FATIGUE

La fatigue est un symptôme affectant fréquemment les patients atteints de cancer. Sa prévalence est difficile à établir mais elle affecte la qualité de vie de manière importante. La fatigue liée au cancer est multifactorielle. Seule est abordée ici la fatigue au cours du traitement du cancer[K].

1. Evaluation de la fatigue

Elle peut être facilement évaluée par une échelle visuelle analogique – de 0 à 10 – de la même manière que l'EVA de la douleur. Le Brief Fatigue Inventory (BFI), un questionnaire plus détaillé, peut aussi être utilisé[L]. On définit alors une fatigue sévère au-dessus de 6-7 et une fatigue modérée au-dessus de 3-4 (80). Enfin, l'ESAS (ou échelle d'Edmonton) est également très simple et peut être utilisée ici.

Grade 1	Fatigue corrigée par le repos
Grade 2	Fatigue non corrigée par le repos, limitant les activités instrumentales de la vie courante
Grade 3	Fatigue non corrigée par le repos, limitant la capacité du patient à prendre soin de soi

Tableau 22 – Cotation de la fatigue selon la classification CTCAE v5.0

2. Prise en charge de la fatigue

Face à une fatigue, la première étape est de rechercher une ou des causes associées et / ou favorisantes et potentiellement corrigeables : anémie, douleur, dénutrition, déshydratation, troubles hydro-électrolytiques, hypothyroïdie, ménopause, troubles du sommeil, détresse émotionnelle, dépression, anxiété, progression de la maladie, insuffisance d'organe (insuffisance cardiaque, respiratoire…) (45).

Échelle d'évaluation des symptômes EDMONTON ASSESSMENT SYSTEM - ESAS

Date : **Heure :** **Nom / Prénom :**

REMPLI PAR : ☐ Patient ☐ Famille ☐ Soignant ☐ Patient aidé par le soignant

Tracer sur les lignes ci-dessous une barre verticale (ou une croix) correspondant le mieux à ce que vous ressentez actuellement :

Pas de douleur		Douleur maximale
Pas de fatigue		Fatigue maximale
Pas de nausée		Nausées Maximales
Pas d'anxiété		Anxiété maximale
Pas de somnolence		Somnolence maximale
Pas de manque d'appétit		Manque d'appétit maximal
Aucun essoufflement		Essoufflement maximal
Je me sens bien		Je me sens mal

Autres symptômes (sudation, bouche sèche, vertige, sommeil, etc.) :

Figure 5 – Echelle d'Edmonton (ESAS)

En l'absence – ou après correction – de ces troubles associés on peut proposer la prise en charge suivante :

- Pour les fatigues légères (EVA ≤ 3 ou BFI ≤ 3-4) : Traitements non pharmacologiques
  - **Psychothérapie**, thérapies cognitivo-comportementales +/- hypnose (81).
  - **Conseils** pour la gestion du stress et de l'anxiété, relaxation, thérapie par le sommeil.

[K] Pavic M *et al*. Fatigue et cancer. Les référentiels Soins Oncologiques de Support. Lyon, décembre 2012. Sous le patronage du Réseau Espace Santé Cancer Rhône-Alpes. N°PRA-SOS-1012FATIGUE. http://espacecancer.sante-ra.fr/Ressources/referentiels/PRA-SOS-1012FATIGUE.pdf
[L] Version anglaise accessible sur : www.npcrc.org/files/news/brief_fatigue_inventory.pdf

- L'acupuncture reste débattue dans cette indication (82,83).
- **L'activité physique adaptée** (APA) (en l'absence de contre-indication) a démontré son efficacité sur la réduction de la fatigue mais essentiellement chez des femmes atteintes de cancers du sein à un stade curable. Un essai randomisé a donc été mené chez des patients atteints de cancer et dont l'espérance de vie était inférieure à 2 ans (n=231 dont 15% environ de cancer broncho-pulmonaire). Le groupe test bénéficiait d'un exercice physique (60 min x 2/sem pendant 5 sem) et le second n'en bénéficiait pas. L'objectif principal – l'évaluation de la fatigue ressentie par le patient mesurée par questionnaire – n'était pas améliorée dans le groupe test par rapport au groupe contrôle. Toutefois, la force musculaire était significativement améliorée dans le groupe ayant recours à l'exercice physique (84). Un autre essai clinique, comparant un programme d'entraînement de 12 semaines contre un programme de repos, montrait des résultats similaires (85). Une meta-analyse publiée en 2014 retrouve des résultats convergents (86). Une étude de faisabilité auprès de patients atteints d'un cancer du poumon avancé ou métastatique, pendant les traitements, a montré une amélioration de la tolérance à l'exercice, de la force des grands groupes musculaires, un maintien de la qualité de vie, de la dépression et de la fatigue, après 8 semaines d'exercices combinés de résistance et d'aérobie, et ce, sans effet indésirable (87). Une méta-analyse de 3 études contrôlées randomisées a aussi indiqué une amélioration de la tolérance à l'exercice, un maintien ou une amélioration de certains domaines de la qualité de vie, un maintien du volume expiratoire forcé et de la force musculaire (88,89). Il est apparu qu'une tolérance à l'effort plus importante (+50 mètres au test de marche de 6 minutes) était associée avec une réduction du risque de mortalité (-13%) chez des patients atteints d'un cancer bronchique non à petite cellules métastatique (90). Enfin, les programmes d'APA sont faisables chez les patients atteints de cancer métastatique et apportent une amélioration des symptômes dus au cancer ainsi que de la qualité de vie (91). Une seule étude (avec un faible effectif) a été conduite auprès de patients traités par thérapies ciblées pour un cancer du poumon métastatique et a démontré qu'une telle activité était faisable avec un impact positif sur la qualité de vie (92).
- Une étude présentée récemment à l'ASCO a étudié la faisabilité et l'acceptabilité de l'utilisation d'une *Apple Watch©* et d'un *Iphone©* pour mesurer l'activité physique. Le nombre de pas quotidiens était très significativement associé à la fatigue, aux fonctions physiques, à l'état général global, à l'impact social et aux troubles du sommeil[M].
- Le yoga et le *tai-chi* ont tous les deux été testés dans des essais randomisés montrant leur intérêt dans cette indication (93,94).

- Pour les fatigues modérées à sévères (EVA ≥ 4 et BFI ≥ 3-4) : Associations aux mesures précédentes de traitements pharmacologiques :
  - Antidépresseur et anxiolytique en cas de dépression ou d'anxiété avérée associée.
  - Le methylphenidate (RITALINE® / QUASYM® / CONCERTA®) – de la classe des amphétamines – a été assez largement étudié dans cette indication. Deux essais randomisés contre placebo (n=112 et 152) ont montré une efficacité sur l'intensité de la fatigue (95). Toutefois un troisième essai randomisé n'a pas montré de supériorité de cette molécule sur l'amélioration de la fatigue comparée au placebo (96). Plus récemment, un dernier essai randomisé a comparé le methylphenidate plus un conseil téléphonique personnalisé par une infirmière au conseil téléphonique seul et ne retrouvait pas non plus de différence significative sur la fatigue sous traitement (97). Par conséquent, **l'utilisation du methylphenidate dans cette indication ne soit plus une option**.
  - L'acétate de megestrol (MEGACE®) et la L-Carnitine (98) sont inutiles dans cette indication.

[M] Thompson C-A et al. Patient-reported outcomes, emoji, and activity measured on the Apple Watch in cancer patients. ASCO 2018 #6501, disponible à https://meetinglibrary.asco.org/record/158434/abstract (consulté le 02/01/2019).

- Deux essais randomisés contre placebo ont étudié le modafinil (MODIODAL®) dans cette indication et sont tous les deux négatifs (99,100). Enfin, un autre essai d'un analogue – l'armodafinil – est lui aussi négatif (101).
- Un essai randomisé a comparé l'effet de la dexamethasone (4 mg po/j pendant 15 j) contre placebo chez 84 patients atteints de fatigue modérée à sévère. L'objectif principal était l'évaluation de la fatigue par l'échelle FACIT-L à J15 ainsi que la qualité de vie associée. L'amélioration moyenne de l'intensité de la fatigue était tout à fait significative dans le groupe DXM comparé au placebo (9 [±10,3] *vs* 3,1 [± 9,59] ; p=0,008). La qualité de vie était également significativement améliorée mais pas l'échelle globale d'intensité des symptômes ni le score de détresse psychosociale. Les auteurs ne notaient pas de différence dans la fréquence de survenue des effets secondaires mais l'effectif était petit et la durée de prescription des corticoïdes courte (102). Un autre essai randomisé portant sur près de 600 patients et publié dans le JCO en 2014, rapporte que 16 mg de methylprednisolone orale pendant 7 jours, permettait de réduire la fatigue et la perte d'appétit chez des patients souffrant de douleur chronique sous opioïdes (103).

Recommandations

- Le traitement de la fatigue légère et le traitement de première intention de la fatigue modérée à sévère reposent sur des mesures non pharmacologiques : conseils personnalisés, psychothérapie, exercice physique.
- La corticothérapie en cure courte est la seule option médicamenteuse possible devant une fatigue modérée à sévère en cas d'échec des traitements non-médicamenteux.

Fatigue légère (EVA ≤ 3 ou BFI ≤ 3-4)	Fatigue modérée à sévère (EVA ≥ 4 et BFI ≥ 3-4)
Activité physique adaptée (Ex : 60 min x 2/sem)	
+/- psychothérapie, thérapies cognitivo-comportementales, hypnose (acupuncture)	
	Cure courte de corticothérapie (Ex : 16 mg de méthylprédnisolone orale 7 jours)

Tableau 23 – Proposition de prise en charge symptomatique de la fatigue

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