

Meta-analysis about Atrial Natriuretic Peptide (ANP)

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Abstract

Among the topics studied in physiology and aging, a hormone has been drawing attention from the scientific community: the Atrial Natriuretic Peptide (ANP). The ANP, which is produced by the cardiac atria, has demonstrated decisive action in endocrine mechanisms of action inhibiting sodium reabsorption in nephrons, revealing a direct influence on physiological mechanisms linked to aging and chronic stress. The overall objective of this study was to assess and analyze scientific literature on the ANP in the Pubmed database from 2010 to 2012. 30 articles were collected, verifying authorship and gender division of species, instruments and types of research. The results showed that the research of multiple authorship appeared mostly with 99.1%, being 51.8% of male authorship, 17.9% of female authorship and 29.5% of publications not identified. Research with only one author appears with 0.8% in total. As the types of species used, it was observed 50.3% of the works with humans, 40% with animals and 6.7% mixed (animal / human). As to the instruments used, the biochemical markers were the ones that stood out, with 30%, followed by label arterial pressure with 12, 2%, drugs, with 11.1% and microscopic studies with 10%. In the typology of research, biochemical research appears first, with 33.3%, followed by research morphophysiological/biochemical research, with 30%, Physiological / biochemical, with 26.7%, Physiological with 6.7% and Morphophysiological with 3.3%. We can conclude that the publications about the hormone ANP are still little explored when the focus is aging. In the analyzed publications, there is important information about the physiological and biochemical role of ANP as well as on their molecular composition.

Keywords: Atrial Natriuretic Peptide (ANP), heart disease, nephropathy and aging.

1 Introduction

According to Witter (2005), the objective of a meta-analysis of scientific production is to reveal the production and dissemination of topics surveyed in a given area of knowledge and its quality as a material for the advancement of science.

Lourenço (1997) affirm that the scientific production is the sum of works about a specific subject of interest from a specific scientific community that can contribute to science and research. States that scientific production refers to a dynamic process and unfinished, worthy of constant revision.

Christofi and Witter (2007) are of opinion that scientific work is fundamental to evaluate the advancement of a particular area of knowledge. The research metascience enable investigation, evaluation and definition, not only on the quality of studies, but also on the quality of scientific periodic and communications.

The adoption of computer resources and the existence of the Internet made possible an expansion of the possibilities of access to academic production becoming more accessible to search and obtain bibliographic sources, as well as analyzing data and writing papers (CASTIEL and SANZ-VALERO, 2007).

The increase of the elderly population in the last century and concern for the quality of life is unquestionable (VECCHIA, RUIZ, BOCCHI et al., 2005). Seid and Zannon (2004) go even further when they report an increase in chronic diseases in the elderly, raising concepts of quality of life for this age group.

Man has been researching more and more about aging in living organisms and their adaptive molecular evolution in order to increase the longevity and quality of life (JACOB FILHO and GORZONI, 2008). According to these authors, there are more than three hundred theories on aging, which demonstrates the complexity of the process and its systematization. For these authors, the disparity between chronological and biological age may be influenced by intrinsic and extrinsic factors and extrinsic factors have a greater impact on aging.

A hormone that has been researched and is linked to the aging process and also to biological rhythms is the hormone atrial natriuretic peptide (ANP) (CHARLOUX, BRANDENBERGER, PIQUARD et al., 2007). The granules of atrial natriuretic peptide were first described by Bruno Kisch in 1956 in mice (SILVA, FERREIRA, BLACHER et al., 2003). Subsequently, when it was found that these granules containing a chemical natriuretic factor that acted as a chemical substance has for the first time, to be called atrial natriuretic peptide (PALADE, 1961).

Human Natriuretic peptides are a family of peptides structurally similar but genetically distinct, including the atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and type C natriuretic peptide (CNP), all being important for cardiorenal homeostasis (CHEN, CHEN, ZHU et al., 2011). Afzal, Qvigstad and Aronsen et al. (2011) states that very high plasma levels of ANP, BNP and

CNP, produced by the myocardium, are direct consequences of heart failure.

Natriuretic peptides have numerous actions that inhibit the hypertrophy of cardiomyocytes, among them diuretic, natriuretic, and vasodilatory actions also autocrine / paracrine actions in cardiomyocytes (HORIKAWA, PANNEERSELVAM, KAWARAGUCHI et al., 2010). The ANP has demonstrated decisive action in endocrine mechanisms of activation, by inhibiting sodium reabsorption in the nephrons in both the proximal and distal segments, including the collecting ducts (ZHAO, PANSY and NAVAR, 2010). Soualmia, Djeridane, Eurin et al. (2007) reported that the ANP is produced by the atria and secreted into the bloodstream in response to various stimuli, including the autonomic nervous system (ANS) and the renin-angiotensin system.

Most of the ANP granules are located near the nucleus, in combination with the components of cardiomyocytes functionally involved with the production and secretion of ANP (MAKSIMOV, KOROSTYSHEVSKAYA, MARKEL et al., 2004). The ANP, when released into the bloodstream, will act in the renal tubules to produce lowering of blood pressure by increasing the secretion of sodium and water as the consequent decrease in blood volume (CLERICO, ZUCHELLI, PILO et al., 2006; PAN, 2008). Wu, Cai, Chen et al. (2009) suggest that this system exists in all vertebrates from the most primitive species. Authors such as Woodman, Malakul, Cao et al. (2008) also claim that the ANP brings not only extremely beneficial effects on the cardiovascular system, but also excellent antioxidant activities.

Heart disease is still the leading cause of death worldwide killing twice as much as cancer, reaching 20 million deaths annually. The role of the cardiologist remains one of the most important within the medical field in an attempt to reduce these numbers as alarming. More and more the control of blood pressure has become a common place in doctor's office. Problems of chronic stress, wrong diet and lack of sleep, are just some of the causes of high blood pressure. We know that diseases such as myocardial infarction, stroke and aneurysm can be directly linked to an imbalance of pressure. The trend of these factors worsen over time in society is fact because humans are increasingly subjected to social pressures, raising the stress level too. The human body, suffering from external pressures, will always be pre-disposed to serious consequences to health, mainly related to cardiac physiology.

In the present study, we conducted an evaluation of the scientific production of ANP in the last three years, 2010-2012, either in young or elderly reporting differences between authorship and genres, the most frequently used

tools, division of species (animals and / or humans) and typology of research.

2 Materials and Methods

The material analyzed consisted of journal articles on the ANP, indexed in Pubmed, seeking the relationship of this hormone with aging and age-related diseases. The data were collected between 2010 to 2012 totaling 30 items. The search of articles was made through the keywords: atrial natriuretic peptide or ANP, ANP and aging, ANP and heart / heart failure, ANP and renal / kidney failure.

3 Results and Discussion

In Table 1, we can see the prevalence of multiple author ship in international work on the ANP, with 99.1% of publications, and, among them 51.8% of publications with male author, 17.9% with female author and 29.5 % of publications were not identified. Only 0.8% was unique publications, being exclusively with male author.

It is evident that, international publications related to ANP are, mostly, with several authors with very few publications with one author and no with two authors. Perhaps this shows the complexity of the work related to the hormone ANP and the need for multiple authors to perform these kinds of searches. Typically researches on the ANP are descriptive or experimental laboratory works, requiring considerable complexity. Therefore, it is normal to have several authors in one work so that it is prepared correctly and efficiently.

In contrast, in a study of meta-analysis on the relationship of the ANP precursor gene linked to hypertension, the author Niu (2011), developed his work on single authorship, contradicting what most works present today in the area of physiology. However, a meta-analysis research requires less work from one author's than experimental work, because in this case the authors need a chronology of the animals / humans that can hardly be taken individually.

Another work of one author that caught our attention was that of Pandey (2011), which presents an approach on the ANP receptors and the advantages of using this peptide with therapeutic purposes. However, this work was undertaken in the form of review, i.e., there was no need to use animals or humans to develop quantitative work.

It is clear that all descriptive studies and / or experimental require multiple authorship. Nowadays, in the field of physiology, it is unlikely that the work of a single author could be well regarded in the scientific community. Its complexity and form of conduct in the experiment almost make impracticable an individual research without the cooperation of others.

Table 1. Frequency of authors and genre in publications of ANP.

Authors	Male		Female		No identified		Total	
	F	%	F	%	F	%	F	%
Multiple Authors	116	51.8	40	17.9	66	29.5	222	99.1
One Author	2	0.8	-	-	-	-	2	0.8
Total	118	52.7	40	17.9	66	29.5	224	100

Table 2. Types of Specimens used in researches about ANP.

	Young	Aged	Both	Not Mentioned	Total	%
Human	4	2	1	9	16	53.3
Animal	5	-	1	6	12	40.0
Animal/Human	-	-	-	2	2	6.7
Total	9	2	2	18	30	100

In Table 2, we can see the dominance of research on ANP in humans. Of the 30 studies published 16 were in humans, 12 with animals and 2 were mixed, i.e., in animal / human.

The ANP had, in the majority of the cases, greater number of publications in humans, according to the survey carried out in the present work. Although 40% of works are in mice, being a quite significant number, 53.3% of the work produced in humans are due to the high prevalence of heart disease that reflect the health system according to data from the World Health Organization (WHO), 2011, reporting that 17.3 million people worldwide die from heart disease every year, being one of its main causes, the hypertension.

Therrien, Kim, Terunuma et al. (2010) demonstrated a skin gene therapy approach which can regulate blood pressure and to treat systemic hypertension expressing ANP being able to lower blood pressure in human bioengineered skin equivalents. Cannone, Boerrigter, Cataliotti et al. (2011) in a study of genetic evaluation of cardiovascular disease also showed that susceptibility for cardiometabolic diseases support the possible protective role of natriuretic peptides for their favorable effects on metabolic function. However, replication studies are needed to confirm these findings. Chen, Chen, Zhu et al. (2011) went further by reporting that natriuretic peptides are the new candidate therapies for cardio-renal diseases. The results mentioned in the above works, seem clear that therapies of natriuretic peptides is a fact in control of cardiac diseases. Experimental studies in humans will be a more frequent need for dose adjustments, time use, pharmacokinetics and pharmacodynamics of the hormone, to find the correct way to administer it, and can be used even as a prophylactic treatment.

WHO have a series of priorities for the coming years, including increased attention to cardiovascular diseases and improve care to patients suffering from heart disease and stroke, promoting diets focused on the well-being of the heart and physical activities for the entire population, to improve the detection and control of high blood pressure worldwide. If a new drug can help all these factors, we may experience a reduction in the numbers of heart disease in the next decade thanks to new works with this hormone.

In Table 3, we can see that in relation to the instruments used in the works, the biochemical markers appear more frequently, with 30%, followed by marker blood pressure, 12.2%, drugs, with 11.1% and microscope 10%.

Studies with hormones require biochemical evidence for a more accurate assessment on the quality of the research. This is one of the factors that can prove the veracity of research in the area of health. Authors give much importance to these markers, because with them it is possible to analyze and evaluate the comparisons established in their respective goals and then conclude the results more accurately.

Biochemical markers are substances normally found within cells which can be released into the circulation, as

Table 3. Different materials used in researches about ANP.

	F	%
Biochemical markers	26	30.0
Arterial pressure markers	11	12.2
Drugs	10	11.1
Microscopy	9	10.0
Infusion of ANP	7	7.8
Human tissue	7	7.8
Other	7	7.8
Animal tissue	6	6.6
Echo/electrocardiogram	5	5.6
Catheter	2	2.2
Total	90	100

in cases of injury, depending on the marker. Normally present indisputable usefulness in quantitative research, both descriptive and experimental. According to Arias, Mazza and Funke (2003), biochemical methods to detect hormone has the advantage of working with quantitative results being very common in the research with ANP. We can consider that because the need of the credibility of the research, these markers are essential, being used with increasing frequency.

According to Vieira (1999), the increased use of biochemical markers is due to the emergence of new research methods and the need for a better understanding of the pathophysiology of the diseases. Niu (2011) demonstrated, in a work of meta-analysis the relationship of the ANP gene with hypertension, in which the materials were, mostly, biochemical markers which were used in the analysis of the results and in the comparison results. Cunha, Ribeiro and Oliveira (2006) reported that biochemical markers may provide relevant information for an accurate and reliable diagnosis, thus avoiding higher probabilities of errors in the results of the research.

It seems clear that the use of biochemical tests is a consensus among materials used in research in physiology. Vieira (1999), Arias, Mazza and Funke (2003) and Cunha, Ribeiro and Oliveira (2006) showed, in all their researches, the importance of these materials in the veracity of the data surveyed. Likewise, the results presented in this paper can prove, as in the work of Niu (2011), in their meta-analysis, these markers are essential in the development of research in physiology. New methods have been used to allow the results to be more accurate, showing increasingly, publishing best work. Biochemical tests depend directly on advances in technology to continue progressing as a direct tool in research work in the area of physiology, which will determine the veracity of results.

In Table 4, we can see that the biochemical research on ANP were predominant, with 10 publications in 30 studies

Table 4. Types of researches about ANP.

	Descriptive	Experimental	Meta-analysis	Total	%
Biochemical	5	4	1	10	33.3
Morphophysio/biochemical	2	7	-	9	30.0
Physiological/biochemical	2	6	-	8	26.7
Physiological	1	1	2	6.7	
Morphophysiological	1	-	-	1	3.3
Total	10	18	2	30	100

analyzed, followed closely by research Morphophysiological / biochemical, research with 9 publications and the physiological / biochemical, with 8 papers, physiological, with 2 works and 1 Morphophysiological publication.

Biochemical researches appear as most publications on the hormone ANP and there is very little difference compared to the other types, according to the search 2010-2012. Thus, it seems clear the diversity of types of published research with the hormone ANP. However, we can see that, there are a few works with only morphophysiological and physiological research. This can be explained by the fact that research morphophysiological / biochemical and physiological / biochemical enable a range of significantly higher results in one study compared to other studies that focus on only one area.

In a meta-analysis research, Niu (2011) studied the genetic polymorphism of hypertension associated with the ANP, demonstrating a significant heterogeneity, in developing a major physiological / biochemical descriptive research. In this work, it was studied the relationship between the Polymorphism of Natriuretic Peptide Precursor T2238C gene and hypertension. These types of researches on the hormone ANP are relatively new. Physiological / biochemical descriptive researches are very important in order to know more about the action of ANP and its correlation with the genetic system.

Clearly, in studies on molecular and / or cellular biology, there will always be a clear need for a greater focus on experimental aspects, since, descriptive studies and literature reviews have been extensively explored and published. Experimental work will bring new insights into the physiology of hormone or any other marker to be studied.

Pandey (2011) demonstrated this fact in his physiological / biochemical descriptive review when reporting the benefits of therapies using ANP. Likewise, the research of Niu (2011), also physiological / biochemical descriptive, but about meta-analysis on the ANP gene, can bring significant contributions to future experimental research on this hormone. Further work in the area of physiology will be more experimental rather than descriptive. This fact indicates that the new studies will be focused on the development of drugs and / or supplements that may directly or indirectly influence the physiological action of the hormone in the prevention or treatment of diseases.

4 Conclusion

The natriuretic peptide hormones, apparently has his role established in cardiac physiology. However, the publications on the hormone ANP are not yet exhausted especially when the focus is aging. It was observed by the publications

analyzed, that there is important information about the physiological and biochemical action of ANP as well as about its molecular constitution and genetic polymorphism. However, specific works on some aspect of aging are scarce in the databases. For example, we expected to find more information about physiological aspects of ANP in various age groups of mammals. Thus, further studies are needed to demonstrate the relationship of blood pressure and deficient synthesis of ANP or if ANP synthesis is increased to combat the rise in pressure caused by different factors such as hardening of the arteries due to aging.

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