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BLEEDING TIME AND SCOLIOSIS

ALF UDÉN, INGA MARIE NILSSON & STIG WILLNER

Departments of Orthopaedic Surgery and the Coagulation Laboratory, Malmö General Hospital (University of Lund, Malmö, Sweden

Collagen abnormalities in idiopathic scoliosis are on record. Since there is a correlation between the platelet aggregating power of the collagen and the bleeding time in patients with scoliosis, the bleeding time was studied in 195 cases with scoliosis and in 318 controls. The bleeding time was longer in the females, especially in those with idiopathic scoliosis (n = 149). Patients with paralytic scoliosis (n = 5) also had a significantly longer bleeding time than non-scoliotic controls. The patients with congenital scoliosis (n = 13) did not differ significantly from the controls or from patients with idiopathic scoliosis. The bleeding time in idiopathic scoliosis did not vary with age or magnitude of the scoliosis. Our data support the view that collagen abnormalities play a role not only in the aetiology of idiopathic scoliosis, but also in other forms of scoliosis.

Key words: bleeding time; collagen; scoliosis

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Collagen is responsible for most of the tensile strength of the connective tissue. It also plays an important role in normal haemostasis. When a vessel wall is damaged platelets adhere to the exposed subendothelial collagen, and this contact initiates a chain of reactions resulting in the formation of a platelet thrombus (Gordon 1979).

Collagen abnormalities have been described in idiopathic scoliosis (Francis et al. 1977, Bushell et al. 1978, Udén et al. 1980a). In adolescent idiopathic scoliosis the platelet aggregating power of collagen is decreased and the bleeding time prolonged (Udén et al. 1980a). Similar abnormalities are sometimes seen also in congenital scoliosis (Udén et al. 1980b). These observations have been made in collagen from fascia specimens obtained at surgery of patients because of moderate or severe scoliosis (>45°). We do not think it ethical to obtain biopsy specimens of fascia from patients with only mild scoliosis not requiring surgery. Therefore, nothing is known about the collagen in such cases. However, there is a correlation between the platelet aggregating power of the collagen and the bleeding time in scoliosis (Udén & Nilsson 1979). It was therefore decided to study the bleeding time in idiopathic, congenital and paralytic scoliosis with respect to sex, age and magnitude of the scoliosis.

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CLINICAL MATERIAL

The material consisted of 108 patients operated on for scoliosis at the Department of Orthopaedic Surgery, Malmö General Hospital, and 86 patients who were treated conservatively with a brace or only expectantly. The material is summarized in Table 1.

The patients with congenital scoliosis had a unilateral bar on the concave side and/or one or several hemivertebrae. Of the 5 patients with paralytic scoliosis 2 had cerebral palsy, one had had poliomyelitis, one had the progressive neuromuscular atrophy of Charcot-Marie Tooth and one suddenly developed paraplegia (anterior

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Table 1. Age and sex distribution of patients with scoliosis

Type	Males	Years AV±SD	Females	Years AV±SD
Idiopathic				
operated on	(13)	18±4	(79)	18±4
not operated on	(14)	16±2	(70)	14±2
Congenital				
operated on	(5)	17±1	(6)	14±3
not operated on	–	–	(2)	13±1
Paralytic				
operated on	(3)	19±1	(2)	24±12
not operated on	–	–	–	–

Figures within brackets indicate number of patients.

Table 2. Age and sex distribution of the controls

	Males	Years AV±SD	Females	Years AV±SD
Controls	(167)	41±19	(151)	39±19
≤ 25 years	(37)	14±5	(46)	15±5
≥ 26 years	(130)	49±14	(105)	49±13

Figures within brackets denote number of patients.

spinal artery syndrome) at 13 years of age. Twenty-four healthy volunteers and 357 patients without known bleeding diathesis and tested at the Coagulation Laboratory, Malmö General Hospital, prior to microsurgery served as controls (Table 2). Since the mean age of the controls was higher than that of the groups with scoliosis and since only a few of the patients with scoliosis were older than 25 years, the controls were divided into two groups, one below 26 years and one 26 years or above.

METHODS

The following determinations were made in the 108 patients operated on for scoliosis.

Coagulation time in glass and plastic tubes, recalcification time, bleeding time according to Duke and Ivy, platelet count, platelet adhesiveness in whole blood according to the method of Hellem and according to the method of Salzman, factor VIII, factor IX, factor XI, factor XII, one-stage prothrombin time, Owren's P & P test (prothrombin factor VII and factor X), factor V, fibrinogen, fibrinolytic activity of plasma and resuspended euglobulin precipitate on unheated fibrin plates, euglobulin clot lysis time, plasminogen by an immunological method, and fibrin degradation products (FDP) (Nilsson 1974).

In all the patients and the controls the *bleeding time* was determined according to *Ivy*, as modified by Borchgrevink & Waaler (1958) and Nilsson et al. (1963). A cuff was wrapped round the upper arm and inflated to a pressure of 40 mm Hg. About 30 to 60 seconds later two transverse incisions were made just below the elbow fold. The incisions were made either with the blade of a surgical knife (Swan Morton No. 11) or with a disposable Simplate II™. The incisions were 1 mm deep and 10 mm long when made with a blade and 5 mm long when made with a Simplate II™. The blood was blotted every 30 seconds as long as bleeding continued. The mean of the bleeding times after the two incisions was taken as the bleeding time. The values found did not vary with the technique used. Thus, in 255 patients the surgical blade technique gave a bleeding time of 7.75 ± 2.26 (AV ± SD) and the Simplate II™ technique gave 7.69 ± 2.40 (AV ± SD) (Nilsson et al. 1979).

Statistical methods used were Student's *t*-test, for checking the significance of differences between means, and Pearson's correlation test.

RESULTS

The bleeding time in the different groups with scoliosis and in the controls is given in Table 3. In

Table 3. Ivy bleeding time in patients with scoliosis and controls

	Males	AV±SD	Females	AV±SD	Total	AV±SD
Idiopathic scoliosis	(27)	8.5±2.0	(149)	10.0±2.8	(176)	9.8±2.8
Congenital scoliosis	(5)	7.5±1.6	(8)	9.2±2.2	(13)	8.5±2.1
Paralytic scoliosis	(3)	10.3±3.2	(2)	12.0±1.0	(5)	11.0±2.5
Controls ≤ 25 years	(37)	8.3±1.9	(46)	8.7±2.0	(82)	8.5±2.0
Controls > 25 years	(130)	7.8±2.4	(105)	8.2±2.2	(236)	8.0±2.3
Controls total	(167)	7.9±2.3	(151)	8.3±2.3	(318)	8.1±2.3

Figures within brackets denote the number of patients or controls.

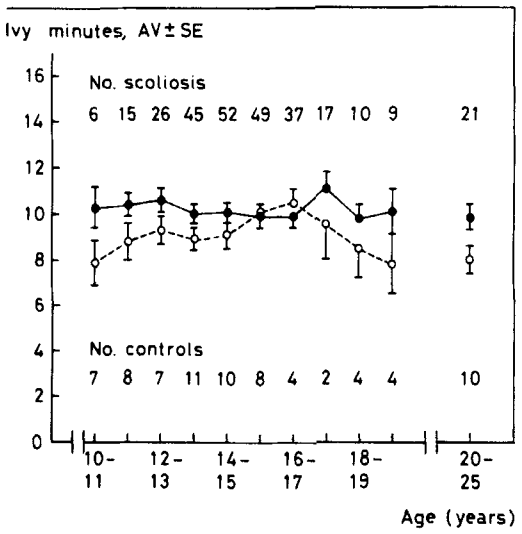

Figure 1. Bleeding time (Ivy) in relation to age. Running average and standard error for females with idiopathic scoliosis and female controls. No significant correlation.

all the groups the mean bleeding time was longer in the females. But the difference was statistically significant only in the idiopathic scoliosis group ($P < 0.01$) and if all the females were pooled and compared with all the males ($P < 0.001$). There were no significant correlations between age and bleeding time, either in the controls or in the group with idiopathic scoliosis (Figure 1). Thus the coefficient of correlation was –0.08 in the male controls ($n = 167$) and –0.02 in the females ($n = 151$); in the males with idiopathic scoliosis it was 0.32 ($n = 27$) and in the females 0.14 ($n = 149$). However, since the bleeding time was somewhat longer though not significantly in controls below 26 years than in controls 26 years or older (Table 3), the scoliosis groups were also compared with this age-matched control group.

The mean bleeding time in the females with idiopathic scoliosis was longer than in the female controls ($P < 0.001$). It was also longer than in the age-matched female controls ($P < 0.005$). However, the males with idiopathic scoliosis did not differ significantly from the male controls.

The mean bleeding time in patients with congenital scoliosis did not differ significantly from that in the controls or from that in patients with idiopathic scoliosis. The mean bleeding time in the 5 patients with paralytic scoliosis was significantly longer than that in the controls ($P < 0.01$). Compared with the bleeding time in the age-matched controls the difference was also significant ($P < 0.02$). No correlation was found between age at onset of the scoliosis and the bleed-

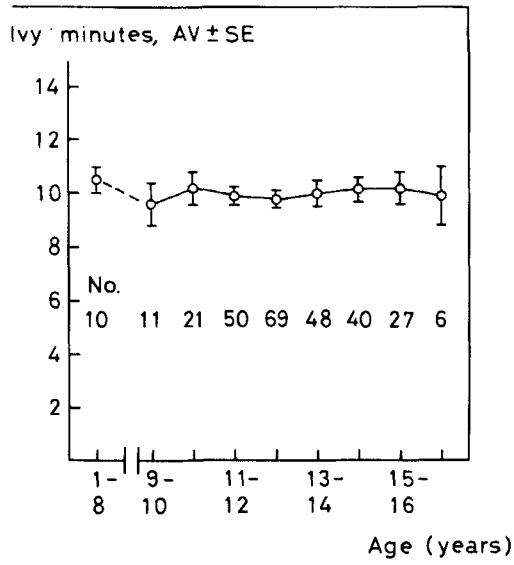

Figure 2. Bleeding time (Ivy) in relation to age (CA) at onset of the scoliosis. Running average and standard error for females with idiopathic scoliosis. No correlation between age at onset and bleeding time.

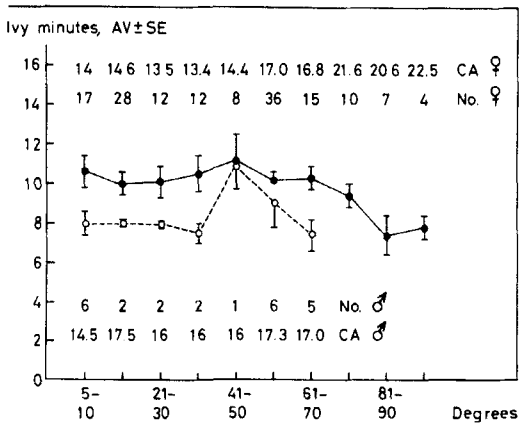

Figure 3. Bleeding time (Ivy) in relation to the magnitude of the scoliosis. Average and standard error for males and females with idiopathic scoliosis. No significant correlation between magnitude of the curves and bleeding time.

ing time (Figure 2). Neither was any correlation found between the bleeding time and the magnitude of the scoliosis in the idiopathic cases (males $r = 0.29$, $n = 27$, females $r = -0.15$, $n = 149$. This is also illustrated in Figure 3.

Of 79 females operated on for idiopathic scoliosis, only 16 showed minor abnormalities in the coagulation and bleeding tests. The fibrinolytic activity was slightly to moderately increased in 12 of them, and the platelet adhesiveness was slightly decreased in 4. In one patient factor VII was low (50 per cent). In this group of patients with minor abnormalities in the haemostatic tests, the mean bleeding time was 10.3 ± 3.1 minutes (AV ± SD). The mean value for the other 63 females was 9.7 ± 2.5 (AV ± SD). The difference was not statistically significant.

DISCUSSION

The Ivy bleeding time modified in the way described by Nilsson et al. (1963) is a sensitive test capable of detecting even small abnormalities in primary haemostasis. The mean bleeding time in the patients with scoliosis was longer than that in the controls, but the bleeding time in most of the patients with scoliosis was within the normal range, and in the few in whom it was prolonged it was not attended by any detectable increase in blood loss at surgery for scoliosis.

Laboratory studies of the patients operated on for scoliosis did not show any abnormalities, such as von Willebrand's disease or platelet defects, which could otherwise explain the prolonged bleeding time. In some patients with scoliosis the fibrinolytic activity was slightly increased. Such an increase can be due to stress during blood sampling (Brozovic 1977) and a similar increase could also be expected in the controls who were also exposed to the same stress.

A correlation between the platelet-aggregating power of the collagen and the bleeding time has been reported in an earlier paper (Udén & Nilsson 1979). It is therefore tempting to assume that the prolonged bleeding time in scoliosis might be caused by abnormalities of the collagen and possibly play a role in several types of scoliosis since the bleeding time was prolonged not only in the females with idiopathic scoliosis but also in the few cases with paralytic scoliosis. In fact, collagen abnormalities have been reported also in congenital scoliosis (Francis et al. 1976, Udén et al. 1980b). One possible explanation for these abnormalities in all three types of scoliosis might be secondary alterations due to an increased turnover of collagen caused by rebuilding of the connective tissue during the progress of the scoliosis, but since the bleeding time is prolonged also in adults in whom the scoliosis is supposed to be non-progressive, this explanation is not likely. Nor is the bleeding time more prolonged in the severe cases, which would be the case if the abnormalities were secondary.

A tempting hypothesis is that the scoliosis can be initiated by other factors, such as disturbed equilibrium in idiopathic scoliosis (Sahlstrand 1977), paralytic muscles, as in paralytic scoliosis, or malformations of the vertebrae, as in congenital scoliosis, and that the defective collagen allows the curvature to progress as proposed by Bushell et al. (1979). Our data do not lend support to the assumption that collagen has a major influence on the progress of scoliosis for no correlation was found between the bleeding time and the severity of the scoliosis, possibly because the bleeding time is too crude an indicator of collagen abnormalities.

The bleeding time was longer in the females although the difference was statistically significant only in idiopathic scoliosis. This sex difference remains unexplained. However, it could be relevant since clinically important scoliosis is more common in females. Again, this is true for idiopathic and congenital cases (Winter et al. 1968, Nordwall 1973), but not for paralytic scoliosis (James 1976).

Genetic studies support a multifactorial aetiology of idiopathic scoliosis (Filho & Thompson 1971, Riseborough & Wynne-Davies 1973) and neuromuscular, hormonal and constitutional factors may be involved (Sahlstrand 1977, Willner 1974, Willner et al. 1976). In congenital scoliosis the malformation is of obvious importance and in paralytic scoliosis the paralysis. However, our findings suggest that also collagen abnormalities may play a role in the development not only of idopathic scoliosis, but also of other forms of scoliosis.

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Correspondence to: Alf Udén, M.D., Department of Orthopaedic Surgery, Malmö General Hospital, S-214 01 Malmö, Sweden