

Use of the aromatase inhibitor letrozole in pubertal boys to improve final height: laboratory, auxological and bone age data

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Conclusion: 2,5 mg Letrozole per day slightly increases calculated final height in the majority, but not in all treated boys. Letrozole-induced decrease of IGF-I-SDS could eventually induce an antagonistic effect on growth. Additional delay of bone age as well as estradiol suppression were achieved after 12 months, so it is to be discussed if a higher dose of letrozole, at least during the first 6 to 12 months could show better effects.

Background / Aims: The aromatase inhibitor letrozole is used to improve final height in boys with predicted small stature by delaying bone age maturation due to suppression of estradiol levels. As there are few data about its effects, especially when used as single medication, we analysed our data.

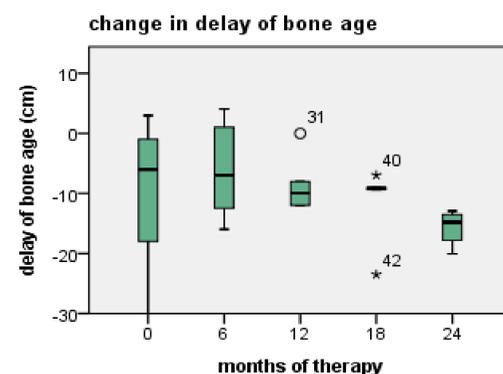
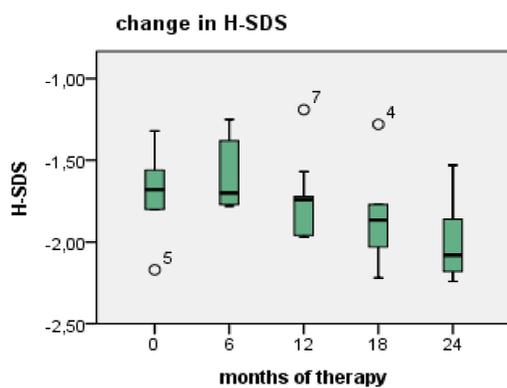
Methods: 10 pubertal boys with predicted low final height (< 166 cm) treated with letrozole 2,5 mg/d p.o. (no other medication) for up to 24 months were analysed for auxological, laboratory and bone age data.

Results:

Auxological data:

- Height-SDS showed only small changes during the time of treatment. In the mean it even decreased (mean -1,75 at 0 months to -1,90 at 24 months) with a wide interindividual variability. A significant increase was seen in only one patient (+0,64 SDS), in the other patients changes of H-SDS were between 0,08 and -0,79 SDS.
- BMI continuously raised until 18 months of treatment (mean: +0,45 SDS).
- In most patients, there was a slight delay of bone age (BA) vs. chronological age (CA) at start (mean: - 9,5 months). While this delay first even declined at 6 months (mean: -8,5 months), a significant increase of the difference between bone age and chronological age compared to baseline was first seen at 12 months (mean: -12,5 months) which remained constant at 18 months and showed further delay at 24 months (mean: -15,6 months). Yet, on the whole, the additional delay was small in all patients (-1,21 to +0,69 years).

month of therapy	n	age	H-SDS	BMI-SDS	delay of BA (months)	
0	10	mean	13,65	-1,75	-0,48	-9,6
		SDS	0,89	0,72	0,97	11,4
6	10	mean	14,30	-1,71	-0,11	-8,5
		SDS	0,79	0,82	0,83	13,3
12	9	mean	14,89	-1,98	-0,23	-12,5
		SDS	0,86	0,85	0,81	11,8
18	6	mean	15,18	-1,84	0,09	-11,6
		SDS	0,85	0,32	0,93	6,7
24	5	mean	15,51	-1,98	-0,07	-15,6
		SDS	0,77	0,29	1,17	3,1

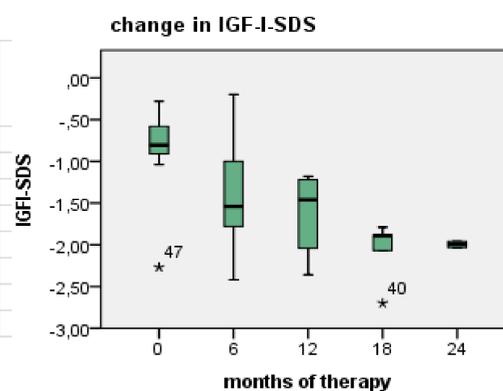


Laboratory data:

As blood tests were not performed at all control times in every patients, especially at the end of treatment, numbers were too low for analyses at 24 months.

- IGF-I-SDS decreased continuously in all until 18 months of treatment, falling below -2 SDS in 3 patients.
- All patients had pubertal values for testosterone at start of treatment (mean at 0 months: 109 ng/dl). This parameter showed a continuous and quite large raise during the whole period of treatment (mean at 24 months: 2591 ng/dl).
- Suppression of estradiol is the main effect of letrozole. Yet, in 5 of the 10 patients, estradiol levels were still detectable after 6 months and suppressed in 5 of 6 only after 12 months.

month of therapy	n	IGF-I-SDS	testosterone (ng/dl)	estradiol (pg/ml)	
0	10	mean	-0,73	109	11,5
		SDS	0,79	105	8,69
6	9	mean	-1,39	845	11,6
		SDS	0,64	437	8,2
12	6	mean	-1,62	1492	6,6
		SDS	0,48	1537	4,00
18	5	mean	-2,07	2577	5,0
		SDS	0,37	2591	0,00



Predicted final height:

- Changes of predicted final height varied widely interindividually between a loss of 5,0 cm to a gain of 7,47 cm compared to the initial prognosis in the 6 patients who already finished therapy or were treated for 18 months at the end of data collection. Interestingly, almost all patients showed temporary decreases in predicted final height, raising again and vice versa during the course of treatment.

month of therapy	n	predicted height (cm)	change of predicted height (cm)	
0	10	mean	166,2	
		SDS	3,72	
6	10	mean	167,4	-0,02
		SDS	3,46	3,28
12	9	mean	165,0	0,21
		SDS	3,34	3,17
18	6	mean	167,4	1,11
		SDS	4,28	4,78
24	5	mean	168,4	2,53
		SDS	3,19	5,21

