

Hyperparathyroidism and Asthenia. A New Deal?

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Opinion

The profile of primary hyperparathyroidism (PHPT) changed profoundly over the course of the twentieth century. The highly symptomatic forms reported in the 1960s have progressively been replaced by forms with few symptoms and in some cases totally asymptomatic forms. As of 1991, with the increasing frequency of these new forms, several consensus meetings designed to define the criteria for establishing the operability of minimally-symptomatic hyperparathyroidism have been organized [1]. However, the criteria chosen are in some cases deemed too restrictive as they do not take into account general and neuro-psychic symptoms which are frequently associated [2]. Since 1995, with the aim of extending operable criteria several publications including at least 12 prospective and three meta-analyses [3-5] have shown an improvement in the quality of life of patients operated for asymptomatic hyperparathyroidism. Unfortunately these studies which support an approach of operating all patients, have limited practical application. Considered too general, they are rarely appropriate on an individual level. Really the reason for proposing surgical intervention is generally two-fold: to reduce the risks (or

the negative prognosis) of disease pathology or to reduce one or more symptoms whose presence and severity hamper the patient's daily quality of life. In the latter case, the improvement of quality of life is an expected consequence of the reduction or elimination of bothersome symptoms but is not the direct motivation behind the surgery. In 1998, based on a study including 5202 post-menopausal women, Ewa Lundgren demonstrated that, relative to the control population, patients suffering from PHPT complained more of fatigue, sleepiness during the day, and feeling weak [6]. For several years now, we consider these symptoms to fall within the context of asthenia, fatigue without a physiological cause (effort or lack of sleep) and which is only partially relieved by rest. So when fatigue is beyond normal physiologic conditions, the more appropriate term to employ is "asthenia". It is associated with 50% to 98% of PHPT cases [7,8] however it is rarely singled out as a symptom and the majority of recent publications on hyperparathyroidism do not directly address asthenia, but include "fatigue" as a criterion for the quality of life. Despite this, the discomfort patients experience is real and represents a true handicap improved by the cure of the PHPT as the Table 1 shows when asthenia is isolated from these studies (Table 1).

Table 1:

Authors	Years	Type	N	Follow Up Months	Feel tired	Worm Out
Deutch [9]	2000	Scale ordinal fatigue	25	3	<0,05	
Greutelaers [10]	2004	Pasiëka	71	3	p<0,05	
Quiros [11]	2003	SF36		Mar-24	<0.05	p<0.05
Edward [12]	2006	SF36		06-Dec	<0,007	p<0,01
Tsukahara [13]	2007	Scale: 0,1,2	25	12	0,24*	
Ramakant [14]	2011	PAS parameters	27	6	<0,005	
Brito [5]	2015	Pasiëka	238	06-Dec	p<0,001	metanalysis
Zanocco [15]	2016	PROMIS**		3	8,8***	

*8 of 25 patients have no fatigue

**Patient-Reported Outcomes Measurement Information System

***Significant if >5.

There are at least three possible explanations for this:

i. Firstly, the universal nature of fatigue limits its specificity, particularly as semantically it is associated with several and varied

qualifiers, which are polymorphic in both French ("affaibli, accablé, fatigué, épuisé, éreinté, exténué, harassé") and English (fatigue, tiredness, worn out, weakness). This richness of traditional and

even slang semantics offers a good understanding the intensity of the fatigue (for example in French “coup de pompe” reflects a slight fatigue, while “éreinté” indicates intense fatigue, and in English “pooped” and “shattered” represent slight and intense fatigue, respectively) with stronger or weaker terminology according to the sensations of the individual. So we think that it is thus logical to ask patients to qualify fatigue using an analogic scale which allows translation of this linguistic richness into a figure. In our experience, all patients, including very elderly patients, were able to evaluate their condition without difficulty.

ii. Secondly, in contrast to “classic” symptoms of PHPT, there is no known explanation for the physiopathology of fatigue, other than the publication by Soren Deutch which demonstrated a reduction in muscular strength followed by an increase following treatment for PHPT [9].

iii. Finally, fatigue, i.e., the sensation of bodily reduced strength, is generally considered as a normal physiologic state which most individuals experience are able to evaluate the intensity.

Conclusion

In conclusion, we think that we must now be interested in fatigue-symptom i.e. asthenia of HPTH and the best way to do this is to use an analog scale as is done for other symptoms and as we use it in our daily practice.

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