in muscle tone might have contributed to the lack of stability. In this part of our research project we studied the following in a population of children with Down's syndrome: (1) the reliability of the atlantoaxial distance measured on radiographs, (2) the influence of the magnification on the distance measured on the radiographs, and (3) the influence of gender and age on the atlantoaxial distance.

Subjects and methods

The population for this study consisted of 400 children with Down's syndrome, aged 6–17 years, from special schools all over the Netherlands. Exact figures about the total number of children with Down's syndrome in these schools are not available, but a realistic estimation is between 1000 and 1500 in this age group. The parents were informed about the purpose of the research project and about the benefits and the risks; all subjects gave their written consent by proxy. The parents themselves arranged that the radiographs of the cervical spine of their child were taken in a nearby hospital. About 40 different hospitals were involved. All parents received a letter with instructions for the radiologist. This letter explained the reason for x ray imaging and the background of the entire project about Down's syndrome and sports. Lateral radiographs of the cervical spine were taken in two positions: in neutral position and in active flexion. In order to assess the magnification factor, we gave the instruction that a marker (a large paperclip) should be fixed with adhesive tape to the nape of the neck, overlying the spinal processes of the cervical vertebrae. The paperclip was then attached to the radiograph and measured. The magnification factor was

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Age and sex distribution of 279 children studied (158 boys, 121 girls).

calculated from the ratio between the lengths of the real marker and its image projected on the radiograph. All radiographs were assessed by a single radiologist.

This study is based on the radiographs of 279 children that we could collect at a set time. The age and sex distribution of the children are shown in the figure. The two peaks in the age distribution, with a division at about 11 years, correspond with the number of births to women over 35 years in the Netherlands in the years these children were born.

The atlantoaxial distance is the distance between the posterior rim of the anterior arch of the atlas and the adjacent axis. When these lines did not run parallel, the smallest and largest distances between these lines were averaged. After nine months 25 radiographs were chosen at random and reassessed by the same radiologist, without access to the previous results. These radiographs were also assessed by a second radiologist.

On the basis of the study of Locke *et al*⁷ we decided to consider an atlantoaxial distance greater than 4 mm as abnormal. All children with an abnormal atlantoaxial distance on the first radiograph took part in a further study on participation in sports. All children were examined neurologically by the first author at least once. This included assessment of muscle power of the biceps and triceps, flexion and extension of the wrist, flexion and extension of the fingers, flexion of the hip, and flexion and extension of the knee and foot. Jaw, knee, and ankle jerks and the plantar reflexes were also examined, as was muscle tone and passive movement of the elbow, wrist, knee, and ankle. Only (sub)clonus of the knee or ankle jerk or Babinski's sign were considered as pathological.

Results

The results of x ray imaging are listed in table 1, separately for sex and age. The division in age classes was chosen in accordance with the bimodal distribution in the study group. The atlantoaxial distance, uncorrected for magnification, varied between 0.6 and 6.5 mm. The magnification factor ranged from 1.02 to 1.73 (mode 1.17, mean 1.20). When an atlantoaxial distance of 4 mm was taken as threshold value, uncorrected, as in all other studies, 88 of the 279 children (32%) had atlantoaxial instability. To eliminate the possible difference in film-focus distance in the 40 hospitals that were involved in this study, we used the real

atlantoaxial distance, that is the distance after correction for magnification. We then found 41 of the 279 distances greater than 4 mm (15%, table 2).

The test-retest and interobserver reliability of atlantoaxial measurements made by two radiologists is shown in tables 3 and 4. On average, observer 1 reported longer distances for the first measurements than for the second, and on both occasions the measured distances were greater than those reported by observer 2. There was no significant difference between measurements of radiographs in test-retest or in interobserver comparison neither in neutral position nor in flexion. Cohen's κ , a measure for agreement between two observers, which takes account of agreement by chance (maximum value 1.0), was 0.49 when the measurements were divided into three categories. This indicates moderate agreement.⁹

The variance in measured atlantoaxial distances may be partially explained by sex and age (table 5). Analysis of variance with sex and age as independent factors, in a two by two factorial design, resulted in a coefficient of

Table 1 Atlantoaxial distance: mean (SD) and 95% confidence interval (CI)* in mm, corrected for magnification (n=279)

	Mean (SD)	No	95% CI
All subjects			
Neutral	2.37 (0.80)	279	2.28 to 2.47
Flexion	3.10 (0.85)	279	3.00 to 3.20
Boys ≤ 11 years			
Neutral	2.69 (0.71)	84	2.54 to 2.85
Flexion	3.47 (0.79)	84	3.30 to 3.64
Boys > 11 years			
Neutral	2.31 (0.90)	64	2.09 to 2.54
Flexion	2.99 (0.92)	64	2.76 to 3.22
Girls ≤ 11 years			
Neutral	2.17 (0.67)	64	2.00 to 2.33
Flexion	2.94 (0.75)	64	2.75 to 3.13
Girls > 11 years			
Neutral	2.18 (0.80)	52	1.96 to 2.41
Flexion	2.88 (0.80)	52	2.66 to 3.10

*95% CI is the range of values which contains the true population mean with a probability of 0.95.

Table 2 Number (%) of children with Down's syndrome and atlantoaxial instability

	Before correction		After correction	
	≤ 4 mm	> 4 mm	≤ 4 mm	> 4 mm
Boys				
≤ 11 years	42 (52)	39 (48)	60 (74)	21 (26)
> 11 years	52 (67)	25 (33)	68 (88)	9 (12)
Girls				
≤ 11 years	49 (77)	15 (23)	60 (94)	4 (6)
> 11 years	48 (84)	9 (16)	50 (88)	7 (12)
Total	191 (68)	88 (32)	238 (85)	41 (15)

Table 3 Mean (SD) and 95% confidence interval (CI) of the uncorrected atlantoaxial distance in mm and of the magnification factor for repeated measurements (n=25)

	Mean (SD)	95% CI
Observer 1, measurement 1		
Neutral	3.4 (1.1)	2.9 to 3.9
Flexion	4.4 (0.9)	4.0 to 4.9
Magnification	1.2 (0.1)	1.2 to 1.3
Observer 1, measurement 2		
Neutral	3.3 (1.4)	2.6 to 3.9
Flexion	4.3 (1.1)	3.8 to 4.8
Observer 2		
Neutral	2.9 (1.3)	2.3 to 3.5
Flexion	4.3 (1.0)	3.8 to 4.7
Magnification	1.2 (0.1)	1.2 to 1.3

Table 4 Mean, SD, and SE of the differences between test-retest and interobserver measurements of the atlantoaxial distance in mm made in neutral position and in flexion

	Neutral			Flexion		
	Mean	SD	SE	Mean	SD	SE
Test-retest, observer 1	0.145	0.692	0.148	0.205	0.700	0.149
Interobserver	0.305	0.717	0.153	0.123	0.630	0.134

determination of 9.4%. Thus, more than 90% remains unexplained by the factors sex and age. Besides the inaccuracy of measurements, other factors may be relevant to explain the differences in the atlantoaxial distances in children, such as genetic predisposition or sporting practice.

The presence or absence of abnormal reflexes was not related to either the threshold value of 4 mm or the difference in the distance measured in flexion and in the neutral position. This lack of relation was also observed for the other threshold values (table 6).

Discussion

The prevalence of atlantoaxial instability among people with Down's syndrome depends on several factors, particularly on the threshold value and on whether or not correction is made for magnification on the radiograph. The threshold value of 4 mm is based on the study of Locke *et al*⁷ and is used by several investigators.^{2 3 10} In contrast, Semine *et al* used 4.5 mm as a threshold value,¹¹ and Martel and Tishler¹² and Pueschel and Scola 5 mm.¹ In our opinion the normal value for the atlantoaxial distance in children with Down's syndrome should take into account the inaccuracy of the measured distance. Error might be caused by technical aspects such as the quality of the film or by observer inconsistency. Hinck and Hopkins emphasised that 'the error resulting from the use of crude measuring techniques, though unimportant in measuring distances of several centimeters, may take on statistical significance when measuring 1 or 2 mm. This becomes particularly critical when working with values considered to be at the limits of the normal range'.⁶ We confirmed that, on repeated measurement, the differences between the means of two measurements of distances in neutral position were greater than those in flexion. This is probably because the absolute distance is somewhat greater in flexion than in the neutral position. Similarly, the greater length of the paperclip probably explains why there is no difference in the mean of this measured length, although the less distinct borders of bony structures may also influence the variability of the atlantoaxial

Table 6 Relation between appearance of abnormal reflexes and atlantoaxial distance

	≤4 mm	>4 and ≤5 mm	>5 mm
No abnormal reflexes	140	26	3
With abnormal reflexes	27	6	1
Total	167	32	4

χ² 0.33, p=0.84.

distance. On the whole the results for the test-retest and interobserver reliability were satisfactory on group level. But the result of a single radiograph can differ substantially, according to the standard deviations in table 4. To decrease error in the measurement of atlantoaxial distances, it would be best to use the average value of two measurements made by different observers. Pueschel *et al* think that the difference in the atlantoaxial distance, measured on a radiograph and on a computed tomogram, can be explained by magnification.¹³ As far as we know only the study of Martel and Tishler took the magnification factor into account.¹² Our method is easy to perform and the magnification factor is reliable; the device proposed by Singer *et al* is more sophisticated.¹⁴ With correction for magnification (and an uncorrected threshold value of 4 mm), we found the percentage of children with atlantoaxial instability (15%) similar to that of other studies (performed in one centre) without correction.¹⁻³ The question arises whether the threshold value found by Locke *et al*⁷ should also be corrected for magnification. After adjustment for magnification, using the mode of the magnification factors we found, the cut off value of Locke *et al* would be 3.4 mm; 100 of the 279 children had longer distances (35%).

In our group of 279 children, the maximum atlantoaxial distance was 6.5 mm. With a threshold value of more than 4 mm, it does not mean that children who have a longer atlantoaxial distance are definitely at risk of spinal cord damage. No relation was found between abnormal reflexes and the atlantoaxial distance. An explanation for this could be that the appearance of abnormal reflexes is not specific for spinal lesions at the cervical level.

x Ray imaging is one of the best methods to detect atlantoaxial instability, and is better than laxity assessment.¹⁵ The current normal range for values is not adequate, however, as it does not take magnification into account and the measured distances are not reliable enough in that range. Screening, in general, is only useful if prevention of accidents is possible or treatment in an early stage is

Table 5 Differences in atlantoaxial distance (mm) in neutral position and in flexion between boys and girls and between ages

	Boys		Girls		Difference (SE) between ages		Difference (SE) between boys and girls	
	≤11 years (n=84)	>11 years (n=64)	≤11 years (n=64)	>11 years (n=52)	Boys	Girls	≤11 years	>11 years
Neutral	2.69	2.31	2.17	2.18	-0.38 (0.14)**	0.01 (0.16)	0.52 (0.14)**	0.13 (0.16)
Flexion	3.47	2.99	2.94	2.88	-0.48 (0.14)**	-0.06 (0.16)	0.53 (0.14)**	0.11 (0.16)

**p<0.01.

available. The advice that, if atlantoaxial instability exists, certain sports should be avoided to prevent accidents has not been supported by evidence from our studies¹⁶ and those of others.

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