Systematic review of central nervous system anomalies in incontinentia pigmenti

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Additional file 1

Central nervous system anomalies in incontinentia pigmenti in the perod 1906-1993

In addition to investigation of the period 1993-2012, 82 references for the periods 1906-1975 and 1976-1992 were collected in the same manner and were analyzed, comparing results from three different periods. The data of IP patients for the period between 1906 and 1975 were used from Carney's review [1976]. These references are listed in Additional references published in the period of 1906-1993.

The results of the present systematic review for the period 1906-2012 are presented in Additional Table 1. It contains the summarized data of IP patients, CNS anomalies, and their distribution by sex and by the period of investigation. The data of IP patients for the period 1906-1975 were from Carney's review [1976], where the data for the periods 1976-1992 and 1993-2012 refers to IP patients for which data from the literature were collected.

The total number of IP patients found in the literature for the 1906-2012 period was 2,291 (91.83% females, 5.85% males, and 2.32% with unspecified sex). There were 752 CNS anomalies registered in 450 IP patients for the period 1906-2012. The total number of CNS anomaly types per patient for the periods 1906-1975, 1976-1992, and 1993-2012 were 1.81, 1.54, and 1.62, respectively. For the three investigated periods, no significant difference in the total of CNS anomaly types per patient (χ^2=2.58; df=2; p=0.28>0.05) was found. Among neurologically investigated IP patients, CNS anomalies were observed in 31.25% of the patients in the cumulative period 1906-2012. The proportions of patients with CNS anomalies for the periods 1906-1975, 1976-1992, and 1993-2012 were 30.54%, 36.67%, and 30.44%, respectively, and they did not differ significantly (χ^2=1.93; df=2; p=0.38>0.05). Only for the 1976-1992 and 1993-2012 periods were data adequate for calculating the number of CNS anomalies according to sex. For the periods 1976-1992 and 1993-2012 higher values for the percentage of female IP patients with CNS anomalies than in males, 38.55% and 15.38% (1976-1992) and 30.74% and 27.63% (1993-2012), respectively, were found. In the present study for the periods 1976-1992 and 1993-2012 there was no significantly higher number of anomalies per patient in females than males, 1.55 and 1.50 (1976-1992) and 1.63 and 1.52 (1993-2012), respectively. For the cumulative 1906-2012 period the most frequent CNS anomalies were seizures, motor impairment, and mental retardation, which comprise 34.04%, 27.66%, and 24.73% of the total number of anomalies, respectively. Microcephaly was found in 5.58%, and unspecified anomalies were found in 7.98%. For the three investigated periods a significant difference in the distribution of CNS anomaly types (χ^2=27.47; df=8; p=0.001<0.05) was found. The difference is also significant for three anomaly types: seizures, mental retardation, and motor impairment (χ^2=22.95; df=4; p=0.0001<0.05). For the three investigated periods a significant difference in the distribution of patients with mild and severe CNS anomalies (χ^2=15.36; df=2; p=0.001<0.05) was also found.

Additional Table 1 Main findings of IP patients and CNS anomalies by sex and for different periods of investigation

Observed period and sex	Number of					Distribution of CNS anomaly types in numbers					Percentage of		
	IP patients	Neurologically investigated IP patients	Neurologically investigated IP patients with CNS anomalies	CNS anomalies	CNS anomaly types per patient	Seizures	Mental retardation	Motor impairment	Microcephaly	CNS anomalies found in small number or unspecified	Neurologically investigated IP patients with CNS anomalies	IP patients with mild CNS anomalies	IP patients with severe CNS anomalies
Total* 1906-2012	2,291	1440	450	752	1.67	256	186	208	42	60***	31.25	11.80	19.45
Female 1906-2012	2,104	1339	422	712	1.69	242	177	200	41	52	31.52	11.79	19.72
Male 1906-2012	134	100	28	40	1.43	14	9	8	1	8	28.00	13.00	15.00
Total* 1906-1975	653	465	142	257	1.81	62	76	77	19	23	30.54	14.19	16.34
Female 1906-1975	593	454	137	252	1.84	62	75	77	19	19	30.18	13.66	16.52
Male 1906-1975	16	11	5	5**	1**	0	1	0	0	4	45.46	36.36	9.09
Total* 1976-1992	245	180	66	102	1.54	29	30	30	7	6	36.67	6.67	30.00
Female 1976-1992	216	166	64	99	1.55	28	29	29	7	6	38.55	6.62	31.93
Male 1976-1992	26	13	2	3	1.50	1	1	1	0	0	15.38	7.69	7.69
Total* 1993-2012	1,393	795	242	393	1.62	165	80	101	16	31***	30.44	11.57	18.86
Female 1993-2012	1,295	719	221	361	1.63	152	73	94	15	27	30.74	11.68	19.05
Male 1993-2012	92	76	21	32	1.52	13	7	7	1	4	27.63	10.52	17.10

*In all observed periods there were some patients without adequate data regarding sex in literature so total number of patients is always higher then sum of females and males.

**Insufficient data for exact calculating because adequate detailed information about number and type of CNS anomalies was not available.

***The task of counting and identifying anomalies in some references was challenging because there were only lists of observed anomalies with no exact numbers. These lists included frequent types of CNS anomalies such as seizures, motor impairment, mental retardation, and microcephaly. These anomalies were classified as unspecified anomalies together with different anomalies presented in small numbers. In this investigation, for the period 1993-2012, of 31 registered rare or unspecified CNS anomalies, 15 were unspecified but frequent types of CNS anomalies (seizures, motor impairment, mental retardation, and microcephaly). Because of these difficulties, the exact number of frequent types of CNS anomalies such as seizures, motor impairment, mental retardation, and microcephaly was actually higher than those presented in the Table.

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