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Neurological and Pharmacological Action of Adrenaline-Review

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ABSTRACT

The adrenergic system which is called the parasympathetic system, where the neurochemicals are formed from the precursor aminoacid named phenylalanine. The main neurochemicals encompassed in the adrenergic nervous system is adrenaline (epinephrine), nor adrenaline (nor epinephrine), dopamine. These neurochemical have immense pharmacological action in human system. Among the adrenergic neurochemical adrenaline act as vasoconstrictor, it acts in wound healing; it is used in the treatment of anaphylactic shock etc.

KEYWORDS: *neurochemicals, adrenergic nervous system, adrenaline (epinephrine), nor adrenaline (nor epinephrine), dopamine*

INTRODUCTION

Adrenergic System

Adrenergic is a term availed to describe proteins and drugs that interact with adrenaline or noradrenaline, also known as the epinephrine and norepinephrine, respectively.

- For example, adrenergic receptors are membrane proteins (macromolecules) that are the target for epinephrine andnorepinephrine, while the adrenergic transporters are proteins that carry norepinephrine across the cell membrane of the nerve cells.
- An adrenergic agonist is a drug that typically produces the same effect as epinephrine or the norepinephrine.
- Whereas an adrenergic antagonist is a drug that generally ceases the effects of epinephrine andnorepinephrine(Motiejunaite et al.,2021).

- Epinephrine and the norepinephrine act as hormones and neurotransmitters in the numerous biological processes.
- When epinephrine is released, it contracts and mainly relaxes smooth muscle and increased blood pressure.
- Epinephrine can also increase the level of the glucose and fatty acids in the blood, generally leading to increased energy production within the cells.
- In addition, epinephrine and norepinephrine initiate the flight-or-fight response.
- The Norepinephrine typically increases the heart rate and blood flow to muscles during the stressful situations and affects the part of the brain that is responsible for attention and response. It also elevates blood glucoselevels, thus providing needed energy for cells. The Norepinephrine also acts as an anti-inflammatory agent when it is released as a neurotransmitter between the nerve cells of the brain (Hou et al., 2023).

The Characteristics of Adrenergic Agonist: Most of the adrenergic drugs are derivatives of β-phenyl ethylamine. The Substitutions on the benzene ring or on the ethylamine side chains produce a variety of the compounds with varying abilities to differentiate between α and β receptors and to penetrate the CNS. Two important structural characteristics of these drugs are

1) the number and location of THE OH substitutions on the benzene ring and

2) the nature of the substituent on the amino nitrogen.

A. The Catecholamines

Sympathomimetic amines that comprises the 3, 4-dihydroxybenzene group (such as epinephrine, norepinephrine, isoproterenol, and the dopamine) are called catecholamines.

These compounds share the following properties:

1. The High potency: Catecholamines (with –OH groups in the 3 and 4 positions on the benzene ring) show the highest biopotency in directly activating α or β receptors.
2. The Rapid inactivation: Catecholamines are metabolized by COMT postsynaptically and by the MAO intraneuronally, as well as by COMT and MAO in the gut wall, and by the MAO in the liver. Thus, catecholamines have only a brief period of action when given parenterally, and they are inactivated (ineffective) when administered orally.
3. Poor penetration into the CNS: The Catecholamines are polar and, therefore, do not readily penetrate into the CNS. Nevertheless, most catecholamines have some bioclinical

effects (anxiety, tremor, and the headaches) that are attributable to action on the CNS(Perman et al.,2023).

B. The Non-catecholamines

Compounds lacking the catechol hydroxyl groups have longer half-lives, because they are not inactivated by the COMT. These include phenylephrine, ephedrine, and the amphetamine. These agents are poor substrates for MAO (an important route of metabolism) and, thus, show much of a prolonged duration of action. Increased lipid solubility of many of the non-catecholamines (due to the lack of polar hydroxyl groups) permits greater access to the CNS.

The Mechanism of action of adrenergic agonists:

1. Direct-acting agonists: These drugs act directly on the α or β receptors, producing effects similar to those that occur following stimulation of the sympathetic nerves or release of epinephrine from the adrenal medulla (Zhong et al.,2023). The Examples of direct-acting agonists include epinephrine, norepinephrine, isoproterenol, and the phenylephrine.

2. Indirect-acting agonists: These agents may block the reuptake of the norepinephrine or cause the release of norepinephrine from the cytoplasmic pools or the vesicles of the adrenergic neuron. The norepinephrine then traverses the synapse and binds to the α or β receptors. Examples of reuptake inhibitors and agents that cause norepinephrine release encompass cocaine and amphetamines, respectively.

3. The Mixed-action agonists: Ephedrine and its stereoisomer, pseudoephedrine, both simulate adrenoceptors directly and release norepinephrine from the adrenergic neuron.

The Direct-acting agonists: Direct-acting agonists bind to adrenergic receptors on effector organs without interacting with the presynaptic neuron. As a group, these bioagents are widely used clinically.

Epinephrine

The Epinephrine is one of the four catecholamines (epinephrine, norepinephrine, dopamine, and the dobutamine) commonly used in therapy. The prime three are naturally occurring neurotransmitters, and the latter is a synthetic compound. In the adrenal medulla, the norepinephrine is methylated to yield epinephrine, which is stored in chromaffin cells along

with the norepinephrine. On stimulation, the adrenal medulla releases about approx. 80% epinephrine and 20% norepinephrine directly into the circulation(Lee et al.,2019).

THE THERAPEUTIC USES OF EPINEPHRINE

1. **Anaphylactic shock:** epinephrine is the life-saving drug in the anaphylactic shock. It rapidly reverses the manifestations of the severe allergic reactions when given IM.
2. **Bronchial asthma (Goodall et al.,2017):** the Adrenaline is a powerful bronchodilator and has rapid onset but short duration of action. It is useful for the acute attack. Its use has declined because of its dangerous cardiac-stimulant effect. It ismainly given subcutaneously. It can be given by nebulization (as inhalation).
3. **Cardiac resuscitation:** In the treatment of the cardiac arrest due to drowning or electrocution, epinephrine is injected IV along with the other supportive measures such as external cardiac massage, as a part of the advanced life support.
4. **Prolongs the Duration of the local anesthesia:** epinephrine by its vasoconstrictor effect (α1) delays the systemic absorption of the local anesthetic and prolongs the duration of local anesthesia and promotes the local hemostasis.
5. **Controls Epistaxis and other capillary oozing (Evans et al., 2021):** Epinephrine is availed as a local haemostatic to control bleeding following tooth extraction and during the surgical procedures in nose, throat, larynx, etc. because of its vasoconstrictor effect.
6. **The Intraocular surgery:** Epinephrine is used in the induction and maintenance of mydriasis during the intraocular surgery.

Adverse effects of epinephrine

Epinephrine can produce adverse CNS effects that encompass anxiety, fear, tension, headache, and tremor. It can mainly trigger cardiac arrhythmias, particularly if the patient is receiving digoxin. Patients with the hyperthyroidism may have an increased production of adrenergic receptors in the vasculature, leading to an copioused response to epinephrine, and the dose must be precisely reduced in these individuals. Inhalation anesthetics also sensitize the heart to 5 the effects of the epinephrine, which may lead to tachycardia. Epinephrineaggrandizes the release of endogenous stores of glucose. In diabetic patients, dosages of insulin may have to be aggrandized (Golden et al.,2024).

Nonselective β-blockers prevent vasodilatory effects of epinephrine on β2 receptors, leaving

the α receptor stimulation unopposed. This may lead to increased peripheral resistance, and aggrandized blood pressure. Routes of administration: SC (slow absorption). IM (rapid absorption). IV (in emergency: rapid onset of action). Inhalation (in bronchial asthma). The Intracardiac IC (in resuscitation). The IV and IC routes are very dangerous (must be diluted to 1:10000).

Contraindications

1. Severe hypertension.
2. Cardiac disease.
3. The clinical manifestation of Thyrotoxicosis.

Norepinephrine

When administered in the therapeutic doses, the α- adrenergic receptor is most affected.

Effects: The Norepinephrine causes a rise in peripheral resistance due to intense vasoconstriction of most vascular beds, encompassing the kidney (α1 effect). Both systolic and diastolic blood pressures increase.

[Note: The Norepinephrine causes greater vasoconstriction than the epinephrine, because it does not induce compensatory vasodilation via β2 receptors on the blood vessels supplying skeletal muscles. The weak β2 activity of the norepinephrine also explains why it is not useful in the treatment of bronchospasm or anaphylaxis.]

Therapeutic uses: The Norepinephrine is used to treat shock (for example, septic shock), because it elevates vascular resistance and, therefore, increases blood pressure. It has no other clinically significant uses. The Pharmacokinetics: Norepinephrine is given IV for the rapid onset of action. It is rapidly metabolized by MAO and COMT.

Adverse effects: These are similar to the neurochemical epinephrine. In addition, norepinephrine is a bio-potent vasoconstrictor and may cause blanching and sloughing of skin along an injected vein. If the extravasation (leakage of drug from the vessel into tissues surrounding the injection site) occurs, it can also cause tissue necrosis. It should not be administered in peripheral veins, if possible. The Impaired circulation from norepinephrine

may be treated with the α receptor antagonist phentolamine. Isoproterenol: The Isoproterenol is a direct-acting synthetic catecholamine that stimulates both β1- and the β2adrenergic receptors. Its non-selectivity is a disadvantage and the reason why it is rarely availed therapeutically. Dopamine: The Dopamine occurs naturally in the CNS in, where it functions as a neurotransmitter, as well as in the adrenal medulla. Dopamine can mainly activate α- and β-adrenergic receptors (Mehta et al.,2023).

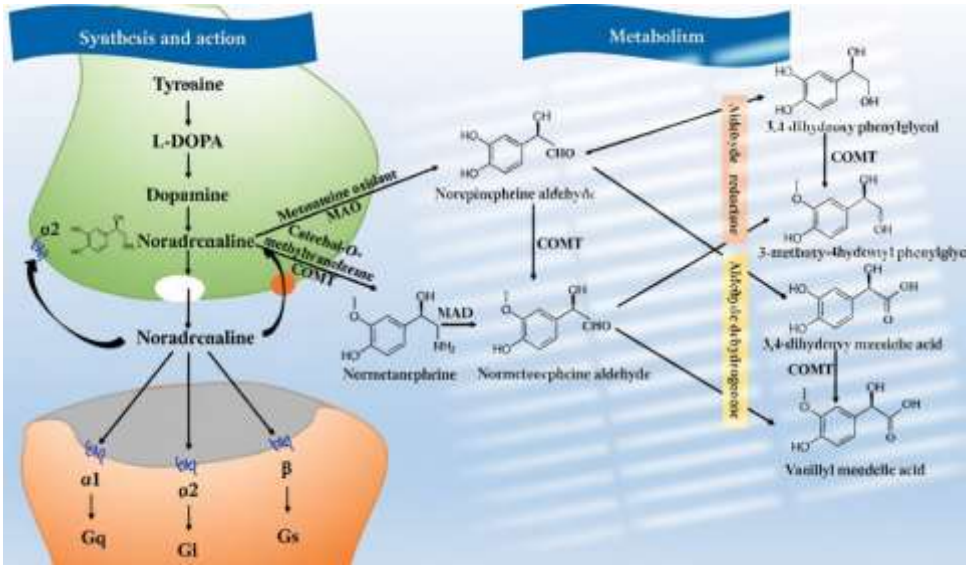

Figure: 1

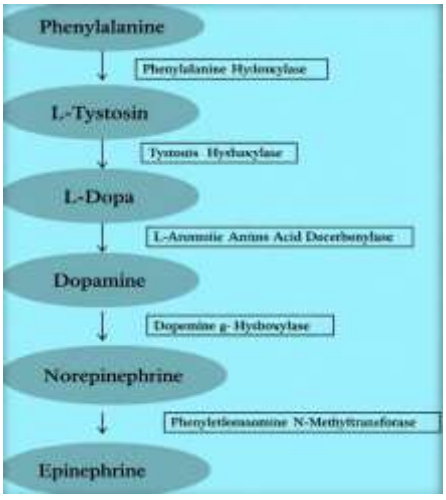

Figure: 2

The wiring of the brain with neural system is intriguing (Dr. S. Sreeremya,2025a).These system helps in signalling and processing the signals(Dr. S. Sreeremya,2025b). The various

disease associated with neural system can more or less be assessed with the neurochemicals (Dr. S. Sreeremya,2026).

Therapeutic uses: Dopamine can be availed for cardiogenic and septic shock. It raises blood pressure by stimulating the β1 receptors on the heart to elate cardiac output, and α1 receptors on blood vessels to increase total peripheral resistance.

Fenoldopam: It is availed as a rapid-acting vasodilator to treat severe hypertension in hospitalized patients, acting on the coronary arteries, kidney arterioles, and mesenteric arteries (Ellis et al.,2024).

The Dobutamine: is a synthetic, direct-acting catecholamine that is primarily a β1 receptor agonist. The Dobutamine is availed to increase cardiac output in acute heart failure as well as for inotropic support after cardiac surgery.

Oxymetazoline: simulates both α1- and α2-adrenergic receptors(Patel et al.,2021). The drug Oxymetazoline is found in many overthecounter nasal spray decongestants, as well as in the ophthalmic drops for the relief of redness of the eyes associated with swimming, colds, and contact lenses. Oxymetazoline directly simulates α receptors on blood vessels supplying the nasal mucosa and also conjunctiva, thereby producing vasoconstriction and decreasing congestion. Local irritation and the sneezing may occur with intranasal administration. Use for greater than 3 days is not mainly recommended, as rebound congestion and the dependence may occur.

Phenylephrine: binds primarily to α1 receptors causing vasoconstriction. Phenylephrine mainly acts as a nasal decongestant when applied topically or taken orally (Sacha et al.,2019).

Clonidine: is an α2 agonist availed for the treatment of hypertension. It can also be availed to minimize symptoms of withdrawal from opiates, tobacco smoking, and benzodiazepines. Both the clonidine and the α2 agonist guanfacine may be availed in the management of attention deficit hyperactivity disorder. Clonidine acts centrally on the presynaptic α2 receptors to produce inhibition of sympathetic vasomotor centers, decreasing sympathetic outflow to the periphery.

The Albuterol: is a short-acting β2 agonist (SABAs) availed primarily as bronchodilator and administered by a metered-dose inhaler. Albuterol is the SABA of choice for the management of the acute asthma symptoms. When these drugs are administered orally, they may mainly cause tachycardia or arrhythmia (due to the β1 receptor activation), especially in patients with underlying cardiac disease.

Salmeterol, formoterol, and the indacaterol: are long-acting β2 selective agonists (LABAs) used for the management of the respiratory disorders such as asthma and chronic obstructive pulmonary disease. The LABAs are not recommended as monotherapy for the treatment of asthma, because they have been shown to elate the risk of asthma-related deaths; however, these agents are potently efficacious when combined with an asthma controller medication such as an inhaled corticosteroid. The Mirabegron: is a β3 agonist that relaxes the detrusor smooth muscle and aggrandizes bladder capacity. It is used for patients with overactive bladder. Mirabegron may elate blood pressure and should not be availed in patients with uncontrolled hypertension(Lyng et al.,2019).

CONCLUSION

The adrenaline as neurochemical, which is a part of adrenergic neural system or sympathetic nervous system has two main reeptors named alpha and beta. This adrenaline has catechol nuleus so it is also called catecholamines. There are several precise actions of alpha and beta receptors in human body.

REFERNCES

1. Lyng JW, White CC, Peterson TQ, Lako-Adamson H, Goodloe JM, Dailey MW, Clemency BM, Brown LH. Non-Auto-Injector Epinephrine Administration by Basic Life Support Providers: A Literature Review and Consensus Process. Prehosp Emerg Care. 2019 Nov-Dec;23(6):855-861
2. Sacha GL, Bauer SR, Lat I. Vasoactive Agent Use in Septic Shock: Beyond First-Line Recommendations. Pharmacotherapy. 2019 Mar;39(3):369-381.
3. Patel N, Chong KW, Yip AYG, Ierodiakonou D, Bartra J, Boyle RJ, Turner PJ. Use of multiple epinephrine doses in anaphylaxis: A systematic review and meta-analysis. J Allergy Clin Immunol. 2021 Nov;148(5):1307-1315

4. Ellis AK, Casale TB, Kaliner M, Oppenheimer J, Spergel JM, Fleischer DM, Bernstein D, Camargo CA, Lowenthal R, Tanimoto S. Development of *neffy*, an Epinephrine Nasal Spray, for Severe Allergic Reactions. Pharmaceutics. 2024 Jun 14;16(6)
5. Mehta GD, El Zein J, Felippe Baroni I, Qadir M, Mita C, Cash RE, Camargo CA. Epinephrine treatment of food-induced and other cause anaphylaxis in United States and Canadian Emergency Departments: a systematic review and meta-analysis. Expert Rev Clin Immunol. 2023 Jul-Dec;19(9):1171-1181.
6. Golden DBK, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J, Shaker MS, Wallace DV, Abrams EM, Bernstein JA, Chu DK, Horner CC, Rank MA, Stukus DR, Collaborators. Burrows AG, Cruickshank H, Workgroup Contributors. Golden DBK, Wang J, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J, Shaker MS, Wallace DV, Waserman S, Joint Task Force on Practice Parameters Reviewers. Abrams EM, Bernstein JA, Chu DK, Ellis AK, Golden DBK, Greenhawt M, Horner CC, Ledford DK, Lieberman J, Rank MA, Shaker MS, Stukus DR, Wang J. Anaphylaxis: A 2023 practice parameter update. Ann Allergy Asthma Immunol. 2024 Feb;132(2):124-176.
7. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, Machado FR, Mcintyre L, Ostermann M, Prescott HC, Schorr C, Simpson S, Wiersinga WJ, Alshamsi F, Angus DC, Arabi Y, Azevedo L, Beale R, Beilman G, Belley-Cote E, Burry L, Cecconi M, Centofanti J, Coz Yataco A, De Waele J, Dellinger RP, Doi K, Du B, Estenssoro E, Ferrer R, Gomersall C, Hodgson C, Møller MH, Iwashyna T, Jacob S, Kleinpell R, Klompas M, Koh Y, Kumar A, Kwizera A, Lobo S, Masur H, McGloughlin S, Mehta S, Mehta Y, Mer M, Nunnally M, Oczkowski S, Osborn T, Papathanassoglou E, Perner A, Puskarich M, Roberts J, Schweickert W, Seckel M, Sevransky J, Sprung CL, Welte T, Zimmerman J, Levy M. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021 Nov;47(11):1181-1247
8. Goodall N. Guideline review: Epinephrine use in anaphylaxis (AAP guideline 2017). Arch Dis Child Educ Pract Ed. 2020 Feb;105(1):38-40.

9. Lee JH, Jung JY, Lee HJ, Kim DK, Kwak YH, Chang I, Kwon H, Choi YJ, Park JW, Paek SH, Cho JH. Efficacy of low-dose nebulized epinephrine as treatment for croup: A randomized, placebo-controlled, double-blind trial. Am J Emerg Med. 2019 Dec;37(12):2171-2176.
10. Dr. S. Sreeremya, Neurological Physiotherapy Diagnostics Journal, Clinical Aspects of Neuroplasticity-Review, Vol 1(2),pp-52-59.2025a.
11. Dr. S. Sreeremya, Journal of Pharmacology, Toxicology and Therapeutics, Amanita Muscaria –Overview, Vol 7(1),pp-1-12.2025b.
12. Dr.Sreeremya.S , Book title-Distinct Diseases, 2026, pp-280, paperback . ISBN- 978-93-6631-903-2
13. Zhong H, Yin Z, Kou B, Shen P, He G, Huang T, Liang J, Huang S, Huang J, Zhou M, Deng R. Therapeutic and adverse effects of adrenaline on patients who suffer out-of-hospital cardiac arrest: a systematic review and meta-analysis. Eur J Med Res. 2023 Jan 12;28(1):24.
14. Perman SM, Elmer J, Maciel CB, Uzendu A, May T, Mumma BE, Bartos JA, Rodriguez AJ, Kurz MC, Panchal AR, Rittenberger JC., American Heart Association. 2023 American Heart Association Focused Update on Adult Advanced Cardiovascular Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2024 Jan 30;149(5):e254-e273.
15. Hou M, Dong S, Kan Q, Ouyang M, Zhang Y. Is epinephrine still the drug of choice during cardiac arrest in the emergency department of the hospital? A meta-analysis. Acta Pharm. 2023 Sep 01;73(3):325-339.
16. Motiejunaite J, Amar L, Vidal-Petiot E. Adrenergic receptors and cardiovascular effects of catecholamines. Ann Endocrinol (Paris). 2021 Jun;82(3-4):193-197.