Risk Factors for Fragility Fractures in Persons With Developmental Disabilities

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Abstract

Persons with moderate to severe developmental disabilities are at risk for low-trauma fractures but the associated risk factors have not been well-delineated. A chart review of 224 persons with developmental disabilities living in a residential care facility found that 40 (18%) had sustained 47 low-energy fractures of the appendicular skeleton. Logistic regression demonstrated a strong association between Aboriginal ethnicity and fractures that was not accounted for by other measured variables (adjusted odds ratio [OR] 3.03, 95% CI 1.38-6.69). Phenobarbital use was also a strong independent predictor (OR 2.69, 95% CI 1.18-6.12). The recognition of the high rate of fractures in this population as well as these risk predictors may help to direct screening and targeted interventions for those found to be at highest risk.

The epidemiology, pathogenesis and impact of osteoporosis have been well-described in the general population in recent years. Osteoporosis affects one in four women and one in eight men over the age of fifty years, and is associated with a considerable morbidity. Risk factors for osteoporotic fractures have been established by large long-term epidemiological studies primarily focused on elderly ambulatory populations (Cummings et al., 1995; Dargent-Molina et al., 1996). The risk factors in less-mobile institutionalized groups have not been as well studied. One such population, children and young adults with moderate to severe developmental disabilities, have been shown to have a high rate of fractures after minimal trauma (Lee & Lyne, 1990; Peabody & Stasikelis, 1999). There are limited data describing the incidence of osteoporosis in people with severe intellectual or physical disability, either in a residential facility or living in the community. There has certainly been no cohesive effort to delineate specific risk factors for osteoporosis in this subgroup.

St. Amant Centre in Winnipeg, Canada, offers a wide range of individualized programs and services for children and adults with developmental disabilities and their families, including residential care. Although the resident population is relatively young (oldest resident aged 48 years), several low-trauma fractures are observed each year in a population of only 224 residents. This prompted a systematic review of medical and demographic data of the residents to try to isolate specific factors that might put them at higher risk for low-energy fractures.

Method

The study population included all residents (n=224) at the facility between 1996 and 1999. There were no exclusion criteria. The residents are typically admitted to the facility in childhood or adolescence and there is relatively little turnover in the population. This study was approved by the Research Ethics Board at St. Amant Centre.

Demographic data and medical records were available for all subjects. Charts of these residents were reviewed to establish a fracture history at any time during the resident's admission. All fractures were confirmed by radiographs reviewed by a radiologist. Low energy fractures (also known as fragility fractures) were defined as fractures that occurred with no trauma or falling from a standing height or less. The charts were reviewed for demographic data and risk factors for fracture identified in other populations (Brown & Josse, 2002), as well as factors known to affect bone metabolism, such as long term administration of anti-seizure therapy. Anthropometric measurements including height, weight, and triceps skin fold thickness (TSF) were also obtained from a large subset of residents (88%). Standing height was measured using a stadiometer. Where an individual was unable to stand, height was measured in a recumbent position using a measuring tape. Triceps skin fold thickness was measured by a dietician using a standard technique. The dietary intake of all residents is carefully monitored by registered dieticians, and decisions regarding calcium, vitamin D, or multivitamin supplementation were left to the discretion of the dietician and the resident's physician. Biochemical investigations were only done as clinically appropriate.

Univariate between-group differences were assessed using analysis of variance (ANOVA) for continuous variables and Pearson's Chi-Square test for categorical variables (SPSS for Windows, Chicago IL). The level of statistical significance used was $p<0.05$. Factors contributing to fracture risk were analyzed using multivariate logistic regression. Variables with a $p<0.2$ on univariate analysis were entered into the logistic regression model.

Results

Of the 224 residents evaluated during the study period, there were 109 females and 115 males. There were 43 residents of Aboriginal ethnicity defined as having Treaty Status or a Band number. The other residents were of European ancestry. One hundred and forty-five residents (65%) were determined to be immobile, and were wheelchair users or restricted to a bed. Many of the residents (43%) had one or more joint contractures and most (75%) had a seizure disorder requiring medication. Other demographic data is summarized in Table 1.

Table 1: Demographics and medical characteristics of the study population.

	Mean ± SD	Range
Age (years)	25 ± 9	4-48
Height (cm)	152.1 ± 13.6	107.0-189.0
Weight (kg)	48.6 ± 12.4	18.3-93.1
Body mass index (kg/m2)	20.8 ± 3.4	13.5-39.8
Triceps skinfold thickness (mm)	17 ± 6	5-35
Female	109 (49%)	
Aboriginal	43 (19%)	
Immobile	145 (65%)	
Joint contracture	96 (43%)	
Seizure disorder	169 (75%)	
Seizure medications		
phenobarbital	84 (38%)	
phenytoin	28 (13%)	
carbamazepine	43 (19%)	
valproic acid	46 (21%)	

Forty (18%) of the residents sustained one or more low-energy fractures. A total of 47 fractures were observed as some residents experienced multiple fracture events. All fractures were appendicular with femur being the predominant site (Table 2).

Comparisons between individuals who sustained fractures and the non-fracture residents are detailed in Table 3. Fifteen (38%) of the fracture group were of Aboriginal ethnicity, compared with only 28 (15%) of the non-fracture group and the difference was statistically significant ($p <= 0.001$). The proportion of residents receiving phenobarbital was also significantly greater (56% fracture versus 33% non-fracture, $p = 0.004$). None of the other

anti-epileptic agents showed this relationship. The triceps skin-fold measurement showed a borderline difference (fracture and non-fracture groups means 18.6 mm and 16.3 mm, respectively, *p*=0.059). There also appeared to be a slight predominance of females (60% fracture group versus 46% non-fracture group, *p*=0.11), but the difference was not statistically significant. Age, height, weight, and body mass index were similar. Primary diagnosis, immobility and gonadal status were also unrelated to the presence of a fracture history.

Table 2:   Distribution of low-energy fracture sites (% of all fractures).

	Fracture sites
Femur	27 (57%)
Humerus	11 (23%)
Tibia	4 (9%)
Fibula	2 (4%)
Clavicle	1 (2%)
Radius	1 (2%)
Metacarpal	1 (2%)

Table 3:   Univariate comparisons between fracture and non-fracture groups.

	Fracture (n=40)	*Non-fracture (n=184)*	*p*
Age (years)	28.6 ± 10.8	29.8 ± 8.8	>.2
Female	24 (60%)	85 (46%)	.11
Aboriginal	15 (38%)	28 (15%)	.001
Immobile	28 (70%)	117 (64%)	>.2
Seizure disorder	30 (75%)	139 (76%)	>.2
Seizure medication			
phenobarbital	23 (56%)	61 (33%)	.004
phenytoin	4 (10%)	24 (13%)	>.2
valproate	7 (18%)	39 (21%)	>.2
carbamazepine	11 (28%)	32 (17%)	.14
Total number of seizure drugs	1.5 (1.3)	1.2 (1.1)	.17
Joint contractures	19 (48%)	77 (42%)	>.2
Height (cm)	149.8 ± 11.0	152.5 ± 14.0	>.2
Weight (kg)	47.5 ± 9.5	48.9 ± 12.9	>.2
Body mass index (kg/m2)	21.1 ± 3.5	20.7 ± 3.4	>.2
Triceps skinfold thickness (mm)	18.6 ± 6.6	16.1 ± 5.8	.059

The logistic regression analysis is summarized in Table 4. Triceps skinfold thickness (TSF) was excluded from the base model as measurements were not available for 54 of the residents. This demonstrated that Aboriginal ethnicity (odds ratio [*OR*] 3.03, 95% *CI* 1.38-6.69) and use of phenobarbital were still strong predictors of fractures (*OR* 2.69, 95% *CI* 1.18-6.12). A second regression model which included TSF did not change the effect of Aboriginal ethnicity (*OR* 3.16, 95% *CI* 1.22 - 8.21), but eliminated the contribution of phenobarbital (*OR* 1.01, 95% *CI* 0.41 - 2.50). A final regression model included age and immobility but again did not change the effect of Aboriginal ethnicity (*OR* 3.12, 95% *CI* 1.34 - 7.30) or phenobarbital use (*OR* 2.45, 95% *CI* 1.17 - 5.13).

Table 4: Multivariate logistic regression analysis of factors associated with a low-energy fracture.

Variable	Odds Ratio (95% CI)	p
Female	1.36 (0.65-2.8)	>0.2
Phenobarbital	2.69 (1.18-6.12)	.0184
Carbamazepine	2.31 (0.84-6.34)	.104
Aboriginal	3.03 (1.38-6.69)	.006
Total seizure medications	0.91 (0.59-1.39)	>0.2

Fractures of the proximal and distal femur accounted for 57% of the total fragility fractures. A subsequent logistic regression analysis was restricted to femoral fractures. There appeared to be an even stronger relationship between Aboriginal ancestry and femoral fractures (*OR* 4.55, 95% *CI* 1.84-11.23). The relationship with phenobarbital use appeared to be maintained, but was no longer statistically significant (*OR* 1.96, 95% *CI* 0.77-4.98).

The Aboriginal and non-Aboriginal residents were compared in univariate analyses (Table 5). The Aboriginal residents were younger (*p*<0.001) and had proportionately more females (*p*=0.086). A slightly higher proportion were taking phenobarbital (*p*=0.40), and the mean weight was lower (*p*=0.017). These factors did not weaken the association between ethnicity and fractures when included in a final regression model, however.

Table 5:   Univariate comparisons between Aboriginal and non-Aboriginal groups.

	Aboriginal (n=43)	Non-Aboriginal (n=181)	p
Age (years)	23.7 ± 6.9	31.0 ± 9.0	<.001
Female	60.5 %	45.9%	.086
Immobile	63.5%	69.8%	>.2
Seizure disorder	79%	75.0%	>.21
Seizure medication			
phenobarbital	51.1%	34.3%	.040
phenytoin	9.3%	13.3%	>.2
valproate	18.6%	18.6%	>.2
vigabatrin	4.7%	2.2%	>.2
Joint contractures	41.9%	43.1%	>.2
Height (cm)	149.4 ± 12.3	152.7 ± 13.8	.188
Weight (kg)	44.1 ± 9.4	49.6 ± 12.8	.017
Body mass index (kg/m2)	19.5 ± 2.3	21.0 ± 3.6	.026
Triceps skinfold thickness (mm)	16.9 ± 5.5	16.4 ± 6.1	.701

Discussion

This study demonstrates a high rate of low energy fractures in a relatively young population. The major risk factors for osteoporosis described in other populations (Brown & Josse) are not prevalent in this population, which suggest that there are other factors contributing to bone fragility that are more specific to this setting. Most (65%) of the population were restricted primarily to bed or wheelchair, and this immobility could be expected to contribute significantly to fracture risk. The lack of effect of immobility on the observed fracture rate is probably related (at least in part) to fewer falls in this group who are non-ambulatory. Unfortunately, we are unable to accurately estimate the incidence of falls in our study population. We also do not have more specific measures of mobility in the non-immobile group, many of whom have limited ambulation.

Factors that did contribute to fracture risk in our analysis included use of anti-epileptic drugs (AED), and more specifically phenobarbital (*OR* 2.69). The risk of fracture with carbamazepine use also appeared to double, but

was not significant. The effect of various AED on bone density and quality is well-described, and has been attributed in part to changes in vitamin D metabolism (Farhat et al., 2002; Sato et al., 2001). Phenytoin, phenobarbital, primidone, and valproic acid have all been specifically linked with these changes, but there is little data on the effects of newer AED such as lamotrigine, topiramate, vigabatrin and gabapentin. Seizure activity itself can cause fractures in an immobile person due to the sudden strong muscle contraction on a weakened bone, or can precipitate falls in an ambulating person. The strong contribution of phenobarbital to fracture risk in this study underscores the importance of interventions such as prophylactic vitamin D supplementation. Biochemical measures were not performed systematically in this study population, but 25-hydroxyvitamin D concentrations and alkaline phosphatase measurements were not impressively different in individuals sustaining fractures or using AED (data not shown). In studies of ambulatory populations using anti-epileptic drugs, vitamin D deficiency has been identified, but does not correlate well with bone mineral density measurement (Farhat et al., 2002). This suggests that the impact of these drugs on bone quality is only partly mediated through vitamin D effect.

Independent of the effect of AED, the prevalence of vitamin D deficiency is high in elderly residents of longterm care facilities, especially but not limited to winter months (Liu et al., 1997). Recent Canadian guidelines recommend a daily vitamin D intake of 400 units per day in the general population under age 50, and 800 IU per day above age 50 for men and women (Brown & Josse, 2002). Given the data on prevalence of vitamin D deficiency in institutions, the high rate of AED use, and the high fracture rate, routine supplementation with vitamin D 800 units should be considered in settings described in this study.

Other studies have looked at the effects of the joint contractures, where even routine care can fracture a long bone due to the levering action against a fixed joint such as hip, knee or shoulder (Brunner & Doderlein, 1996). This was not found to be a factor in our study, however.

The association with Aboriginal ethnicity and increased fracture rates has been previously identified in the general adult population through a retrospective analysis of administrative health databases (Leslie, W. D., et al., 2000 & 2004). Increased fracture rates were seen in both males and females and at all ages. The threefold increase in risk of all types of fracture seen in our Aboriginal cohort with developmental disabilities living in a residential care facility cannot be attributed to other measured factors. The effect is also seen when restricting the analysis to femoral fractures, which

are especially associated with morbidity. The mechanism of the effect of ethnicity in this specific setting or in the larger population is not clear, and should be the focus of further study. Measurements of bone mineral density (BMD) would be valuable, as this is the best predictor of fracture risk in other populations. BMD measurements of proximal femur and lumbar spine are practically difficult to obtain in this population given the prevalence of joint contractures and other deformities, as well as the logistical issues in transferring immobile subjects to and from the densitometer. Peripheral measures of bone density and biochemical markers of bone turnover may provide further insight.

In summary, the high rate of fractures in persons with moderate to severe developmental disabilities is not widely appreciated. The identification of reliable risk predictors could serve as the basis for targeted testing and intervention for those found to be at highest risk. More widespread consideration of vitamin D supplementation may be justified given its low cost and toxicity, and the association between fractures and drugs known to affect vitamin D metabolism such as phenobaribital.

Acknowlegements

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