2. Traitement

2.1 Objectif du traitement

Le traitement et la vitesse de correction de l'hyponatrémie dépendent de son retentissement clinique et de sa vitesse d'installation :

- Une hyponatrémie chronique dont le retentissement clinique est faible devra être corrigée lentement (+ 8-10 mmol/l par 24 h).
- Une hyponatrémie aiguë mal tolérée neurologiquement devra être corrigée (partiellement) plus rapidement, sous couvert d'une surveillance rapprochée en soins critiques.

Le risque d'une correction trop rapide de la natrémie en cas d'hyponatrémie chronique est la myélinolyse centro-pontine. Les facteurs de risque de myélinolyse centro-pontine sont :

- la chronicité de l'hyponatrémie,
- une natrémie inférieure à 105 mmol/l,
- une hypokaliémie,
- l'alcoolisme,
- la dénutrition,
- une cirrhose,
- le sexe féminin,
- la faible masse musculaire.

2.2 Modalités et indications de traitement

- **Mesures générales :**
  - Traitement étiologique, à débuter dès que possible (notamment anticancéreux en cas de SIADH) ;
  - Assurer un apport nutritionnel suffisant ;
  - Éliminer les facteurs (notamment médicamenteux) pouvant aggraver l'hyponatrémie : diurétiques thiazidiques ou situations pourvoyeuses de SIADH ;
  - Rechercher et corriger les facteurs de risque de myélinolyse centro-pontine, notamment hypokaliémie ;
  - Assurer une surveillance clinique et biologique stricte : poids et diurèse quotidiens, biologie urinaire régulière.
- **Restriction hydrique** : la première ligne de traitement est systématiquement la restriction hydrique :
  - L'ensemble des apports liquidiens (café, soupe, « perfusettes ») doit être pris en compte ;
  - Son volume est celui de la diurèse des 24 h moins 500 cc ;
  - Certains éléments sont associés à un échec de la restriction hydrique :
    - osmolalité urinaire > 500 mosm/l,
    - diurèse inférieure à 1500 ml/24h,
    - hausse journalière de la natrémie inférieure à 2 mmol/l dans les 24-48 premières heures.
- **Sérum salé hypertonique à 3%** : 150 ml en 20 minutes, uniquement en cas d'hyponatrémie symptomatique, de préférence en milieu réanimatoire.
- **Tolvaptan (Samsca®) :**
  - Il s'agit d'un antagoniste des récepteurs V2 de l'AVP.
  - L'initiation doit être hospitalière avec une surveillance rapprochée pendant au moins 48 heures avec natrémie de contrôle toutes les 4 à 6 heures. La restriction hydrique doit être levée pendant les 24 à 48 premières heures d'utilisation. Il ne doit pas être utilisé conjointement aux autres traitements.
  - Pas de données dans les hyponatrémies asymptomatiques inférieures à 120 mmol/L.
  - La posologie initiale est de 15 mg/jour (possibilité d'augmenter progressivement jusqu'à 60 mg).
  - **AMM : traitement des patients adultes présentant une hyponatrémie secondaire à un SIADH chez lesquels une restriction hydrique est inefficace ou impossible.**

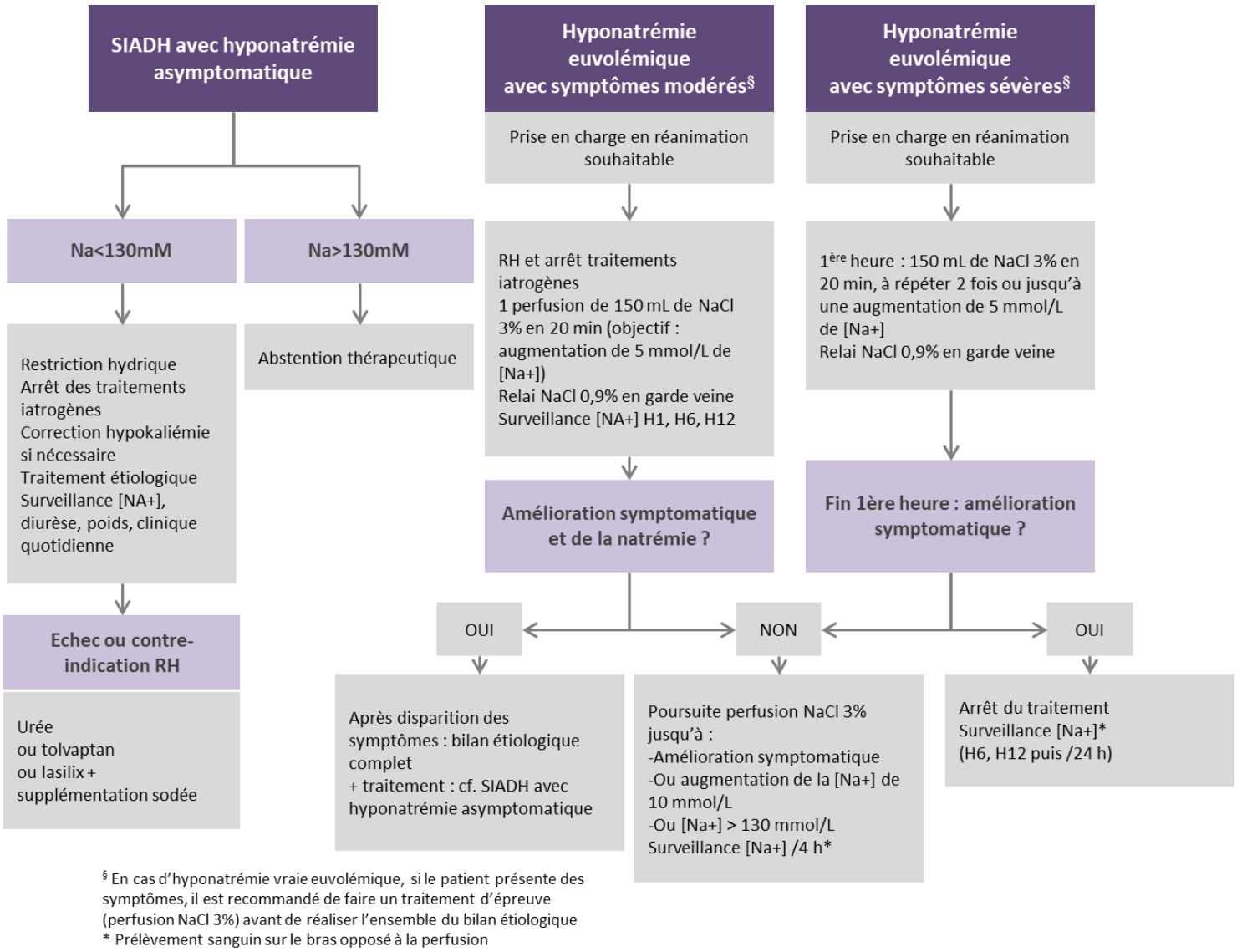
- Inconvénients : non recommandé par les experts européens (contrairement aux américains) en raison des risques de correction trop rapides de la natrémie, durée d'utilisation limitée à 4 semaines (recommandation FDA en raison de la survenue d'hépatopathie), molécule onéreuse.
- Une analyse *post-hoc* poolée des deux études de phase 3 comparant l'utilisation de Tolvaptan *vs* placebo chez des patients présentant un SIADH para-néoplasique a montré une efficacité et un profil de tolérance correct dans cette population (125).

- **Urée** :
  - Posologie : de 0,25 à 0,50 g/kg/jour.
  - Inconvénients : goût (à boire avec du jus d'orange, préparation pharmaceutique en sachet : urée 10 g + NaHCO3 2 g + acide citrique 1,5 g + sucrose 200 mg, à dissoudre dans 100 mL d'eau), préparation pharmaceutique.
- **Furosémide + supplémentation sodée :**
  - Posologie : 20-40 mg de furosémide par jour selon volémie et réponse clinique, associé à 2-4 g de sel en plus de l'alimentation (pour un total de 10-12 g).
  - Surveillance du ionogramme et de la volémie.
- **Ne sont pas indiqués pour le traitement correctif de l'hyponatrémie :**
  - Sérum salé isotonique (NaCl 0,9%).

Plusieurs traitements sont proposés en 2ème ligne par les différentes recommandations, après échec ou intolérance de la restriction hydrique. Aucun n'a démontré de supériorité par rapport aux autres, et le praticien devra tenir compte de la tolérance, de la disponibilité des traitements, de ses habitudes et du coût dans le choix d'une thérapeutique.

	Recommandations européennes 2014 (124)	Recommandations américaines 2013 (126)
Urée	**Recommandé en 2ème ligne après RH**	**Recommandé en 2ème ligne après RH**
Lasilix + supplémentation sodée	**Recommandé en 2ème ligne après RH**	Non mentionné
Tolvaptan	Non recommandé	**Recommandé en 2ème ligne après RH, avec précautions d'emploi nécessaires**

Tableau 28 – Recommandations européennes et américaines sur l'indication des traitements de 2ème ligne du SIADH.



§ En cas d'hyponatrémie vraie euvolémique, si le patient présente des symptômes, il est recommandé de faire un traitement d'épreuve (perfusion NaCl 3%) avant de réaliser l'ensemble du bilan étiologique
* Prélèvement sanguin sur le bras opposé à la perfusion

Figure 8 – Prise en charge thérapeutique d'une hyponatrémie

2.3 Conduite à tenir en cas de correction trop rapide

En cas d'augmentation de la natrémie supérieure à 10 mmol/L dans les 24 premières heures ou supérieure à 8 mmol/L/jour ensuite :

- Arrêt du traitement correctif en cours.
- Avis néphrologique pour perfusion de glucose (10 ml/kg en 1 heure) et/ou perfusion de desmopressine 4 µg.

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DECLARATION DES LIENS D'INTERETS

Les personnes ci-dessous ont déclaré des liens d'intérêt en oncologie thoracique pour des participations à des congrès, séminaires ou formations ; des bourses ou autre financement ; des rémunérations personnelles ; des intéressements ; ou tout autre lien pertinent dans les 3 dernières années :

ARPIN D : Takeda, Roche
AUDIGIER-VALETTE C : Roche, Abbvie, BMS, MSD, Takeda, Boehringer, AstraZeneca, Pfizer, Novartis, Fabre, Amgen, Lilly
AVRILLON V : BMS, Abbvie.
BARANZELLI A. : Roche, Takeda, BMS, MSD
BAUD M. : Boehringer
BAYCE BLEUEZ S. : Roche, BMS, AMGEN
BERARD H : Roche, Pfizer, Boehringer
BERNARDI M. : BMS, Sandoz, Roche
BOMBARON P : Roche, AstraZeneca, BMS, Boehringer.
COURAUD S. : AstraZeneca, Boehringer Ingelheim, Lilly, Merck, MSD, Novartis, Pfizer, Roche, Sysmex Innostics, Chugai, Laidet.
DELCLAUX B : BMS, Boehringer, AstraZeneca, Novartis, Roche.
DEMIR S : Pfizer, BMS
FALCHERO L. : Roche, Boehringer, AstraZeneca, BMS, Pfizer, Amgen.
FOUCHER P : AstraZeneca, Roche, BMS, MSD, Chugai, Vifor, IFCT, PFIZER
FOURNEL P. : Lilly, Amgen, BMS, MSD, Roche, Pfizer, Astelas, Boehringer, AstraZeneca, Takeda, Novartis, PFO
GERINIERE L : Lilly
GIAJ LEVRA M. : MSD, BMS, Roche, AstraZeneca, Novartis, Pfizer, Boehringer
GONZALEZ G. : Roche, Novartis, Pharmadom
GOUNANT V : Takeda, Lilly, Roche, AstraZeneca, BMS, Boehringer, Pfizer, Novartis.
GROUET A. : Boehringer, Novartis
HAMMOU Y : Chiesi, ISIS, Elia
JACOULET P : Boehringer
JANICOT H. Boehringer
LARIVE S. : TEVA Santé, Pfizer, Boehringer, BMS, MSD, AstraZeneca.
LE TREUT J. : AstraZeneca, Boehringer, Roche, BMS, MSD
LOCATELLI SANCHEZ M. : Boehringer, BMS, AstraZeneca, LFB
LUCIANI S : Pfizer
MARTIN E. : Astra Zeneca
MASTROIANNI B : Amgen
MERLE P : MSD, AstraZeneca, BMS, Pfizer
MORO-SIBILOT D : Roche, Pfizer, Lilly, Boehringer, MSD, BMS, Takeda, AstraZeneca, Novartis, Amgen, Abbvie
NAKAD A : BMS
ODIER L. : Lilly, Amgen, Pfizer
PAULUS V : MSD, Roche
PEROL M. : Roche, AstraZeneca, Boehringer, Lilly, Takeda, BMS, MSD, Pfizer, Novartis, Chugai
PERROT E. : AstraZeneca
PINSOLLE J. : Takeda, MSD, Roche, Pfizer, Agiradom.
RANCHON F : CELGENE, JAZZPHORNA
SAKHRI L : Pfizer, BMS.
SOUQUET P.-J. : Amgen, AstraZeneca, BI, CHUGAI, P FABRE, LILLY, MSD, BMS, Pfizer, Novartis, Sandoz, Roche, Takeda, Bayer, Merrimack, Merck, Astellas,
TAVIOT B : Chiesi
TISSOT C : Amgen, Sandoz, BMS
WATKIN E. : MSD, AstraZeneca, Boehringer, Pfizer, Roche, BMS
ZALCMAN G. : Roche, AstraZeneca, BMS, Pfizer, Novartis, Abbvie, MSD, Boehringer, GSK, Inventiva

Les autres participants et membres des groupes de travail n'ont déclaré aucun lien d'intérêt en oncologie thoracique.
Aucun participant ou membre d'un groupe de travail n'a rapporté de lien d'intérêt avec l'industrie du tabac.

MENTIONS LEGALES

La réunion de mise à jour des référentiels (édition 2019) a été organisée par l'Association de Recherche d'Information Scientifique et Thérapeutique en Oncologie Thoracique (ARISTOT).
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Pour citer le référentiel :
Couraud S, Etienne-Mastroianni B, Fontaine-Delaruelle C, Giaj Levra M, Toffart A-C, et le comité de rédaction des référentiels Auvergne Rhône-Alpes en oncologie thoracique. Référentiel sur les Soins de Support et Nutrition : actualisation 2019. ARISTOT ; 2019. ISBN 978-2-490858-07-1. Téléchargeable sur http://espacecancer.sante-ra.fr/Pages/referentiels.aspx et sur www.lecancer.fr

Couraud S, Etienne-Mastroianni B, Fontaine-Delaruelle C, Giaj Levra M, Toffart A-C, on behalf of the editing committee of Auvergne Rhône-Alpes Guidelines in Thoracic Oncology. [Guidelines on Supportive Care and Nutrition in Lung Cancers: 2019 Update]. ARISTOT; 2019 [French]. ISBN 978-2-490858-07-1. Available from http://espacecancer.sante-ra.fr/Pages/referentiels.aspx and from www.lecancer.fr

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