UNIVERSITE D'ANGERS

FACULTE DE MEDECINE

Année 2014 **N°……**

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pour le

DIPLOME D'ETAT DE DOCTEUR EN MEDECINE

Qualification en : RHUMATOLOGIE

Par

Aurélie DESLANDES

Née le 08/11/1985 à Laval

Présentée et soutenue publiquement le : 01/10/2014

PREVALENCE ET FACTEURS ASSOCIES AUX DOULEURS ARTICULAIRES ET RACHIDIENNES DANS UNE POPULATION DE 381 FEMMES TRAITEES PAR INHIBITEURS DE L'AROMATASE DEPUIS TROIS ANS.

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LISTE DES ABRÉVIATIONS

AI : Aromatase inhibitors

MSK : Musculoskeletal

ER+: Estrogen receptor-positive

BMI: Body Mass Index

PTH: Parathyroid hormone

FSH: Follicle stimulating hormone

LH: Latinizing hormone

SBP : Sex binding protein

LS : Lumbarspine

BMD : Bone mineral density

NSAIDs: Nonsteroidal anti-inflammatorydrugs

25(OH)D : 25 hydroxyvitamin D

HER : Human epigermalgrowthfactorreceptor

ANOVA : Analysis of variance

PLAN

RÉSUMÉ

Introduction : Le traitement par inhibiteur de l'aromatase (AI) réduit le risque de rechute du cancer du sein mais peut induire des douleurs musculo-squelettiques (MSK) conduisant à une mauvaise observance thérapeutique. Plusieurs études ont montré la survenue précoce de cet effet indésirable, mais aucune n'a recherché les facteurs associés à ces douleurs après une utilisation prolongée des AI. L'objectif de notre travail était de déterminer la prévalence des douleurs MSK et d'identifier les facteurs cliniques, biométriques et biologiques associés à leur chronicité chez les femmes ménopausées traitées par AI depuis 3 ans. Patients et méthodes : il s'agissait d'une étude monocentrique, transversale, incluant 381 femmes ménopausées traitées par AI pour un cancer du sein. Toutes les patientes ont rempli un auto-questionnaire collectant des informations sur la fréquence, la localisation, le retentissement et les conséquences des douleurs. Résultats : 83,7% des femmes avaient des rachialgies et 74% avaient des arthralgies. Les patientes avec rachialgies chroniques avaient significativement plus d'arthralgies chroniques, pratiquaient moins d'activité physique et étaient moins satisfaites de leur prise en charge médicale. Les patientes avec des douleurs articulaires chroniques avaient un poids et une masse grasse significativement plus importants et significativement plus de rachialgies chroniques. Conclusion : la prévalence des douleurs MSK est élevée chez les femmes traitées depuis 3 ans par AI. Certains facteurs associés aux douleurs MSK chroniques, comme le surpoids et une faible activité physique, sont aussi des facteurs de risque de cancer du sein. Des mesures hygiéno-diététiques pourraient être conseillées à l'initiation du traitement par AI.

ABSTRACT

Introduction: the aromatase inhibitors (AI) treatment reduces the risk of breast cancer recurrence but is responsible to musculoskeletal (MSK) pains leading to a discontinuation of AI. Previous studies have reported early MSK pains associated with AI treatment but none of them assessed factors associated with MSK pains after a prolonged use of AI. The aim of our study was to identify the prevalence of MSK pains and the clinical, biometric parameters and the biological factors associated with chronic MSK pains in post menopausal women with ER+ breast cancer after 3 years of AI treatment. Patients and Methods: we conducted a monocentric, cross-sectional study including 381 post-menopausal women with non-metastatic ER+ breast cancer treated by AI for 3 years. Each patient answered to a self-reported pain questionnaire collected information on MSK symptoms comprising the location, the frequency, the feeling and the consequences of pains. Results: 83.7% of patients had back pain and 74% had arthralgia. Patients with chronic back pain had significantly more chronic arthralgia, had less physical activity and were less satisfied with the medical care. Patients with chronic arthralgia had a significant higher weight and body fat mass on bone densitometry and had more chronic back pain. Conclusion: the prevalence of MSK pains is high in women taking chronically AI treatment. Some factors associated with chronic MSK pains, such as low walking activity and higher weight, are also implicated as risk factor for breast cancer recurrence. Weight management and physical activity should be advised for each women treated with AI.

INTRODUCTION

Aromatase inhibitor (AI) treatment has become the standard of care for the adjuvant endocrine treatment of hormone receptor-positive (ER+) early-stage breast cancer in post - menopausal women. Its effectiveness has been proven in terms of disease-free survival, time to recurrence, life expectancy and incidence of contralateral breast cancer[1, 2].

AI treatment leads to a total estrogen deprivation that can induce side effects such as joint symptoms, vaginal dryness, bone loss and osteoporotic fractures[1, 3, 4].

The musculoskeletal (MSK) pains occur in 30 to 50% of cases[1, 2, 5, 6].The pain affects the hands/wrists in more than 60% of cases[7] and less frequently the other joints and the spine[8, 9, 10, 11]. The pain can be associated with morning stiffness, decreased grip strength and with a detrimental effect on daily activities. Arthritis and tenosynovitis have also been described leading to carpal tunnel syndrome[3, 12, 13]. The median time of occurrence of MSK pains is one to 3 months after the start of AI treatment and the pain tends to reach its peak intensity during the 6th first month[8, 11].

MSK pain is responsible to a discontinuation of AI treatment in 11 to 20% of cases[14, 15]. Despite conflicting results, obesity (BMI >30)[9,16], prior hormonal treatment for menopause[12,16], neoadjuvant chemotherapy[16], previous history of arthralgia[12,17], menopause occurring less than five years ago[11] and low concentration of 25(OH) vitamin D, seem to be associated with AI-induced MSK pains. On the other hand, a prior tamoxifen therapy could be associated with lower risk of MSK pain[9].

Previous studies have assessed factors associated with joint pains but only in the first year of treatment. The aim of our study was to identify the prevalence of MSK pains and the clinical and biological factors associated with chronic MSK pains in post-menopausal women with a prolonged use of AI treatment (at least 3 years).

PATIENTS AND METHODS

Patients

We firstly conducted a prospective and longitudinal study between January 2006 and January 2009 including 497 post-menopausal women with ER+ breast cancer to assess bone consequences of AI treatment. These data have been already published [4, 18].

After 3 years of AI treatment, 381 of these women were included in a cross-sectional study to assess arthralgia and back pain with a self-reported pain questionnaire.

The inclusion criteria were:

- ER+ breast cancer without bone or visceral metastasis
- AI treatment initiated and taken for at least 3 years
- A good knowledge of the French to read and understand the questionnaire
- A signed consent to participate in this study
- The absence of psychiatric disorders or dementia

Outcome assessment

Clinical assessment

An extensive medical history and a physical examination were obtained for each subject including age, age at onset of menopause, weight, height, body mass index (BMI), cancer characteristics (size, nodal status, tumour grade, hormone receptors), treatment of cancer (surgery, radiotherapy, chemotherapy, tamoxifen), alcohol and tobacco use, physical activity, calcium and vitamin D supplementation.

Pain questionnaire

The pain questionnaire was a self-reported questionnaire collecting data on MSK symptoms. The questionnaire was divided in three parts.

The first part concerned back pain, the second one concerned peripheral joint pains and the third one explored the patient satisfaction level.

The first two parts of the questionnaire explored:

1-The presence or the absence of pain

2- The detailed location of pain including neck, thoracic and lumbar spine, but also fingers, wrists, shoulders, elbows, toes, ankles, knees and hips.

3- The pain frequency: each day, once a week, once a month, or less

4- The pain feeling: “my pain has quickly disappeared”, “I have pains but I can bear them” or as “I have pain and they are ruining my life”.

5-The consequences of pain in terms of care consuming: analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) use, medical imaging and visits to doctors, physiotherapists or osteopaths.

Finally the third part of the questionnaire explored the patient satisfaction level with respect to medical care comprising four items ranging from 0-5each. The final score was 0-20, 20 being the best score. It evaluated:

- the global satisfaction with respect to rheumatologic care (score from 0-5)
- the satisfaction with the schedule, the location and the duration of the appointment (score from 0-5)
- the satisfaction with the information given by the rheumatologist (score from 0-5)
- the satisfaction with the achievement of medical tests (score from 0-5)

Bone assessment

Fasting serum samples were assayed for calcium, phosphate, albumin, creatinine, 25-hydroxy vitamin D [25(OH)D], parathyroid hormone (PTH), bone formation markers (osteocalcin and bone alkaline phosphatase) and bone resorption marker (C-telopeptide).

Bone mineral densitometry (BMD) measurement has been described previously[18]. Briefly it was measured using dual energy X-ray absorptiometry (DXA) operating in fan-beam mode (Hologic QDR 4500A densitometer, Hologic Inc., Waltham, MA). Lumbar spine BMD (LS BMD) was assessed from L2 to L4, in the posteroanterior view incidence and fractured vertebrae were excluded from analysis. Total hip BMD was measured at upper left femur. As usually, the results were expressed in absolute values (g/cm2) and using the T-score [standard deviation (SD)]. Furthermore, the body composition divided in fat mass, and lean soft tissue mass was provided by whole-body scan on DXA.

Anteroposterior and lateral lumbar and thoracic spinal radiographs were taken the same day as DXA to diagnose the presence, the number and the grade of vertebral fractures.

Statistical analysis

Statistical analysis was performed using the software Statistical Package for the Social Sciences (SPSS Version 15.0). Baseline characteristics of patients were expressed in mean ± one standard deviation.

To analyze factors associated with pain, we decided to assess only chronic pain. We defined “chronic arthralgia” as having arthralgia more than once per month since 3 years. “Chronic back pain” was defined as having back pain more than once per month since 3 years.

The comparison of groups was performed for continuous variables by analysis of variance (ANOVA) and for binary variables by the Pearson Chi2 test. Univariate logistic regression was performed to analyze factors associated with chronic arthralgia and chronic back pain. Studied factors were: age (in years), weight (every 10 kg), height (in cm), BMI (in kg/m^2), body fat mass (every 10 kg), lean fat mass (every 10 kg), age of menopause (in years), physical activity (in hours of walking per week), tobacco consumption (any vs. none), alcohol consumption (any vs. none and by glass per week), diary products consumption (number per day), calcium supplementation (any vs. none), vitamin D supplementation (any vs. none), radiotherapy for breast cancer (any vs. none), use of adjuvant chemotherapy (any vs. none), use of tamoxifen therapy (any vs. none), duration of tamoxifen therapy (in years), type of AI (anastrozole vs. exemestane vs. letrozole), tumor size (T1 vs. T2 vs. T3+T4), nodal involvement (positive vs. negative), progesterone receptor status (positive vs. negative), HER status (positive vs. negative), tumor grade (1 vs. 2 vs. 3), PTH concentration (pg/ml), 25(OH) vitamin D concentration (in nmol/l and [25 OH D] >75 nmol/l vs. [25 OH D] <25 nmol/l vs. 25 nmol/l > [25 OH D] < 75 nmol/l), level of creatinine (in µmol/L), calcemia (mmol/L), phosphatemia (mmol/L), osteocalcin (µg/l), bone alkaline phosphatase (ng/ml), C-telopeptide (ng/ml), lumbar spine BMD (every 0.100 g/cm^2), hip BMD (every 0.100 g/cm^2), neck BMD (every 0.100 g/cm^2), chronic arthralgia (any vs. none), chronic back pain (any vs. none), vertebral fracture (any vs. none). Finally, we compared patients who considered that their pains were bearable “I have pain but I can bear them” and patients who considered that their pains were excruciating “I have pain and it's ruining my life”.

Differences were considered significant when $p < 0.05$.

RESULTS

Patients

The study population and cancer characteristics are shown in ***table I***. Briefly the mean age was 66.0 +- 9.2 years, the mean age of menopause was 49.5 +-13.5 years, the mean BMI was 27.2 +- 5.6 kg/m2. 19 women (5%) had a type 2 diabetes and one had a type 1 diabetes. Nobody had inflammatory chronic rheumatism. 72.5% were menopausal at the time of the diagnosis of cancer. Before AI initiation, 98.4% of women have been treated by surgery, 94.5% by radiotherapy and 58% by chemotherapy. 35.6% have been treated by tamoxifen for a mean duration of 12.3 months. Anastrozole was administered in 71.9% of the patients, exemestane in 16.0% and letrozole in 12.1%. Among the 381 women, 18 (4.7%) changed the type of AI during the 3 years of follow-up. The mean 25(OH) vitamin D concentration was 66.8 nmol/l +- 29.3, 33.5% had an optimal 25(OH) vitamin D concentration ([25 OH D]>75 nmol/l) and 1.6 % had a severe 25(OH) vitamin D concentration deficiency ([25 OH D] < 25 nmol/l).

Musculoskeletal pain location, frequency and consequences

83.7% of the patients reported having suffered from back pain in the previous three years. The detail of back pain location and frequency is shown ***table II***.

Among women having back pain, 43% consulted a doctor, 15.7% consulted a physiotherapist, 19.9% used analgesics or NSAIDs and 15.5% had spine CT scan or spine MRI.

74% of the patients had arthralgia in the previous three years. The detail of their location and frequency is shown ***table III.***

Among women having arthralgia, 46.6% consulted a doctor, 13.4% consulted a physiotherapist, 25.5% used analgesics or NSAIDs and 11.3% had joint X-rays.

Parameters associated with chronic back pain

Firstly, we compared the different parameters between the 2 groups, patients with chronic back pain (N = 126) and patients without chronic back pain (N = 222). Patients with chronic back pain had significantly less physical activity (1.5±1.3 hours of walking per week vs. 1.8±1.1 hours of walking per week; p=0.048), were significantly less satisfied

with the medical care (satisfaction score 13.5±2.1 vs. 14.0±1.5; p=0.020) and had more often chronic arthralgia (79.8%±0.4 vs. 27.5±0.5 %; p=0.001).

The cancer characteristics (tumour size, nodal status, tumour grade, presence or not of progesterone hormone receptor, HER expression) did not influence chronic back pain. Others parameters such as age, weight, bone mineral density, type of AI and biological factors were not statistically different between the 2 groups. 25(OH)vitamin D concentration did not influence chronic back pain. It is important to note that the prevalence, the number and the grade of vertebral fracture were not different between the 2 groups.

Univariate logistic regression analysis showed that chronic back pain was associated with the presence of chronic arthralgia (HR=10.42; 95%CI 6.06-17.91; p=0.00), a lower satisfaction score (HR=1.18; 95%CI 1.02-1.35; p=0.027) and a lower walking activity (HR=1.22; 95%CI 1.01-1.49; p=0.049).

Among patients with chronic back pain, we finally compared patients with excruciating back pain and patients with bearable back pain ***(table IV)***. Patients with excruciating back pain were significantly more health care consumers, took more drugs, had more medical imaging and consulted more doctors, physiotherapists and osteopaths. All other parameters were not statistically different.

Parameters associated with chronic arthralgia

Firstly, we compared the different parameters between the 2 groups patients with chronic arthralgia (N = 159) and patients without chronic arthralgia (N = 188). Patients with chronic arthralgia had a significant higher weight (68.8±13.1 kg vs. 65.6±12.9 kg; p=0.030), a higher body fat mass on bone densitometry (27.78±89.61 kg vs. 25.63±80.26 kg; p=0.020), a higher LS BMD (0.876±0.1 g/cm2 vs. 0.934±0.1 g/cm2 p=0.001) and more chronic back pain (62.5±0.5% vs. 13.8±0.4%; p=0.001). Even if there was no difference in 25(OH) vitamin D concentration, patients without chronic arthralgia received significantly more calcium (37.2%±0.4 vs. 25.2±0.5%; p=0.01) and vitamin D supplementation (39.4±0.5% vs. 28.3%±0.5; p=0.03). The cancer characteristics (tumour size, nodal status, tumour grade, presence or not of progesterone hormone receptor, HER expression) did not influence chronic arthralgia.

Univariate logistic regression analysis showed that chronic arthralgia were associated with a higher weight (HR=1.18; 95% CI 1.01-1.40; p=0.038), a higher body fat mass (HR=1.34 [95%CI 1.03-1.73]; p=0.027), a higher lumbar spine BMD (HR=1.32 every 0.100 g/cm^2;

95% CI 1.12-1.55; p=0.001) and the presence of chronic arthralgia (HR 10.42; 95% CI 6.06-17.91; p=0.00) (***table V***). Calcium supplementation (HR=0.57; 95% CI 0.36-0.90; p=0.017) and vitamin D supplementation (HR=0.61; 95% CI 0.39-0.96; p=0.031) were significantly associated with less chronic arthralgia. In multiple logistic regression including the weight, lumbar spine BMD remained significantly associated with chronic arthralgia. 25(OH)vitamin D concentration did not influence chronic arthralgia.

Among patients with chronic arthralgia, we finally compared patients with excruciating arthralgia and patients with bearable arthralgia (***table VI***). Patients with excruciating arthralgia were significantly more health care consumers for MSK pain, they took more drugs, had more medical imaging and consulted more doctors, physiotherapists and osteopaths. All other parameters were not statistically different.

DISCUSSION

This original study assessed the prevalence of arthralgia and back pain in postmenopausal women with ER+ breast cancer treated with AI since 3 years. The population was homogeneous and the cancer characteristics were those usually found in terms of size, nodal status, hormonal status and grade. Previous studies have reported early MSK pain occurring during the first year of AI treatment [8, 9, 11, 19]. To our knowledge, this is the first study assessing MSK pains in patients treated chronically with AI. Furthermore, we analyzed separately joint pain and back pain, specifying their location, their frequency, the feeling of pain and the consequences in terms of health care.

Back pain and arthralgia were frequent in this study. The design of our study did not permit to obtain pain description before AI treatment, so that we cannot specify what is the specific influence of AI treatment on the pain. Pain is common in the general population, especially in menopausal women, independently of AI treatment. According to previous studies, more than half women around the time of menopause (45-55 years) have arthralgia[20, 21] and the prevalence of chronic back pain in the general population of post-menopausal women could reach 20 to 40% [22, 23].

In our study, 83.7% of the patients reported back pain. No previous study had specifically assessed the risk factors associated with chronic back pain in a population of AI treatment. In our study, patients with chronic back pain had a lesser walking activity. Sedentary lifestyle is a well-known risk factor for low back pain and it has been shown that the practice of physical activity during leisure time prevents low back pain occurence[24]. It is important to note that physical activity has also been shown to increase survival after breast cancer[25, 26, 27, 28].

We observed that 74% of women reported chronic arthralgia, which were significantly associated with higher weight and body fat mass**.** It has been similarly demonstrated in a cohort of 292 postmenopausal women that higher BMI were associated with joint pain[23]. In general population, MSK pain occurs more frequently in obese subjects compared to non-obese[29, 30]. It is well illustrated in case of bariatric surgery, with a significant decrease of MSK pains after surgery[31].The link between MSK pain and obesity could be explained by biomechanical stress but also by an inflammatory modulating effect of adipokines within synovial joints[32, 33, 34]. Similarly to physical activity, losing weight has shown its efficacy in terms of survival in breast cancer[35, 36, 37, 38].

In our study, higher LS BMD was strongly associated with chronic arthralgia. Overweight is known to be associated with an increased LS BMD[39], which could explain the link between LS BMD and chronic arthralgia. However in multiple logistic regression LS BMD remained independently associated with chronic arthralgia. Women with a higher LS BMD could have a higher estrogen concentration before AI treatment and have a huge drop in this concentration after the beginning of AI treatment explaining more arthralgia.

The patients of this study had a 25(OH) vitamin D concentration particularly "normal" because they were followed by a rheumatologist for bone assessment and thus were supplemented with vitamin D. The effects of 25(OH)vitamin D concentration on the occurrence of MSK pain are debated. In our study, 25(OH)vitamin D concentration did not influence pain occurrence. It has been suggested that a low 25(OH)vitamin D concentration could play a role in the development of early MSK pain during AI use[40, 41, 42]. In a study, including fifty one patients, 25(OH)vitamin D concentration < 40 ng/ml was associated with clinical tenosynovitis but not with MSK pain[43]. Other studies concluded that 25(OH)vitamin D concentration had no effect on the occurrence of arthralgia[7, 19, 44]. In the IBIS-II study, a multicenter randomized placebo controlled trial with 416 participants, 25(OH)vitamin D concentration did not predict arthralgia within the first year of use[44]. The effects of 25(OH)vitamin D supplementation on MSK pain relief are also debated. A schedule of intense vitamin D3 supplementation may reduce disability from AI-induced arthralgia[40, 41]. But these studies were not randomized, comprised a low number of patients and the pain assessment was done at the third month. In our study even if there was no difference in the final concentration in calcemia and 25(OH) vitamin D concentration, patients receiving calcium and vitamin D supplementation had less chronic arthralgia.

Chronic back pain was more frequent in our patients who were less satisfied with the medical care. In the general population, dissatisfaction is related to depressive disorders[45]. These results are similar to a recent prospective multicenter cohort study assessing risk factors for estrogen deprivation pain syndromes related to one year AI treatment, which observed that personality traits may result in a predisposition to chronic pain development[19]. Menopause is also a period of change in which anxiety and depression are more frequent[46]. In a systematic review, depression, psychological distress, passive coping strategies and fear-avoidance beliefs were found to be linked with chronic low back pain[47]. Furthermore, we showed that patients suffering from chronic back pain had more frequently chronic arthralgia and inversely. This is in line with previous studies, which

have demonstrated that regional pain could develop into chronic widespread pain if psychological factors were associated[48, 49, 50, 51].

Finally, our study showed a huge consumption of health care related to MSK pain: consultations, drugs consumption and imaging. Even if MSK pains are insignificant compared to the benefice of AI in terms of cancer recurrence[52, 53], MSK pain can result in major consequences in term of health costs.

In conclusion, we showed in this original study, comprising 381 postmenopausal women with ER+ breast cancer treated with AI since 3 years, that back pain and arthralgia occurred respectively in 83.7% and 74% of women. Some factors associated with chronic MSK pains, such as low walking activity and higher weight, are also implicated as risk factor for breast cancer recurrence. Weight management and physical activity should be advised for each women treated with AI for a breast cancer to improve the tolerance.

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TABLES

Table I: Study population and cancer characteristics

Variables	Value[1]
Age (years)	66.0±9.2
BMI (kg/m2)	27.2±5.6
Age of menopause (years)	49.5±4.6
Physical activity (hours of walking per week)	1.7±1.2
Current smokers	13.1%
Alcohol consumers[2]	24.1%
Tumour size	
T1	72%
T2	20.5
T3 and T4	7.5%
Nodal status	
Negative	49.2%
Positive	50.8%
Tumour grade	
Grade1 Well differentiated	25.1%
Grade 2 Moderately differentiated	50.8%
Grade 3 Poorly differentiated	24.1
Estrogen hormone receptor positive	100%
Progesterone hormone receptor	
Negative	15.4%
Positive	84.6%
HER expression	
Negative	93.4%
Positive	6.6%
Previous treatment for breast cancer	
Surgery	98.4%
Radiotherapy	94.5%
Chemotherapy	58.0%
Tamoxifen	35.6%
Type of AI[3] (%)	
Anastrozole	71.9%
Exemestane	16.0%
Letrozole	12.1%

[1] Values are given as mean ± SD or as %
[2]Alcohol consumers were defined as drinking at least 1 glass of alcohol per week
[3] AI at the time of the questionnaire
BMI: Body Mass Index ;HER: Human epigermal growth factor receptor AI: Aromatase inhibitor

Table II: Back pain location and frequency

	Every day (N)	Every week (N)	Once a month (N)	Less than once a month (N)	TOTAL (N)
Neck (N)	29	12	19	33	93
Thoracic (N)	23	8	7	27	65
Lumbar (N)	60	22	22	68	172
TOTAL (N)	112	42	48	128	330

Table III: Arthralgia location and frequency

	Every day (N)	Every week (N)	Once a month (N)	Less than once a month (N)	TOTAL (N)
Fingers (N)	52	13	19	27	111
Wrists (N)	35	10	10	27	82
Elbows (N)	18	4	4	6	32
Shoulders (N)	49	9	16	31	105
Toes (N)	21	7	5	8	41
Ankles (N)	25	3	7	8	43
Knees (N)	52	16	18	40	126
Hips (N)	31	8	11	19	69
TOTAL (N)	283	70	90	166	609

Table IV: Comparisons of parameters in patients with excruciating back pain and bearable back pain

Variables (%)	Excruciating chronic back pain (n=33)	Bearable chronic back pain (n=108)	p Value
Health care consumption for chronic back pain			
Medical consultations	90.9±0.3	71.7±0.5	0.001
Pain killers use	51.5±0.5	28.7±0.5	0.090
Physiotherapist and Osteopathic consultations	21.2±0.4	11.9±0.3	0.010
Spine CT scan or spine MRI	42.4±0.5	24.8±0.4	0.030
Health care consumption for arthralgia			
Medical consultations	80.7±0.4	64.5±0.5	0.001
Pain killers use	63.6±0.5	26.9±0.4	0.070
NSAIDs use	21.2±0.4	8.3±0.3	0.001
Joints X-rays	12.1±0.3	16.7±0.4	0.190

NSAIDs: nonsteroidal anti-inflammatorydrugs

Table V: Univariate logistic regression for factors significantly associated with chronic arthralgia

Variables	HR	95% IC	p Value
Weight (kg)	1.18	1.01 to 1.40	0.038
Body fat mass (kg)	1.34	1.03 to 1.73	0.027
Lumbar spine BMD (g/cm2)	1.32	1.12 to 1.55	0.001
Calcium supplementation (%)	0.57	0.36 to 0.90	0.017
Vitamin D supplementation (%)	0.61	0.39 to 0.96	0.031
Chronic back pain (%)	10.42	6.06 to 17.91	0.001

BMD, bone mineral density

Table VI: Comparisons of parameters in patients with excruciating arthralgia and patients with bearable arthralgia

Variables (%)	Excruciating chronic arthralgia (n=40)	Bearable chronic arthralgia (n=154)	p Value
Health care consumption for chronic arthralgia			
Medical consultations	94.7±0.2	64.1±0.5	0.001
Pain killers use	65.0±0.5	24.0±0.4	0.016
NSAIDs use	22.5±0.4	8.4±0.3	0.001
Joints X-rays	27.5±0.5	14.3±0.4	0.001
Health care consumption for chronic back pain			
Medical consultations	79.0±0.4	49.4±0.5	0.001
Pain killers use	38.5±0.5	21.1±0.4	0.001
Physiotherapist and Osteopathic consultations	15.4±0.4	10.5±0.3	0.098
Spine CT scan or spine MRI	30.8±0.5	16.3±0.4	0.001

NSAIDs, nonsteroidal anti-inflammatory drugs

TABLE DES MATIÈRES

PERMIS D'IMPRIMER

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PREVALENCE ET FACTEURS ASSOCIES AUX DOULEURS ARTICULAIRES ET RACHIDIENNES DANS UNE POPULATION DE 381 FEMMES TRAITEES PAR INHIBITEURS DE L'AROMATASE DEPUIS TROIS ANS.

Résumé : Introduction : Le traitement par inhibiteur de l'aromatase (AI) réduit le risque de rechute du cancer du sein mais peut induire des douleurs musculo-squelettiques (MSK) conduisant à une mauvaise observance thérapeutique. Plusieurs études ont montré la survenue précoce de cet effet indésirable, mais aucune n'a recherché les facteurs associés à ces douleurs après une utilisation prolongée des AI. L'objectif de notre travail était de déterminer la prévalence des douleurs MSK et d'identifier les facteurs cliniques, biométriques et biologiques associés à leur chronicité chez les femmes ménopausées traitées par AI depuis 3 ans. Patients et méthodes : il s'agissait d'une étude monocentrique, transversale, incluant 381 femmes ménopausées traitées par AI pour un cancer du sein. Toutes les patientes ont rempli un auto-questionnaire collectant des informations sur la fréquence, la localisation, le retentissement et les conséquences des douleurs. Résultats : 83,7% des femmes avaient des rachialgies et 74% avaient des arthralgies. Les patientes avec rachialgies chroniques avaient significativement plus d'arthralgies chroniques, pratiquaient moins d'activité physique et étaient moins satisfaites de leur prise en charge médicale. Les patientes avec des douleurs articulaires chroniques avaient un poids et une masse grasse significativement plus importants et significativement plus de rachialgies chroniques. Conclusion : la prévalence des douleurs MSK est élevée chez les femmes traitées depuis 3 ans par AI. Certains facteurs associés aux douleurs MSK chroniques, comme le surpoids et une faible activité physique, sont aussi des facteurs de risque de cancer du sein. Des mesures hygiéno-diététiques pourraient être conseillées à l'initiation du traitement par AI.

Abstract: : Introduction: the aromatase inhibitors (AI) treatment reduces the risk of breast cancer recurrence but is responsible to musculoskeletal (MSK) pains leading to a discontinuation of AI. Previous studies have reported early MSK pains associated with AI treatment but none of them assessed factors associated with MSK pains after a prolonged use of AI. The aim of our study was to identify the prevalence of MSK pains and the clinical, biometric parameters and the biological factors associated with chronic MSK pains in post menopausal women with ER+ breast cancer after 3 years of AI treatment. Patients and Methods: we conducted a monocentric, cross-sectional study including 381 post-menopausal women with non-metastatic ER+ breast cancer treated by AI for 3 years. Each patient answered to a self-reported pain questionnaire collected information on MSK symptoms comprising the location, the frequency, the feeling and the consequences of pains. Results: 83.7% of patients had back pain and 74% had arthralgia. Patients with chronic back pain had significantly more chronic arthralgia, had less physical activity and were less satisfied with the medical care. Patients with chronic arthralgia had a significant higher weight and body fat mass on bone densitometry and had more chronic back pain. Conclusion: the prevalence of MSK pains is high in women taking chronically AI treatment. Some factors associated with chronic MSK pains, such as low walking activity and higher weight, are also implicated as risk factor for breast cancer recurrence. Weight management and physical activity should be advised for each women treated with AI.

MOTS-CLES

Aromatase inhibitors
Arthralgia
Chronic pain
Vitamin D
Breast cancer
Back pain
Postmenopausal women
Estrogen deprivation

FORMAT

☐ **Mémoire**
☒ **Article[1] :** ☒ à soumettre ☐ soumis ☐ accepté pour publication ☐ publié

suivi par : Madame le Docteur BOUVARD Béatrice

[1]statut au moment de la soutenance