Aquaretics And Natriuretics Current Therapeutic Uses And Future Prospectives

Essay

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List of Contents

Title Page No.

List of Tables

List of Figures

List of Abbreviations

Abb.	Full term
AA	Amino acid
ACEI	Angiotensin converting enzyme inhibitors
ADH	Antidiuretic hormone
ADHERE	Acute decompensated heart failure registry
ADHF	Acute Decompensated heart failure
ADM	Adrenomedullin
ADPKD	Autosomal dominant polycystic kidney disease
AMPc	Adenosine monophosphate (cyclic)
Ang	Angiotensin
ANP	Atrial natriuretic peptide
AQ2	Aquaporin 2
AQMCV	Aquaporin water channel containing vesicles
AQP	Aquaporin
ARB	Angiotensin receptor blocker
ARBs	Angiotensin Receptor blockers
AS	Aortic stenosis
ASCEND	Acute study of clinical effectiveness of neseritide in decompensated heart failure
AVP	Argenin vasopressin
AVR	Ascending vasrecta
BACH	Biomarkers in acute heart failure
BMI	Body mass index

List of Abbreviations (Cont...)

Abb.	Full term
BNP	Brain natriuretic peptide
cAMP	Cyclic adenosine monophosphate
CD	Collecting duct
CD-NP	Cenderitide
cGKI	cGMP-regulated protein kinase
CGMP	Cyctic guanosine monophosphate
CHF	Congestive heart failure
CNP	C type natriuretic peptide
CNS	Central nervous system
COMPASS	Carperitide effects observed through monitoring dyspnea in acute decompensated heart failure study
CPAP	Continuous Positive airway pressure
CRTP	Cardiac resynchronization therapy pacemaker
CSWS	Cerebral salt wasting syndrome
CV	Cardio-vascular
DI	Diabetes insipidus
DPPIV	Dipeptidyl peptidase IV
DVR	Descending vas recta
ECF	Extracellular fluid
ECFV	Extracellular fluid volume
ED	Emergency department
EMA	European Medicines Agency

List of Abbreviations (Cont...)

Abb.	Full term
ETT	Endotracheal tube
EVEREST	Efficacy of vasopressin antagonism in outcome of heart failure outcome study with Tolvaptan
FDA	Food and drug Administration
GC-A	Guanyl cyclase A
GFR	Glomerular filtration rate
GIT	Gastrointestinal tract
HARMONY	Hypertension analysis of stress reduction using mind fullness medications and Yoga
HF	Heart failure
H-ISDN	Hydralazine and isosorbid dinitrate
HR	Heart rate
ICD	Implantable cardioverter defibrillator
ICU	Intensive care unit
IRAG	Inositol 1, 4, 5 triphsophate associated cGMP kinase substrate
IS-OM	Inner strip of outer medulla
K	Potassium
LBBB	Left bundle branch block
LIBRA	Multicenter randomized double blind placebo controlled study to evaluate the efficacy and safety of oral Lixivaptan capsule in subjects with euvolemic hyponatremia
LVAD	Left ventricle assist device
LVEF	Left ventricle ejection fraction

List of Abbreviations (Cont...)

Abb.	Full term
LVEF	Left ventricle ejection fraction
MICP	Myosin light chain phosphate
MR antagonist	Miniralocorticoid receptor antagonist
MR	Mitral regurje
MRI	Magnetic resonance angiography
MR-ProADM	Mid regional fragement of pro ADM
MR-ProANP	Mid regional fragement of ProANP
Na	Sodium
NEP	Neprilysin
NEPi	Neprilysin inhibition
NF-KB	Nuclear factor K light chain enhancer
NIPPV	Non invasive positive pressure ventilation
NP	Natriuretic peptides
NPR-C	Natriuretic peptide clearance receptor
NTG	Nitroglycermine
NT-ProBNP	N-terminal prohormone BNP
NYHA	New York Heart Association
NYHA	New York heart association
OD	Osmotic demylination
ODS	Osmotic demyelination syndrome
OPC-31260	Mozavaptan
OPC-41061	Tolvaptan
OS-OM	Outer strip of outer medulla

List of Abbreviations (Cont...)

Abb.	Full term
OVLT	Organum vasculosum laminae terminalis
PaO2	Partial pressure of oxygen
PCWP	Pulmonary capillary wedged pressure
PDEs	Phosphodiesterases
PGE2	Prostaglandin E2
PKG	cGMP Protein kinase G
PROTECT	Pro-Btype Natriuretic peptide outpatient tailored chronic heart failure therapy study
PVN	Paraventricula neucleus
RAA	Renin angiotensin adolsterone
RAAS	Renin angiotensin aldosteron system
RGS2	Regulator of G protein signaling subtype 2
SALT	Study of ascending levels of tolvaptan
SHR	Spontaneously hypertensive rats
SIADH	Syndrome of Inapropriate antidiuretic hormone
SIRIUS I	Effects of the renal natruiuretic peptide urodilatin (ularitide) in patients with decompensated heart failure
SIRIUS II	Renal effects of ularitide in patients with decompensated heart failure
SMCs	Smooth muscle cells
SNS	Sympathetic nervous system
SON	Supra Optic Neucleus

List of Abbreviations (Cont...)

Abb.	Full term
SPO2	Saturationof peripheral oxygen
SR	Sarcolasmic reticulum
SR121463	Satavaptan
SR49059	Relcovaptan
TEMPO	Tolvaptan efficacy and safety in management of utosomal dominant polycystic kidney disease
TRPV	Transient receptor potential vanilloid
TRUE-AHF	Trial to evaluate the efficacy of safety of ularitide intravenous infusion in patients suffering from acute decompensated heart failure
UAE	Urinary albumin execretion
UCI	Urea channel inhibitors
URO	Urodilatin
V1a	Vasopressin 1a
V1b	Vasopressin 1b
V1R	Vasopressin 1 receptor
V2	Vasoprwessin2
V2R	Vasopressin 2 receptor
VMAC	Vasodilation in the management of acute congestive heart failure
YM-087	Conivaptan

Abstract

Hyponatremia is the most common disorder of electrolytes encountered in clinical practice. Despite knowledge of hyponatremia since the mid-20th century, this common disorder remains incompletely understood in many basic areas because of its association with a plethora of underlying disease states, and its causation by multiple etiologies with differing pathophysiological mechanisms. Optimal treatment strategies have not been well defined, both due to these reasons, and because of marked differences in symptomatology and clinical outcomes based on the acuteness or chronicity of the hyponatremia. The increased urine output produced by the aquaretics (aquaretics mostly act on vasopressin receptor antagonism leading to water excretion) , is quantitatively equivalent to that of diuretics such as furosemide; qualitatively it is different in that only water excretion results and excretion of urinary solutes is not augmented. Thus, aquaretics produce solute-sparing water excretion in contrast to classic diuretic agents that block distal tubule sodium transporters, leading to simultaneous electrolyte and water losses. For this reason, the renal effects produced by this group of drugs have been termed aquaretic to distinguish them from the renal effects produced by classical diuretic agents, which are natriuretic and kaliuretic as well. This is not simply a semantic issue, because appreciating these important differences in renal effects is crucial for the intelligent clinical use of aquaretics. For example, the negative water balance induced by aquaretic agents has less adverse effect on neurohormonal activation and renal function than comparable degrees of urine output induced by loop diuretic agents, because only one third of the negative water balance induced by aquaretics derives from the ECF, whereas two thirds comes from intracellular water. Selective vasopressin 2 antagonists orally administered include (1) tolvaptan used in slowing progression in APCKD in TEMPO study and in EVEREST study for treatment of heart failure. (2) Mozavaptan present in Japan market for control of hyponatremia in paraneoplastic SIADH. (3) satavaptan showing promising results in controlling hyponatremia in liver cirrhosis patients (4) Lixivaptan involved in studies for treatment of eurovolemic hyponatremia. On the other hand conivaptan a non selective vasopressin antagonist was FDA approved for treatment of euvolemic and hypervolemic hyponatremia in hospitalized patients.

Keywords: Aquaretics, Aquaretics

INTRODUCTION

Hyponatremia is the very most common electrolyte disturbance that occur in hospitalized patients ***(Schrier, 2006).*** It is associated with high mortality and morbidity in patients with liver, heart or neurological disease ***(Goldberg, 2006; Wu et al., 2006; Bhardwaj, 2006).***

Vasopressin receptors play an important role in circulatory and water homeostasis including subtypes. Vasopressin 1a receptors (V1a) are located mainly in blood vessels having vasopressor action, vasopressin 1b receptors (V1b) found in the pituitary gland & are involved in vasopressin – stimulated secretion of adrenocorticotropin ***(Green berg and Verbalis, 2006; Streefkerk and van Zwieten, 2006).***

Vasopressin 2 receptors (V2) are located in basolateral membrane of the cells of collecting duct of the kidney, they induce water reabsorption ***(Morello and Bichet, 2001)***. Aquaretics induce their effect through antagonizing vasopressin. V2 receptor antagonists (in contrast with the effect of diuretics) include a highly hypotonic diuretic effect without substantially affecting the excretion of electrolytes. V2 receptor antagonists include Mozavaptan, Lixivaptan Satavaptan and Tolvaptan ***(Decaux et al., 2008).***

Tolvaptan has been used in a phase III (TEMPO3/4) study to block V2 receptors thus inhibiting cyst growth in adult polycystic kidney disease patients ***(Torres et al., 2011).*** Conivaptan is a V1a, V2 non selective receptor antagonist that has been approved by the US food and Drug Administration as an intravenous infusion treatment of euvolemic and hypervolemic hyponatremia ***(Decaux et al., 2008).***

Some published studies showed V2 receptor antagonists effectiveness in increasing electrolyte free water excretion in various water retention disorders including hyponatremic patients with cirrhosis ***(Wong et al., 2003),*** congestive heart failure ***(Gheoghiade et al., 2006)*** and patients with syndrome of inappropriate antidiuretic hormone secretion ***(Soupart et al., 2006)***.

On the other hand natriuresis; that is sodium execretion in urine is the principal action of natriuretic peptides. This action is concomitant with diurices; vasodilatation, anti-inflammatory and antifibrotic effects as well. This action led to the pursuit of natriuetic peptides and chemically modified peptides as adjunctive therapy in management of myocardial ischemia ***(Kousholt, 2012)***.

Aim of the Work

To review the current therapeutic and diagnostic uses and future prospectives of aquaretics and natriuretics with specific emphasis on their role in nephrology practice.